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MAJOR ARTICLE

Use of Severe Acute Respiratory Syndrome Coronavirus 2 Antibody Tests by US Infectious Disease Physicians: Results of an Emerging Infections Network Survey, March 2022

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Background. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody tests have had limited recommended clinical application during the coronavirus disease 2019 (COVID-19) pandemic. To inform clinical practice, an understanding is needed of current perspectives of United States–based infectious disease (ID) physicians on the use, interpretation, and need for SARS-CoV-2 antibody tests.

Methods. In March 2022, members of the Emerging Infections Network (EIN), a national network of practicing ID physicians, were surveyed on types of SARS-CoV-2 antibody assays ordered, interpretation of test results, and clinical scenarios for which antibody tests were considered.

Results. Of 1867 active EIN members, 747 (40%) responded. Among the 583 who managed or consulted on COVID-19 patients, a majority (434/583 [75%]) had ordered SARS-CoV-2 antibody tests and were comfortable interpreting positive (452/578 [78%]) and negative (405/562 [72%]) results. Antibody tests were used for diagnosing post–COVID-19 conditions (61%), identifying prior SARS-CoV-2 infection (60%), and differentiating prior infection and response to COVID-19 vaccination (37%). Less than a third of respondents had used antibody tests to assess need for additional vaccines or risk stratification. Lack of sufficient evidence for use and nonstandardized assays were among the most common barriers for ordering tests. Respondents indicated that statements from professional societies and government agencies would influence their decision to order SARS-CoV-2 antibody tests for clinical decision making.

Conclusions. Practicing ID physicians are using SARS-CoV-2 antibody tests, and there is an unmet need for clarifying the appropriate use of these tests in clinical practice. Professional societies and US government agencies can support clinicians in the community through the creation of appropriate guidance.

Keywords. SARS-CoV-2; COVID-19; antibody tests; serology; utilization.

Antibody tests are routinely used for a broad array of pathogens at the individual level for clinical decision making [1] and for assessment of occupational risk for healthcare workers [2]. At the population level, antibody tests are used for serosurveillance for known and emerging pathogens [3–5]. Antibody tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), have been available in clinical practice since April 2020 [6]. As of 7 February 2023, 85 SARS-CoV-2 antibody tests have received emergency use authorization (EUA) from the United States (US) Food and Drug Administration (FDA), detecting immunoglobulin M, immunoglobulin G (IgG), and/or total antibodies against either the nucleocapsid antigen of the virus (anti-N), spike protein (anti-S), or receptor-binding domain of the spike protein (anti-RBD). Most available assays detect binding antibodies and are designed to be qualitative, giving results as either positive or negative; 1 assay is quantitative and measures antibody levels, and 15 are designated as semiquantitative binding antibody tests [7]. Only 2 neutralizing antibody tests have received FDA EUA.

The sole approved clinical indication for SARS-CoV-2 antibody tests per FDA EUA is as an aid for identifying individuals with an adaptive immune response to SARS-CoV-2, indicating recent or prior infection [7]. The US Centers for Disease Control and Prevention (CDC) [8] and the Infectious

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Table 1. Characteristics of Survey Participants (N = 747), Emerging Infections Network, March 2022

Characteristic	No. (%)
Specialty	
Adult infectious diseases	555 (74)
Pediatric infectious diseases	192 (26)
Region	
US: New England	55 (7)
US: Mid-Atlantic	104 (14)
US: East North Central	118 (16)
US: West North Central	86 (12)
US: South Atlantic	128 (17)
US: East South Central	33 (4)
US: West South Central	48 (6)
US: Mountain	33 (4)
US: Pacific	134 (18)
Canada and Puerto Rico	8 (1)
Years of experience since ID fellowship	
<5 y	113 (15)
5–14 y	245 (33)
15–24 y	159 (21)
≥25 y	230 (31)
Primary practice setting (hospital)	
University	324 (43)
Nonuniversity teaching	188 (25)
Community	163 (22)
Veterans Affairs or Department of Defense	42 (6)
City/county	26 (3)
Outpatient only	4 (1)
Member type	
Infectious diseases physician	708 (95)
Healthcare professional (eg, PharmD, advanced practice provider)	39 (5)

