

Clinician Perspectives on Monoclonal Antibody Treatment for High-Risk Outpatients with COVID-19: Implications for Implementation and Equitable Access



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BACKGROUND: There is an urgent need to identify and address factors influencing uptake and equitable access to monoclonal antibody (mAb) treatment for high-risk outpatients with COVID-19.

OBJECTIVE: To assess clinician knowledge, beliefs, and experiences regarding obtaining mAb treatment for eligible patients.

DESIGN AND PARTICIPANTS: Survey of clinicians ($N = 374$) practicing in the state of Colorado who care for patients with COVID-19 in primary care, emergency medicine, and other clinical settings.

MAIN MEASURE(S): Diffusion of innovation theory concepts including knowledge, perceived strength of evidence, barriers, and experience with, ease of use, preparedness, and feasibility, appropriateness, and acceptability of mAb referral systems and processes.

KEY RESULTS: Most respondents indicated little to no knowledge about mAb therapies for COVID-19 (67%, 74%, 77%, for bamlanivimab, bamlanivimab+etesivimab, and casirivimab+imdevimab, respectively). About half reported little to no familiarity with eligibility criteria (50.9%) and did not know the strength of evidence (31%, 43%, 52%, for bamlanivimab, bamlanivimab+etesivimab, and casirivimab+imdevimab, respectively). Lack of knowledge or confidence in treatment was a top barrier to mAbs use; other barriers included complicated referral processes, patients not eligible when seen, and out-of-pocket costs concerns. Respondents rated four mAb referral steps as generally acceptable, appropriate, and feasible to complete in their primary outpatient clinical setting. Only 24% indicated their clinical setting was very prepared to facilitate referrals, 40% had ever referred a patient for mAbs, and 43% intended to refer a patient in the next month.

CONCLUSIONS: Clinician education on strength of evidence and eligibility criteria for mAbs is needed. However, education

alone is not sufficient. Given the urgent need to rapidly scale up access to treatment and reduce hospitalizations and death from COVID-19, more efficient, equitable systems and processes for referral and delivery of care, such as those coordinated by health systems, public health departments, or disaster management services, are warranted.

KEY WORDS: COVID-19; primary care; acute care; dissemination and implementation; referral; diffusion of innovations.

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INTRODUCTION

From the earliest days of the COVID-19 pandemic, there was an accelerated search for repurposed and novel treatments.^{1–4} Despite widespread availability of highly efficacious vaccines in most well-resourced countries, vaccine hesitancy⁵ and emerging variants⁶ drive continued spread of the SARS-CoV-2 virus and ongoing need to identify and implement effective therapeutics. Among candidates for early treatment of COVID-19, evidence supports neutralizing monoclonal antibody (mAb) treatments to reduce progression to hospitalization among those at high risk.^{7–12} Though early studies were small, multiple subsequent studies showed mAbs can reduce hospitalizations by 70–80% among high-risk outpatients with mild symptoms of COVID-19, if given within 10 days of symptom onset.^{13–15} Several mAbs have received Emergency Use Authorization (EUA) by the US Federal Drug Administration.^{16–18} The United States' National Institutes of Health COVID-19 treatment guidelines recommend use of mAbs for high-risk patients in ambulatory settings.¹⁹

When mAb treatments for COVID-19 first became available in winter 2020, initial uptake was low, even though there were many patients that might benefit and the medication itself was provided at no charge due to a large federal procurement.²⁰ There were concerns about inequities in treatment access benefiting those with financial resources, high health literacy,

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and social and medical connections. In January 2021, a Rapid Expert Consultation paper from the National Academies of Sciences, Engineering, and Medicine (NASEM) hypothesized that several factors might underlie low uptake, including low perceived strength of evidence (at the time), lack of awareness and interest in the treatment among both patients and health care providers, and logistical concerns such as time, resources to access health care facilities, transportation, and cost barriers associated with a treatment requiring intravenous infusion.²¹

Scant literature exists regarding development and implementation of systems and processes of care for mAb treatment for COVID-19. A primary focus has been on setting up infusion centers with the potential for direct outreach to patients testing positive for COVID-19.^{22–24} Others described mAb administration systems and processes for skilled nursing facilities,^{25,26} mobile satellite emergency departments,²⁷ and pharmacist outreach.²⁸ Beyond brief mention of the need to familiarize outpatient clinicians with how to access infusions,²² there has been little discussion of clinician perspectives on mAb referral systems and processes. This study addresses this gap in the literature by assessing primary care, emergency care, and medical specialist clinician perspectives on knowledge, attitudes, perceived barriers, and experiences with referring patients for mAb treatment. We report results of a statewide survey in Colorado designed to rapidly assess health care provider experiences with and perspectives on factors related to dissemination and implementation of mAb referral systems and processes.

METHODS

Design and Theoretical Framework

This was a cross-sectional survey study administered to clinicians in Colorado in May–August 2021, beginning about 5 months after mAbs first became available. Survey development aligned with diffusion of innovation (DOI) theory, commonly used in implementation science.^{29–31} According to DOI applied in the health care context, successful dissemination and adoption of health innovations are a function of a variety of individual and system-level factors pertaining to the characteristics of potential adopters, the context, and the innovation itself.^{29–31} Results reported here reflect one portion of this investigation; perspectives of community members were assessed using surveys and focus groups, and in-depth interviews were conducted with a number of provider survey respondents. Insights contributed to design and implementation of strategies to enhance broad, equitable use of mAb treatment in Colorado. The study was approved as exempt human subjects research by the Colorado Multiple Institutional Review Board (COMIRB).