Diseases Society of America (IDSA) [9] have provided guidance that a positive antibody test can help support a diagnosis of post-COVID conditions such as multisystem inflammatory syndrome (MIS) or other postacute sequelae of COVID-19. Although not recommended for use after vaccination to determine antibody response to vaccination, CDC has clarified the expected results of anti-S and anti-N tests used to distinguish prior infection from prior vaccination [8].

As the US enters the fourth year of the COVID-19 pandemic in 2023, SARS-CoV-2 serology testing in certain situations could help to guide clinical practice, especially in the era of hybrid immunity from infection and vaccination. With availability of therapeutics, such as monoclonal antibody (mAb) preparations, that have been demonstrated to improve outcomes among hospitalized patients who are seronegative (but not seropositive) [10], and with the potential for future therapeutics, rapid and reliable antibody testing could improve clinical decision making [11]. In addition, some individuals with certain immunocompromising conditions may not mount an adequate immune /response to COVID-19 vaccination [12]. An objective metric may identify those who are less likely to have protective immunologic responses from vaccines and who could benefit most from preexposure prophylaxis or continuing nonpharmaceutical interventions [13]. With limited published literature on the clinical use of SARS-CoV-2 antibody tests [14, 15], there is a need to systematically assess current knowledge, attitudes, and practices among the US clinical community.

Since its founding in 1995, the IDSA Emerging Infections Network (EIN) has evolved into a flexible sentinel network and an established platform for surveying primarily infectious disease (ID) physicians in the US on clinical aspects of emerging infections; a small number of other professionals (eg, ID pharmacists, public health providers) also participate in the network [16]. The overarching goal of the EIN is to assist CDC and other public health authorities with surveillance for emerging infectious diseases and to understand how clinical practices of disease prevention and management need to adapt. EIN provides an opportunity to gain an understanding of current perspectives from ID physicians based primarily in the US on the use, interpretation, and need for SARS-CoV-2 antibody tests in clinical practice.

METHODS

EIN developed and administered a 6-question survey with technical assistance from CDC covering several themes [17]: (1) current patterns of SARS-CoV-2 antibody assay use, including the types of assays ordered or recommended by EIN members while caring for or consulting on COVID-19 patients and the frequency of ordering these assays; (2) based on current knowledge, level of confidence in interpreting antibody test results (both negative and positive results); (3) the clinical scenarios in which antibody tests were ordered or recommended for clinical decision making; and (4) factors that would influence the provider's decision to order or recommend SARS-CoV-2 antibody tests for clinical decision making. Responses were analyzed using descriptive statistics, with χ^2 test used to compare responses among groups. Not all participants responded to all questions, and variation in denominators is reflected when reporting results.

A free-text comment field was also provided with a prompt to enter remarks regarding the survey or the clinical utility of SARS-CoV-2 antibody tests. We analyzed free-text comments provided by a subset of respondents to identify and summarize key themes.

All EIN members (n = 1867) were emailed a request to complete the survey on 1 March 2022, email reminders were sent on 9 and 17 March 2022, and the survey was closed on 28 March 2022.

This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy (45 Code of Federal Regulations [C.F.R.] part 46, 21 C.F.R. part 56; 42 US Code [U.S.C.] §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq).

Table 2. Severe Acute Respiratory Syndrome Coronavirus 2 Antibody Assay Use by Participants[a] Who Managed or Consulted on Coronavirus Disease 2019 Patients (n = 583), March 2022 Emerging Infections Network Member Responses to Survey Questions

Survey Items and SARS-CoV-2 Antibody Assay	No. (%)
SARS-CoV-2 antibody assay types that you most commonly order[b] (n = 583)	
Binding antibody assay, anti-N	212 (36)
Binding antibody assay, anti-S/anti-RBD	219 (38)
Semi-quantitative binding assay	48 (8)
Quantitative binding assay	29 (5)
IgM	42 (7)
IgG	136 (23)
Total antibody	69 (12)
Neutralization antibody assay	15 (3)
Not sure, but I have ordered/recommended an antibody assay	59 (10)
Not applicable: have not ordered or recommended	148 (25)
Frequency of ordered/recommended SARS-CoV-2 antibody test to support clinical decision making (n = 583)	
Rarely (less than once a week)	334 (57)
Often (weekly or more often)	103 (18)
Other (eg, greater than weekly, more often in the past, during surges)[c]	33 (6)
Never	113 (19)
Why SARS-CoV-2 test never ordered[b] (n = 121)	
Not FDA approved	26 (21)
Not available to me	7 (6)
Not reliable	63 (52)
Not covered by insurance	3 (2)
Other (eg, does not change management, results not actionable/clinically useful, interpretation of results not clear)[c]	60 (50)
With current knowledge, comfort interpreting positive SARS-CoV-2 antibody test[b] (n = 578)	
Yes	452 (75)
Evidence of prior SARS-CoV-2 infection (anti-N)	445 (77)
Has mounted a humoral immune response to COVID-19 vaccination (anti-S)	382 (66)
Has mounted an adequate humoral immune response to COVID-19 vaccination	99 (17)
Other (eg, interpretation depends, prior vaccine or infection)[c]	20 (3)
Not comfortable interpreting antibody test results based on current evidence	126 (22)
With current knowledge, comfortable interpreting negative SARS-CoV-2 antibody test[b] (n = 562)	
Yes	405 (72)
No evidence of prior SARS-CoV-2 infection (anti-N)	338 (60)
Has not mounted a humoral immune response to COVID-19 vaccination (anti-S)	338 (60)
Other (eg, interpretation depends, limited utility of negative test, does not exclude prior infection/waning antibody response, no response to SARS-CoV-2 infection)[c]	51 (9)
Not comfortable interpreting antibody test results based on current evidence	157 (28)
Scenarios when SARS-CoV-2 antibody assays were ordered/recommended for clinical decision making at the patient level[b] (n = 520)	
Supporting a diagnosis of COVID-19 complications or PCCs (eg, MIS-C, long COVID)	318 (61)
Determination of prior SARS-CoV-2 infection status	314 (60)
Distinguishing between prior SARS-CoV-2 infection and response to COVID-19 vaccination (using anti-N, anti-S, or anti-RBD assays)	193 (37)
Documenting presence or absence of a measurable humoral immune response to COVID-19 vaccination to determine need for additional or booster doses of COVID-19 vaccine in:	172 (33)
Moderately or severely immunocompromised individuals (at high risk for severe COVID-19)	146 (85)[d]
Immunocompetent individuals	43 (25)[d]
Elderly (≥65 y of age)	30 (17)[d]
Vulnerable populations (nursing home residents, people experiencing homelessness)	20 (12)[d]
Children (≤18 y of age)	16 (9)[d]
For risk stratification	136 (26)
Identifying inpatients most likely to benefit from anti-SARS-CoV-2 mAb therapy	67 (49)[e]
Prioritization of immunocompromised persons for PrEP	66 (49)[e]
Quarantine or isolation involving patients	30 (22)[e]
Eligibility for PEP in those at high risk for severe COVID-19	27 (20)[e]
Quarantine or isolation involving HCWs and essential personnel	8 (6)[e]
To resume social activities	3 (2)[e]
Need for initial COVID-19 vaccination (as in those with prior SARS-CoV-2 infection)	21 (4)
Other (eg, use with other therapies, immunocompromised patients)[c]	…