Outcomes and Measures

The clinician survey included 3 screening items, 13 items assessing professional and personal characteristics, and 51

items reflecting DOI factors. DOI factors included innovation attributes (perceived strength of evidence for the three mAbs available at the time, including bamlanivimab [BAM], bamlanivimab+etesivimab [BAM/ETE], and casirivimab+imdevimab [CAS/IMD], likelihood of referring a patient for treatment in the next month); characteristics of potential adopters (knowledge of mAb treatments for COVID-19, familiarity with eligibility criteria, experience caring for patients with COVID-19 in the outpatient setting, professional and personal characteristics); and experience with and perceptions of the referral process (frequency, effort required, and ease of use of referral systems and processes, for both the State's web-based referral tool or their organization's own referral system, and perceived barriers, feasibility, appropriateness, and acceptability of referral systems and processes in one's own clinical setting).

To assess perceived acceptability, appropriateness, and feasibility of each step towards referring patients for mAb treatment, we adapted survey items from existing implementation outcome measures.³² The four mAbs referral steps are identifying patients eligible for treatment, counseling patients on the opportunity for treatment, finding a treatment site, and generating a referral or order for treatment at the selected treatment site. From the existing multi-item measures, we selected one item with the best face validity and/or the highest loading on factors corresponding to acceptability ("is appealing to me"), appropriateness ("seems suitable for my clinical setting"), and feasibility ("seems doable in my clinical setting").³²

Survey Development and Testing

The study team iteratively developed the survey. Early iterations were pretested using expert review; a revision was used in five cognitive interviews with physicians in Colorado, and a near-final version was administered to a convenience sample of 19 physicians to ensure readability, length, timing, and flow. The final survey is provided in [Supplemental Material A](#).

Participants and Sampling

Eligible respondents were clinicians (physicians, physician assistants, nurse practitioners) with prescribing privileges and currently practicing in the state of Colorado who reported having cared for at least 1 patient in the outpatient setting who had recently been diagnosed with COVID-19. We used convenience sampling and email outreach, seeking to recruit 350 participants, providing a margin of error of 4% at a confidence level of 90%. For email outreach, we obtained a list of 8115 practicing physicians in Colorado from IQVIA, a leading commercial vendor of physician contact information, from which we extracted physicians in 16 specialties likely to care for COVID-19 patients in outpatient settings (i.e., excluding hospitalists, surgical specialties, other inpatient care) and with verified email addresses, resulting in a final email list of 6649 physicians (the "IQVIA email sample").

Survey Administration and Response Validation

We used multiple survey administration methods. An open link to the survey was sent to clinicians via Colorado practice-based research networks, clinical faculty listservs among the authors' University of Colorado academic departments (Family and Emergency Medicine), and to community clinicians via Colorado's Regional Health Connectors.³³ IQVIA email sample physicians were sent personalized survey links via email. Email invitations and reminders were sent in 4 waves during the spring and summer of 2021. Non-respondents were sent three email reminders over the 2 weeks after they were sent the initial invitation. Two additional survey reminders, with revised recruitment language, were sent to all IQVIA email sample non-respondents who had not unsubscribed or returned as undeliverable ($n = 6057$) as of mid-August. Demographics for IQVIA email sample respondents vs non-respondents and IQVIA sample and non-IQVIA sample respondents are shown in [Supplemental Appendix B](#). As findings were similar when including IQVIA sample respondents alone, we used the combined sample.

Data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at the University of Colorado Denver.³⁴ REDCap is a secure, web-based application designed to support research data capture. Responses gathered using the public link were validated by conducting an internet search of the respondent's name to ensure the person with the credentials provided exists and practices in the region indicated. Other information, such as years since completing training and specialty were used for further cross-checks if needed. Respondents with complete and validated responses were offered a \$40 e-gift card for participation; respondents could decline compensation.

Analyses

Descriptive statistics were computed to report measures of central tendency (means, medians, frequencies) and spread (standard deviation, interquartile ranges [IQR]) for continuous and categorical variables as appropriate. Respondents were categorized as primary care clinicians (family or internal medicine practicing in an outpatient setting), emergency department (ED) clinicians (anyone practicing in the ED), and other clinician type (all other specialties). A bar plot was constructed based on the average Likert score for the perceived acceptability, appropriateness, and feasibility for each step in the mAb referral process.

RESULTS

Sample Characteristics

We received and verified 374 eligible survey responses; 316 were physicians from the IQVIA email sample and 58 were other physician, PA, and NP respondents who were not in the

IQVIA email sample. As shown in [Table 1](#), respondents represented a range of specialties and clinical settings, including both academic and non-academic settings. Based on reported ZIP code, nearly every county in Colorado was represented; regional distribution of responses generally corresponded with state population density. Four respondents did not indicate primary clinical setting; $N = 370$ for analyses reporting by clinician type.