Table 2. Continued

Survey Items and SARS-CoV-2 Antibody Assay	No. (%)
Factors that would influence decision to order/recommend SARS-CoV-2 antibody assays for clinical decision making (n = 551)	
Statement from professional societies on clinical use and interpretation	432 (78)
Statement from US government (CDC, NIH, FDA) on clinical use or interpretation	340 (62)
FDA EUA with indications for clinical use in postvaccination settings	223 (40)
Superior test performance characteristics in a variety of clinical settings	184 (33)
FDA approval for antibody assays that could then be used off-label	180 (33)
Clarifying statement on payor coverage from CMS	69 (13)
Other (eg, need correlates of protection, identifying clinical scenarios, improved turnaround time and convenience, peer-reviewed studies)[c]	40 (7)

Abbreviations: anti-N, antibody against the nucleocapsid antigen; anti-RBD, antibody against the receptor-binding domain of the spike protein; anti-S, antibody against the spike protein; CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare and Medicaid Services; COVID-19, coronavirus disease 2019; EUA, emergency use authorization; FDA, Food and Drug Administration; HCW, healthcare worker; IgG, immunoglobulin G; IgM, immunoglobulin M; mAb, monoclonal antibody; MIS-C, multisystem inflammatory syndrome in children; NIH, National Institutes of Health; PCC, post-COVID condition; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Number of participants responding to each question varied and is presented by each variable.

[b]Respondents could select >1 response; percentage may add to >100%.

[c]Examples of provided "other" responses.

[d]Subsample of participants (n = 172) indicating ordering/recommending SARS-CoV-2 antibody to document presence or absence of a measurable humoral immune response to COVID-19 vaccination.

[e]Subsample of participants (n = 136) indicating ordering/recommending SARS-CoV-2 antibody for risk stratification.

RESULTS

Practice Characteristics of EIN Member Respondents

Of 1867 EIN members who were emailed the request and link for the survey, 747 (40%) responded. The majority (527 [71%]) were adult ID physicians, 181 (24%) were pediatric ID physicians, and 39 (5%) were healthcare professionals consisting mostly of pharmacists practicing in ID settings (Table 1). There was representation from all US census divisions, with Pacific, South Atlantic, East North Central, Mid-Atlantic, and West North Central accounting for most of the respondents. The preponderance of the physicians (634 [85%]) had completed their ID fellowship training ≥5 years prior, and nearly all were ID physicians who practiced in the inpatient setting at university, nonuniversity, or community hospitals.

Of the 747 respondents, a majority (583 [78%]) indicated that they managed patients with COVID-19 or consulted on patients for preexposure or postexposure prophylaxis to prevent SARS-CoV-2 infection. All subsequent analyses are limited to this subset.

Antibody Assay Types, Frequency of Ordering, and Turnaround Time

Among the subsample of participants, a majority (435/583 [75%]) indicated that they had ever ordered or recommended a SARS-CoV-2 antibody test in their clinical practice. The majority of the 583 respondents who had ever ordered a SARS-CoV-2 antibody test had ordered anti-N (n = 212) or anti-S/anti-RBD (n = 219) assays that were qualitative in nature (Table 2). Less than 10% had ordered either semi-quantitative or quantitative antibody assays, and only 3% had ordered a neutralization antibody assay for SARS-CoV-2. Of those who had ordered assays to support clinical decision making, a majority (334 [71%]) indicated that they ordered these tests less than once a week in their practice. A few respondents indicated that they had ordered these tests more frequently in the past and during COVID-19 surges. Among respondents who had never ordered an antibody test, the most often cited reasons were that they were not reliable, test results were not actionable, interpretation of results was not clear, or that they were not FDA approved.

Among participants who ordered antibody assays and reported response times (n = 440), 242 (55%) indicated that the turnaround time for antibody assay results was "days" and 175 (40%) indicated "hours." Only 6 respondents (1%) had used a point-of-care antibody assay. Among participants who ordered antibody assays and responded to questions about results being provided to patients (n = 439), most (307 [70%]) indicated that the antibody test results were routinely provided to patients at their institution.

Interpretation of Antibody Test Results

Participants who ordered antibody assays were asked about their level of comfort in interpreting positive and negative results. Of 578 participants responding, 75% (452) reported being comfortable interpreting a positive assay result. The majority indicated that it would be appropriate to interpret a positive anti-N assay result as evidence of prior infection (445 [77%]) and to interpret a positive anti-S assay result as evidence of mounting a humoral response to COVID-19 vaccination (382 [66%]). A minority (126 [22%]) were uncomfortable interpreting a positive result from any assay.

Of 562 participants responding to the survey item, 72% (405) were comfortable interpreting a negative antibody assay result. A majority reported it would be appropriate to interpret a negative anti-N assay result as no evidence of prior infection (338 [60%]) and to interpret a negative anti-S assay result as evidence of not mounting a humoral response to COVID-19 vaccination in a vaccinated person (338 [60%]). A minority (157 [28%]) were uncomfortable interpreting a negative result.

Scenarios for Ordering or Recommending Antibody Tests for Clinical Decision Making

Participants who ordered antibody assays were asked about the scenarios when the ordered test was used to inform their clinical decision making. Among participants who provided responses (n = 520), 318 (61%) indicated that they had ordered or recommended SARS-CoV-2 antibody testing to support a diagnosis of COVID-19 complications, such as MIS in children (MIS-C) or post-COVID conditions/long COVID (Table 2). Similarly, 60% had ordered these tests to determine prior SARS-CoV-2 infection status. Less than 40% had ordered tests for other clinical scenarios, such as distinguishing between prior SARS-CoV-2 infection and response to COVID-19 vaccination (using anti-N, anti-S, or anti-RBD assays).

Of those who had used these tests to document presence or absence of a measurable humoral immune response to COVID-19 vaccination to assess the need for additional or booster doses of COVID-19 vaccine (n = 172), the majority had ordered them for individuals with moderate or severe immunocompromising conditions who were at high risk for severe COVID-19 (146/172 [85%]). Approximately a quarter of the respondents (136/520 [26%]) ordered antibody assays to assess a patient's risk to inform clinical decision making. Of those who had used antibody tests to determine risk stratification (n = 136), the most commonly endorsed scenarios were the identification of inpatients most likely to benefit from anti–SARS-CoV-2 mAb therapy (67/136 [49%]) and the prioritization of individuals with immunocompromising conditions for preexposure prophylaxis with tixagevimab co-packaged with cilgavimab (66/136 [49%]).

Factors That Would Influence Ordering or Recommending Antibody Tests

A majority of respondents indicated that statements from professional societies (432/551 [78%]) and from US government agencies (340/551 [62%]) would influence their decision to order or recommend SARS-CoV-2 antibody assays for clinical decision making (Table 2). Other factors that would influence use of antibody assays included FDA EUA with indications for clinical use in postvaccination settings, superior test performance characteristics in a variety of clinical settings, and FDA approval for antibody assays that could then be used off-label.

Findings by Population Served and Physician Characteristics

With regard to ordering SARS-CoV-2 antibody tests, pediatric ID physicians were significantly more likely than adult ID physicians to have ever ordered antibody tests (153/159 [96%] vs 317/424 [75%], respectively; $P < .001$). Pediatric ID physicians were also more likely than adult physicians to report comfort with interpreting a positive serology result (146/159 [92%] vs 292/424 [69%], $P < .0001$) or a negative serology result (137/159 [86%] vs 289/424 [68%], $P < .0001$). There were no significant differences noted by years of experience since ID fellowship or US census divisions.

Free-Text Comments From Subset of EIN Member Respondents

Overall, 96 of 747 respondents (13%) provided additional free-text comments. A favorable view of serological testing was conveyed by 35 (37%) respondents who described in detail how they used SARS-CoV-2 antibody assays in certain clinical situations, for example, to inform decisions about the use of mAb treatment: "With the caveat that there is more to learn, I feel that it has provided valuable information for certain clinical situations." Fourteen respondents (15%) specifically mentioned the role of serology in assessing patients with suspected MIS-C; as a pediatrician noted, "We use [these tests] almost daily due to MIS-C issues, as most of our patients have been unvaccinated due to age limitations for vaccine." Another 8 respondents described the utility of serologic tests in individuals with immunocompromising conditions including organ transplant recipients and those with human immunodeficiency virus.