Knowledge About mAbs for COVID-19

[Figure 1](#) presents reported knowledge about use of mAbs for patients with COVID-19 by clinician type. The majority of respondents in each clinician type indicated knowing little to nothing about BAM, BAM/ETE, or CAS/IMD mAb treatments for COVID-19. Overall, a third to half indicated they did not know the strength of evidence associated with BAM (31.1% "don't know"), BAM/ETE (43.4% "don't know"), or CAS/IMD (51.6% "don't know"). Overall, 15% of respondents indicated they were very familiar with mAb eligibility criteria; 33.3%, 33.9%, and 17.7% indicated they were moderately, a little, or not at all familiar with eligibility criteria, respectively.

COVID-19 Outpatient Care and mAb Referral Experience

[Table 2](#) shows experiences with mAbs use and caring for outpatients with COVID-19 across clinician types. Less than half had ever successfully referred a patient for mAb treatment. About one in five respondents had attempted to refer or explored referring a patient for mAb treatment but had not completed a referral. Overall, while nearly three-quarters of respondents reported caring for any patients with active COVID-19 in the outpatient setting in the last month, very few patients were estimated to have been eligible for treatment and most clinicians did not make any mAb referrals. ED clinicians reported caring for patients with COVID-19 most often in the last month, whereas primary care clinicians reported having referred patients for mAbs most often. Given survey completion dates, the last month referred to the period of April–July of 2021, when COVID-19 rates had declined in the USA.

Experience with and Barriers to Use of mAb Referral Systems and Processes

The State of Colorado implemented a web-based tool for facilitating mAb referrals to a patient's preferred infusion site; 115/374 (31%) of respondents indicated they had used the State's tool. In contrast, 199/374 (53%) of respondents indicated their own organization had also created internal systems and processes for mAb referrals; 127/199 (64%) had used their organization's own system. [Figure 2](#) shows perceived effort and learnability for the State's tool and for respondents' organizations' own systems. In general, respondents reported

Table 1 Sample Characteristics Overall and Across Medical Specialties

Characteristic	Overall (N = 374*)	Internal Medicine (N = 83)	Family Medicine (N = 142)	Emergency Medicine (N = 90)	Other Specialty (N = 59)
Age (years), mean (SD)	45.3 (10.4)	45.3 (10.1)	46.7 (10.6)	42.1 (9.1)	46.9 (10.9)
Missing	6	2	0	2	2
Gender, N (%)					
Woman	187 (50.8%)	45 (55.6%)	80 (56.7%)	32 (36.4%)	30 (51.7%)
Man	174 (47.3%)	33 (40.7%)	60 (42.6%)	54 (61.4%)	27 (46.6%)
Non-binary or gender expansive	1 (0.3%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Prefer not to answer	6 (1.6%)	2 (2.5%)	1 (0.7%)	2 (2.3%)	1 (1.7%)
Missing	6	2	1	2	1
Race/ethnicity, N (%)					
Black or African American	3 (0.8%)	1 (1.2%)	1 (0.7%)	1 (1.2%)	0 (0.0%)
White or Caucasian	297 (81.6%)	62 (75.6%)	116 (82.3%)	77 (89.5%)	42 (76.4%)
Hispanic or Latinx	16 (4.4%)	3 (3.7%)	8 (5.7%)	1 (1.2%)	4 (7.3%)
Asian or Pacific Islander	31 (8.5%)	12 (14.6%)	10 (7.1%)	2 (2.3%)	7 (12.7%)
Native American or Alaska Native	2 (0.5%)	0 (0.0%)	1 (0.7%)	1 (1.2%)	0 (0.0%)
Other/more than 1	15 (4.1%)	4 (4.8%)	5 (3.5%)	4 (4.7%)	2 (3.6%)
Missing	10	1	1	4	4
Primary clinical setting, N (%)					
Inpatient settings not including emergency departments	31 (8.4%)	20 (24.7%)	3 (2.1%)	0 (0.0%)	8 (13.8%)
Emergency department	95 (25.8%)	0 (0.0%)	4 (2.9%)	89 (100.0%)	2 (3.4%)
Outpatient setting located in a community-based clinic	132 (35.9%)	23 (28.4%)	89 (63.6%)	0 (0.0%)	20 (34.5%)
Outpatient setting located in a hospital or specialty care center	63 (17.1%)	22 (27.2%)	16 (11.4%)	0 (0.0%)	25 (43.1%)
Outpatient setting located in an FQHC or FQHC look-alike	36 (9.8%)	10 (12.3%)	25 (17.9%)	0 (0.0%)	1 (1.7%)
Long-term care facilities (e.g., nursing homes)	6 (1.6%)	6 (7.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other	5 (1.4%)	0 (0.0%)	3 (2.1%)	0 (0.0%)	2 (3.4%)
Missing	6	2	2	1	1
Credentials, N (%)					
MD/DO	341 (91.2%)	81 (97.6%)	123 (86.6%)	81 (90.0%)	56 (94.9%)
NP/PA	33 (8.8%)	2 (2.4%)	19 (13.4%)	9 (10.0%)	3 (5.1%)
Years since training, median (IQR)	13.5 (8.0, 21.0)	14.0 (7.0, 22.0)	10.0 (4.8, 16.0)	14.0 (7.0, 22.0)	13.0 (6.0, 20.8)
Missing	8	1	1	6	0
Faculty in med school, N (%) Yes	160 (43.1%)	43 (51.8%)	42 (29.8%)	49 (55.7%)	26 (44.1%)
Missing	3	0	1	2	0
Hours per week in direct patient care, median (IQR)	35 (24, 40)	33.0 (24.0, 40.0)	35.5 (30.0, 40.0)	30.0 (24.0, 40.0)	38.0 (20.0, 41.2)
Missing	15	2	6	4	3

Note: The "Other Specialty" category included the following self-reported specialties: "Can Med", "Cardiac transplant and heart failure", "Cardiology", "Endocrinology", "Endocrinology and diabetes", "Gastroenterology", "Gyn oncology", "Hem onc", "ID", "Medical oncology", "Nephrology", "Neurology", "Ob/Gyn", "Oncology", "Ophthalmology", "Pulmonary", "Radiation oncology", "Rheumatology", "Hospice and palliative medicine", "Infectious disease", "MRM", "PA Urgent care", "Pediatrics", and "Urgent care"

their organizations' own systems required less effort and were easier to learn than the State's tool.

Table 3 shows perceived barriers to mAb referral. Four of the top six major barriers reflected logistical aspects of referrals for treatment (a long, complicated referral process, patients not being eligible by the time they are seen, and concerns about out-of-pocket costs for patients). Other top barriers reflect lack of knowledge or confidence in the treatment. Very few clinicians saw lack of availability of treatment, lack of patient interest, or lack of access to treatment sites as barriers.

Readiness for Monoclonal Antibody Referral in Outpatient Clinical Settings

Overall, as shown in Table 2, less than half of respondents indicated they were very or extremely likely to refer a patient for mAb treatment in the next month; roughly half indicated their clinical setting was very or somewhat prepared to refer

eligible patients for mAb treatment. Figure 3 shows average Likert scale ratings of perceived acceptability, appropriateness, and feasibility for completing each of four mAb referral steps in a respondent's primary outpatient clinical setting. On average, all steps were rated between a 3 (neither agree nor disagree) and a 4 (agree), indicating that in general the referral steps would somewhat fit into outpatient clinical settings. Steps 1 (identifying eligible patients) and 2 (discussing treatment with patients and family/caregivers) were generally seen as acceptable, appropriate, and feasible to deliver in their clinical settings; steps 3 (locate an accessible treatment site) and 4 (generating a referral and/or order) were rated lower across domains but still above the mid-point on average.

DISCUSSION

To reduce hospitalizations and death from COVID-19, there is a critical, time-sensitive need for dissemination

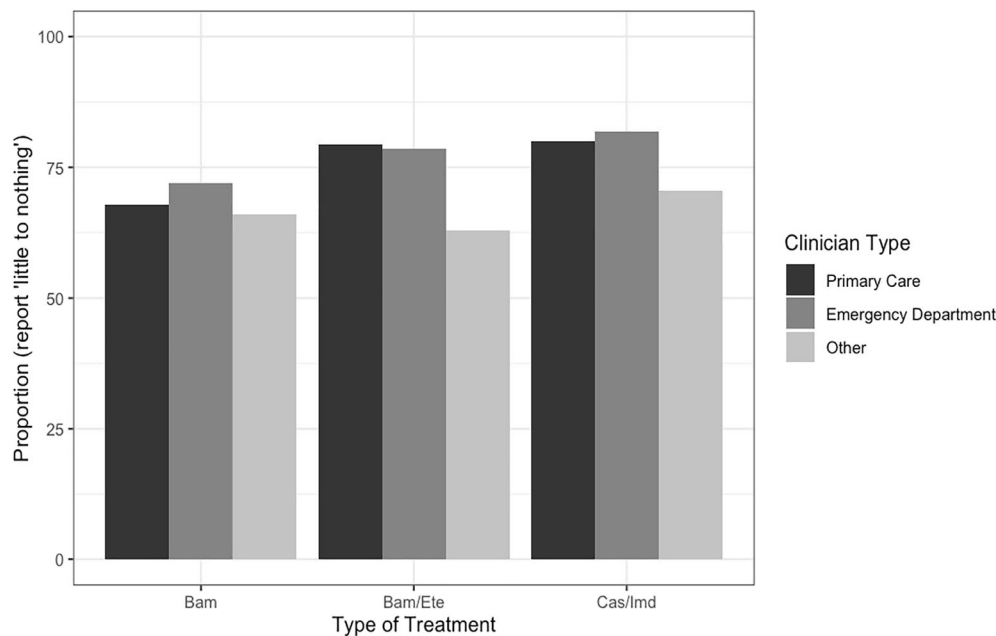


Fig. 1 Clinician-reported knowledge of monoclonal antibody treatment for COVID-19 by clinician type. *Note:* bam, bamlanivimab; bam/ete, bamlanivimab+etesivimab; cas/imd, casirivimab+imdevimab.

and implementation (D&I) strategies for delivering effective treatments such as neutralizing mAbs. It is not unusual for new treatments to require substantial time and implementation support for widespread diffusion and use across clinical settings.^{35,36} However, typical timeframes for diffusion of new treatments are not tenable given the urgency of scaling up access to evidence-based treatment for COVID-19. Our goal was therefore to rapidly assess clinician perspectives on a key component in mAb delivery—identifying and referring eligible people for

treatment. We found clinician education was needed to increase knowledge about the strength of evidence supporting use of mAbs and eligibility criteria as well as how to access referral systems and processes. However, educational strategies are not enough to address inefficiencies and burdens associated the process of identifying and referring patients for treatment. These findings, based on diffusion of innovation theory as applied to health care systems,²⁹ informed several opportunities for D&I of mAb treatment for COVID-19 in Colorado.