Of the 96 free-text respondents, 26 (27%) shared that they did not think serology was useful for clinical decision making currently. These individuals commented that serologic testing "doesn't usually change management," "I have not generally found them useful in practice," and there is "too much variability in individual assays."

Twenty-one respondents (22%) shared that the most important need for SARS-CoV-2 antibody assays going forward was to discern a correlate of immune protection. "Until a correlate protection of vaccine or prior infection is identified and there are data permitting interpretation of the test as indicative or not of protection," a respondent wrote, "use of antibody tests will be limited in my practice." One physician requested "more information about the level of antibody needed to provide protection—or is it just once you are over a level of X you are protected." Another said at their practice, "requests have been for 'am I protected?' for which there is no scientific answer currently."

Respondents recognized the limitations of the antibody tests, called for more studies, and indicated that additional guidance would be beneficial: "Many clinicians order antibody tests but have no idea how to interpret or misinterpret," a provider explained, "so guidelines on usage and when not to use would be extremely helpful."

DISCUSSION

In this systematic assessment of the use of SARS-CoV-2 antibody tests in clinical practice as of March 2022, a majority of US-based ID physicians who responded to the survey indicated that they had ordered or recommended a SARS-CoV-2 antibody test in their clinical practice, but most used these assays infrequently. Most of the assays ordered were qualitative binding antibody assays that provided results as either positive or negative, with very few having ordered a quantitative binding

antibody assay that measures antibody levels or a neutralizing antibody assay. The most frequent indications cited for ordering or recommending of antibody tests by survey respondents were either the FDA EUA indication for detection of prior infection [7], CDC guidance to support a diagnosis of postinfectious MIS, or to distinguish post–COVID-19 vaccination from post–SARS-CoV-2 infection states [8].

The majority of ID physicians were confident in their interpretations of both positive and negative test results based on the type of assay used, with a significant minority expressing discomfort. It is possible that ID physicians, working closely with their clinical laboratory colleagues, have become familiar with the SARS-CoV-2 antibody assays available in their practice settings and have become comfortable with using and interpreting results of those assays for specific clinical scenarios such as identifying previous infection and to assess protective immunity or lack thereof. This has been noted recently with clinical examples for uses of SARS-CoV-2 antibody testing [18].

SARS-CoV-2 antibody tests have had variable availability, acceptance, and adoption as the COVID-19 pandemic has evolved since early 2020 when the clinical, laboratory, and scientific communities were discussing clinical and population-level uses for antibody testing [19]. At that time, poorly performing assays had flooded the market and there were concerns of potential overuse of these tests in situations that were not supported by science and not in keeping with limitations laid out by FDA [20]. Although regulatory scrutiny from FDA has resulted in fewer assays receiving EUA, there is a lack of availability of quantitative assays that are calibrated against an international standard to allow for comparison of results [21] as well as variation in assay performance [22, 23]. Furthermore, confusion and concerns remain regarding the expansion of clinical use and interpretation of positive antibody test results.

A recent publication by Gilbert and colleagues [24] notes that strong evidence has been generated to demonstrate that anti-spike IgG concentrations and anti–SARS-CoV-2 neutralizing antibody titers are serological correlates of protection against symptomatic COVID-19 illness; this concept has also been endorsed by Khoury et al for neutralizing antibodies [25]. Furthermore, FDA has accepted immunobridging studies using comparisons of neutralizing antibody titers for approval of pediatric COVID-19 vaccines and against circulating strains as a correlate for the recently approved COVID-19 bivalent vaccine [26]. It is important to note that routine testing of neutralization titers in clinical practice is not available and, as such, quantitative binding antibody titers would be the practical option. However, in the setting of SARS-CoV-2 variants and concerns for immune escape, a particular individual threshold for protective antibody titers remains elusive.