Table 2 Clinician Experience with and Preparedness for Monoclonal Antibody Referral by Clinician Type

	Overall (N = 370)	Primary care (N = 185)	Emergency department (N = 94)	Other (N = 91)
Cared for COVID-19 patients in last month: N (%)	261 (70.5%)	132 (71.4%)	86 (91.5%)	43 (47.3%)
Yes				
Patients eligible for treatment, median (IQR)	2 (1, 5)	2 (0, 3)	4 (2, 10)	2 (1, 6)
Missing	13	6	6	1
Ever referred a patient for mAbs, N (%)				
Yes, have referred	147 (39.7%)	88 (47.6%)	29 (30.9%)	30 (33.0%)
Attempted to refer/did not complete referral	66 (17.8%)	24 (13.0%)	26 (27.7%)	16 (17.6%)
Have not referred/do not recall	155 (41.9%)	71 (38.4%)	39 (41.5%)	45 (49.5%)
Missing	2	2	0	0
Number of patients referred in the last month, median (IQR)	0 (0, 2)	0 (0, 1)	1 (1, 3)	1 (0, 2)
Missing	18	14	3	1
Ever asked about treatment, N (%)	186 (50.3%)	97 (52.4%)	41 (43.6%)	48 (52.7%)
Likely to refer in the next month, N (%)				
Very/extremely likely	159 (43.0%)	91 (49.2%)	33 (35.1%)	35 (38.5%)
Slightly/somewhat likely	159 (43.0%)	70 (37.8%)	49 (52.1%)	40 (44.0%)
Not at all likely	52 (14.1%)	24 (13.0%)	12 (12.8%)	16 (17.6%)
How prepared is your clinical setting, N (%)				
Very prepared	88 (24.0%)	48 (26.2%)	26 (28.0%)	14 (15.6%)
Somewhat prepared	107 (29.2%)	54 (29.5%)	30 (32.3%)	23 (25.6%)
Slightly prepared	61 (16.7%)	34 (18.6%)	15 (16.1%)	12 (13.3%)
Not at all prepared	89 (24.3%)	42 (23.0%)	15 (16.1%)	32 (35.6%)
Not sure	21 (5.7%)	5 (2.7%)	7 (7.5%)	9 (10.0%)
Missing	4	2	1	1

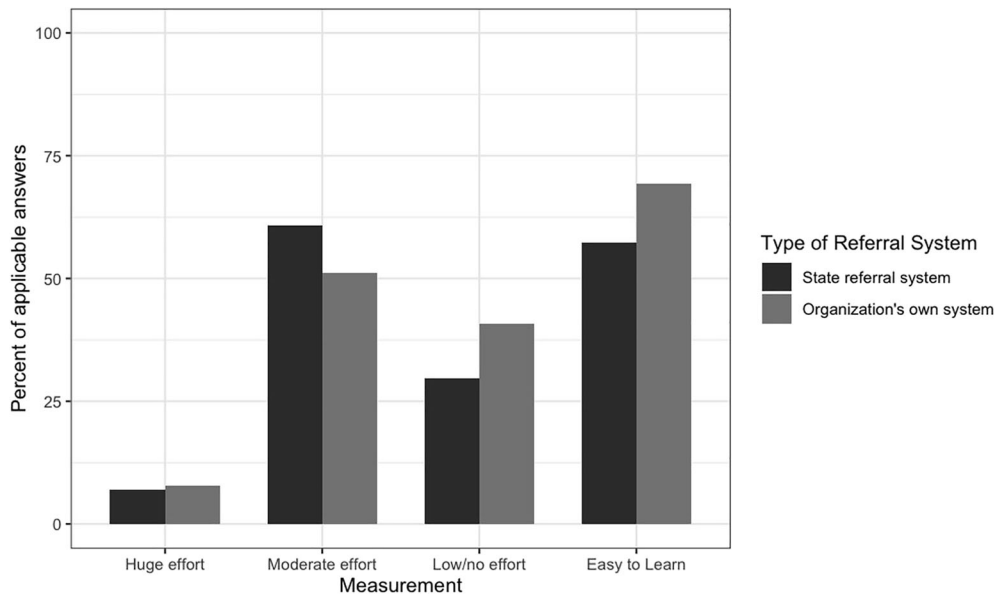


Fig. 2 Clinician-reported effort and ease of learning mAb referral systems and processes.

Health care providers in Colorado who provided outpatient care for people testing positive for COVID-19 in primary care, emergency medicine, and other clinical settings had periodic but not regular opportunity to refer patients for mAb treatment. From May to August 2021, including a time of relatively low case rates and the beginning of the delta variant surge, clinicians typically saw about two patients who would have been eligible for treatment in the last month. It may be challenging to develop efficient routines with such infrequent need to recall referral systems and processes—which can and do change periodically. Available systems and processes for referral for treatment in Colorado, including a statewide infusion center map and the State’s connector tool as well as local health system electronic health record (EHR)–based tools, were perceived as requiring moderate to huge effort to use. While outpatient care providers found it somewhat

appropriate, acceptable, and feasible to implement each referral step in their clinical setting, when considered altogether many reported their clinical settings were not prepared to use existing referral systems and processes.

Together with evidence of provider burnout³⁷ and moral injury³⁸ stemming from the pandemic, we took these results to indicate that a streamlined system and process for referral for treatment that does not rely on direct clinician referrals may be required. While the State’s web-based referral tool helped with some aspects of the referral process, individual community clinicians still needed to perform the most challenging step—identifying a treatment location—prior to issuing the referral. This process also relies upon community clinicians and patients to connect with each other soon after patients test positive for COVID-19. For patients without a regular source of care, such a requirement may be a barrier to equitable access

Table 3 Clinician-Reported Barriers to Monoclonal Antibody Referral

Barrier	Major barrier: N (%)	Moderate barrier: N (%)	Not a barrier: N (%)	Not sure: N (%)	Missing
The process for ordering mAb treatment is too complicated	121 (32.4%)	121 (32.4%)	86 (23%)	46 (12.3%)	0
The process for getting mAb treatment takes too long	87 (23.4%)	106 (28.5%)	114 (30.6%)	65 (17.5%)	2
I have concerns about out-of-pocket costs to my patients	71 (19%)	110 (29.5%)	138 (37%)	54 (14.5%)	1
I don't know enough about mAb treatment	61 (16.4%)	131 (35.2%)	170 (45.7%)	10 (2.7%)	2
My patients are no longer eligible by the time I see them	52 (14%)	144 (38.7%)	128 (34.4%)	48 (12.9%)	2
I am unsure which patients are eligible to receive mAb treatment	50 (13.4%)	117 (31.4%)	196 (52.5%)	10 (2.7%)	1
The evidence that mAb treatments are effective is not convincing	43 (11.6%)	106 (28.6%)	171 (46.2%)	50 (13.5%)	4
There is limited space at nearby infusion centers	42 (11.2%)	78 (20.9%)	141 (37.7%)	113 (30.2%)	0
There is an insufficient supply of mAb treatment in my area	40 (10.8%)	59 (15.9%)	169 (45.6%)	103 (27.8%)	3
I do not typically manage treatment for COVID-19 for my patients	29 (7.8%)	53 (14.3%)	270 (72.8%)	19 (5.1%)	3
Use of mAb treatments has been politicized	24 (6.5%)	75 (20.2%)	205 (55.3%)	67 (18.1%)	3
My patients generally don't want this treatment	24 (6.4%)	105 (28.2%)	163 (43.7%)	81 (21.7%)	1

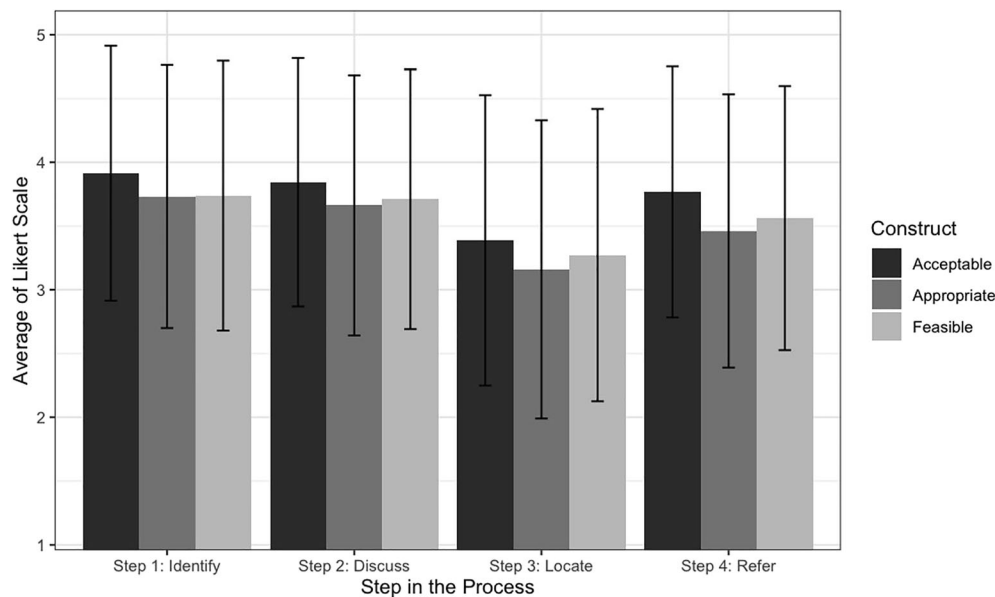


Fig. 3 Clinician perceptions of acceptability, appropriateness and feasibility of mAb referral steps. *Note:* Response scale ranges from 1 (“strongly disagree”) to 5 (“strongly agree”), with a mid-point 3 (“neither agree nor disagree”). Step 1, identify eligible patients for treatment; step 2, discuss treatment options with eligible patients; step 3, locate an accessible treatment site; step 4, refer patient for treatment. The error bars represent one standard deviation.

to timely treatment. A more equitable, efficient model might be staffed with care providers dedicated to performing all steps required for facilitating patient access to mAb treatment. Direct outreach might ensure patients eligible for treatment are identified in a timely manner. Such models may be based in health care systems, public health departments, or disaster management; there is a need for research to determine the most effective, efficient model for ensuring equitable access to treatment during a pandemic.