There has been increased awareness and concern regarding complications of COVID-19 in children, especially MIS-C. In our survey, pediatric ID physicians were significantly more likely to have ordered or recommended SARS-CoV-2 antibody tests. They were also more comfortable interpreting both positive and negative results.

Based on the structured questions and free-text comments, confusion, discomfort in interpreting results, and lack of awareness remain regarding the appropriate use of SARS-CoV-2 antibody tests in clinical practice. In the setting of evolving knowledge and remaining scientific gaps, providing guidance for the appropriate use and interpretation of antibody testing is a challenge. Antibody testing is not currently recommended to assess for immunity to SARS-CoV-2 following COVID-19 vaccination, to assess the need for vaccination in an unvaccinated person, or to determine the need to quarantine after a close contact with someone who has COVID-19 [8]. However, there are certain populations at greater risk for severe outcomes from COVID-19, such as those with immunocompromising conditions, that are in need of objective risk stratification for clinical decision making and advice on the need for continuing to protect against breakthrough infections after vaccination [27, 28]. SARS-CoV-2 antibody testing may be of benefit in these situations. Some of these scenarios, such as prioritization of patients for preexposure prophylaxis, were germane to clinical practice at the time of the survey in March 2022.

We acknowledge several limitations. Experiences of EIN members may not be representative of nonmembers practicing in the community. In general, EIN membership is considered a convenience sample of self-selected ID physicians and is not intended to be either random or necessarily representative of a larger population. Furthermore, other specialists such as oncologists, rheumatologists, and transplant physicians, among others, may be those ordering SARS-CoV-2 antibody tests in their clinical practice. Second, the survey responses were self-reported and have not been validated with chart review at the respondents' institutions. However, real-world data on the extent of SARS-CoV-2 serology testing performed by clinical laboratories have been reported for the general population and are consistent with survey responses [29, 30]. Finally, these results are not directly generalizable to non-ID clinicians in the community.

As these survey results demonstrate, SARS-CoV-2 antibody tests are being used in clinical practice, with concern and lack of consensus among ID physicians regarding the use of these tests. There is a critical need for increasing awareness of the appropriate use of SARS-CoV-2 antibody tests for clinical use, along with refinement of the tests and studies to further delineate correlation with protection and risk stratification. Professional societies and US government agencies can support clinicians in the community through the creation of appropriate guidance with current knowledge and pragmatic clinical experience that would be helpful to clinicians and their patients. These positions should be supported by timely syntheses of available

evidence to endorse current indications for use of SARS-CoV-2 antibody tests in clinical practice and options to expand those indications to account for postvaccination and risk stratification settings. There are several such guidelines now available, with varying degrees of strength of evidence [13, 31, 32]. These messages can be separately tailored to the needs of patients across different age groups and clinical scenarios.

While serological correlates of protection in terms of antibody levels are now well established [24, 25], identifying specific thresholds at the individual level poses challenges particularly as the landscape appears to be constantly shifting due to hybrid immune responses from prior vaccinations and infections as well as immune escape by new SARS-CoV-2 variants and subvariants. This is evident from the recognition of Omicron subvariants with evidence of lack of in vitro susceptibility to anti–SARS-CoV-2 mAbs authorized by FDA for treatment of individuals with mild-to-moderate COVID-19 at high risk for progression to severe COVID-19, and for preexposure prophylaxis in persons with moderate-to-severe immunocompromise; currently, no anti–SARS-CoV-2 mAbs are authorized for prevention or treatment of COVID-19 in the US [33, 34]. Furthermore, the contributions of cellular immunity in protecting against severe disease are known, especially in the setting of viral variants, though measuring and assessing cellular immunity in routine clinical practice remains a challenge with testing restricted to the research setting [35]. In this setting, antibody tests are a relatively low-cost and available tool that can provide additional information to inform the probability of being protected or not. There may be an opportunity to start with the use and interpretation of negative SARS-CoV-2 antibody test results in specific populations in which serologic testing is most likely to be used to guide care decisions [13, 18, 31, 32], such as in patients with immunocompromising conditions.

Notes

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