While the NASEM report²¹ speculated that available health care system resources to conduct direct outreach to eligible patients were a suspected barrier, there are now several models of successful centralized, direct outreach for mAb treatment. Buttressed by findings from our clinician survey, the University of Colorado Health (UCHealth) system expanded its virtual health center to both provide direct outreach to eligible COVID-19 outpatients and field requests from other clinicians to facilitate finding infusion locations and issuing referrals and orders for interested patients. The UCHealth virtual health center model bears similarities to those described by UPMC and the Mayo Clinic, including structured review of EHR reports of COVID-19-positive patients and a centralized team of care providers that perform direct outreach to eligible patients and coordinates referral to treatment sites via a telemedicine platform.^{22,23} UCHealth accepts referral requests from community clinicians and from local public health agency case investigators. Other solutions—such as mass administration sites and standing orders, as the State of Florida has implemented^{39,40}—may also mitigate the challenges associated with finding available infusion centers and issuing referrals and facilitate more equitable access to treatment.

Respondent concerns about patient out-of-pocket costs suggest the need for transparent information about treatment costs. The medication was provided at no charge and the Center for Medicaid and Medicare Services paid for administration for its beneficiaries. However, it was unknown what costs commercial payers would pass on or what patients who are self-pay or on high-deductible plans may be charged for treatment administration costs. Assuring treatment affordability represents another critical equity strategy.

Limitations

Study limitations include a sample focused on Colorado clinicians, reflecting less than 5% of potential respondents in the state, and use of email outreach and convenience sampling. Given the need for rapid insights to inform D&I strategies during a global pandemic, we prioritized pragmatic approaches to recruitment. Furthermore, ~40% of respondents reported they held a faculty appointment in a medical school (vs an estimated 30% statewide, and a range of 5–15% nationwide according to data from the American Medical Association), potentially biasing results towards the experience of such clinicians.

CONCLUSIONS

Clinicians practicing in outpatient settings would benefit from education on the use of mAb treatments for high-risk outpatients with COVID-19. However, there is an urgent need for more efficient systems for identifying eligible patients and directing them to treatment. Direct outreach to facilitate

equitable access to treatment may be more efficient and appropriate than relying upon individual clinicians.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11606-022-07702-2>.

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Declarations:

IRB Approval: This study was approved as exempt human subjects research by the Colorado Multiple Institutional Review Board.

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REFERENCES

- Slaoui M, Greene SE, Woodcock J. Bridging the Gap at Warp Speed - Delivering Options for Preventing and Treating Covid-19. *N Engl J Med*. 2020;383(20):1899-1901.
- Davis JS, Ferreira D, Denholm JT, Tong SY. Clinical trials for the prevention and treatment of COVID-19: current state of play. *Med J Aust*. 2020;213(2):86-93.
- Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the Treatment of Covid-19 - Final Report. *N Engl J Med*. 2020;383(19):1813-1826.
- Cunningham AC, Goh HP, Koh D. Treatment of COVID-19: old tricks for new challenges. *Crit Care*. 2020;24(1):91.
- Aw J, Seng JJB, Seah SSY, Low LL. COVID-19 Vaccine Hesitancy-A Scoping Review of Literature in High-Income Countries. *Vaccines (Basel)*. 2021;9(8):900.
- Gómez CE, Perdiguer B, Esteban M. Emerging SARS-CoV-2 variants and impact in global vaccination programs against SARS-CoV-2/COVID-19. *Vaccines*. 2021;9(3):243.
- Destache CJ, Aurit SJ, Schmidt D, Peet Erkes L, Tierney M, Vivekanandan R. Bamlanivimab use in mild-to-moderate COVID-19 disease: A matched cohort design. *Pharmacotherapy*. 2021;41(9):743-747.
- Anderson B, Smith Z, Edupuganti S, Yan X, Masi CM, Wu HM. Effect of Monoclonal Antibody Treatment on Clinical Outcomes in Ambulatory Patients With Coronavirus Disease 2019. *Open Forum Infect Dis*. 2021;8(7):ofab315.
- Falcone M, Tiseo G, Valoriani B, et al. Efficacy of Bamlanivimab/Etesevimab and Casirivimab/Imdevimab in Preventing Progression to Severe COVID-19 and Role of Variants of Concern. *Infect Dis Ther*. 2021;10(4): 2479-2488.
- Bariola JR, McCreary EK, Wadas RJ, et al. Impact of Bamlanivimab Monoclonal Antibody Treatment on Hospitalization and Mortality Among Nonhospitalized Adults With Severe Acute Respiratory Syndrome Coronavirus 2 Infection. *Open Forum Infect Dis*. 2021;8(7):ofab254.
- McCreary EK, Bariola J, Minnier T, et al. A Learning Health System Randomized Trial of Monoclonal Antibodies for Covid-19. *medRxiv*. <https://doi.org/10.1101/2021.09.03.21262551>.
- Verderese JP, Stepanova M, Lam B, et al. Neutralizing Monoclonal Antibody Treatment Reduces Hospitalization for Mild and Moderate Coronavirus Disease 2019 (COVID-19): A Real-World Experience. *Clin Infect Dis*. 2022;74(6):1063-1069.
- Dougan M, Nirula A, Azizad M, et al. Bamlanivimab plus Etesevimab in Mild or Moderate Covid-19. *N Engl J Med*. 2021; 385:1382-1392.
- GSK. GSK and Vir Biotechnology announce continuing progress of the COMET clinical development programme for sotrovimab [press release]. Available at: <https://www.gsk.com/en-gb/media/press-releases/gsk-and-vir-biotechnology-announce-continuing-progress-of-the-comet-clinical-development-programme-for-sotrovimab/>. Accessed June 21, 2021.
- Weinreich DM, Sivapalasingam S, Norton T, et al. REGEN-COV Antibody Combination and Outcomes in Outpatients with Covid-19. *N Engl J Med*. 2021; 385:e8.
- Mahase E. Covid-19: FDA authorises neutralising antibody bamlanivimab for non-admitted patients. *BMJ*. 2020;371:m4362.
- Food and Drug Administration. Fact Sheet for Health Care Providers Emergency Use Authorization (EUA) of Bamlanivimab and Etesevimab. Available at: <https://www.fda.gov/media/143603/download>. Accessed October 18, 2021.
- Food and Drug Administration. GSK Sotrovimab Letter of Authorization. Available at: <https://www.fda.gov/media/149532/download>. February 23, 2022. Accessed July 1, 2022.
- National Institutes of Health. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Available at: <https://www.covid19treatmentguidelines.nih.gov/>. Accessed October 18, 2021.
- Toy S, Walker J, Evans M. Highly Touted Monoclonal Antibody Therapies Sit Unused in Hospitals. *Wall Street Journal*. December 27, 2020.
- National Academies of Sciences, Engineering, and Medicine. 2021. Rapid Expert Consultation on Allocating COVID-19 Monoclonal Antibody Therapies and Other Novel Therapeutics (January 29, 2021). Washington, DC: The National Academies Press.
- Bariola JR, McCreary EK, Khadem T, et al. Establishing a Distribution Network for COVID-19 Monoclonal Antibody Therapy Across a Large Health System During a Global Pandemic. *Open Forum Infect Dis*. 2021;8(7):ofab151.
- Razonable RR, Aloia NCE, Anderson RJ, et al. A Framework for Outpatient Infusion of Antispike Monoclonal Antibodies to High-Risk Patients with Mild-to-Moderate Coronavirus Disease-19: The Mayo Clinic Model. *Mayo Clin Proc*. 2021;96(5):1250-1261.
- Çağlayan Ç, Thornhill J, Stewart MA, et al. Staffing and Capacity Planning for SARS-CoV-2 Monoclonal Antibody Infusion Facilities: A Performance Estimation Calculator Based on Discrete-Event Simulations. *Front Public Health*. 2022;9:770039. <https://doi.org/10.3389/fpubh.2021.770039>.
- Dale AP, Hudson MJ, Cullen T, et al. Administration of Bamlanivimab to Skilled Nursing Facility Residents During a COVID-19 Outbreak, January-February 2021, Arizona. *J Am Med Dir Assoc*. 2021;22(7):1357-1358.
- Tulledge-Scheitel S, Bell SJ, Larsen JJ, et al. A mobile unit overcomes the challenges to monoclonal antibody infusion for COVID-19 in skilled care facilities. *J Am Geriatr Soc*. 2021;69(4):868-873.
- Morchel H, Clark D, Buenvenida L, Ogedegbe C. Use of a Unique Mobile Medical Asset in COVID Monoclonal Antibody Treatment. *Healthcare (Basel)*. 2021;9(8):990.
- Malashock C, Keifer A, Reisbig K, Reha C, Alexander BT. Pharmacist outreach program for COVID-19 monoclonal antibody distribution. *Am J Health Syst Pharm*. 2021;78(13):1172-1175.
- Greenhalgh T, Robert G, Macfarlane F, Bate P, Kyriakidou O. Diffusion of innovations in service organizations: systematic review and recommendations. *Milbank Q*. 2004;82(4):581-629.
- Dearing JW, Cox JG. Diffusion Of Innovations Theory, Principles, And Practice. *Health Aff (Millwood)*. 2018;37(2):183-190.
- Rogers EM. Diffusion of Innovations. 5th ed. New York, NY: Free Press; 2003.

32. Weiner BJ, Lewis CC, Stanick C, et al. Psychometric assessment of three newly developed implementation outcome measures. *Implement Sci*. 2017;12(1):108.
33. Colorado Regional Health Connectors. Regional Health Connectors. Available at: <https://www.regionalhealthconnectors.org/>. Accessed October 4, 2021.
34. Harris P, Taylor R, Thielke R, Payne J, Gonzalez N, Conde J. Research electronic data capture (REDCap) - A metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 42(2):377-381.
35. Balas EA, Boren SA. Managing clinical knowledge for health care improvement. *Yearbook of Medical Informatics*. 2000;9(01):65-70.
36. Fixsen DL, Blasé KA, Timbers GD, Wolf MM. In search of program implementation: 792 replications of the Teaching-Family Model. *The Behavior Analyst Today*. 2007;8(1):96.
37. Apaydin EA, Rose DE, Yano EM, et al. Burnout Among Primary Care Healthcare Workers During the COVID-19 Pandemic. *J Occup Environ Med*. 2021;63(8):642-645.
38. Litam SDA, Balkin RS. Moral injury in health-care workers during COVID-19 pandemic. *Traumatology*. 2021;27(1):14-19.
39. CDR Maguire Inc. CDR HealthPro. Available at: https://www.patientportallf.com/s/?language=en_US. Published 2021. Accessed October 4, 2021.
40. Chang D, Chacin AC. DeSantis touts monoclonal antibody therapy as Florida hospitalizations for COVID decline. *Miami Herald*. September 17, 2021.

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