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Reimbursement: CMS Mulls Automatic Medicare Coverage of MCIT Breakthrough Devices

Manufacturers of innovative medical devices are on pins and needles right now. That is because the Centers for Medicare and Medicaid Services (CMS) delayed implementation of a final rule that was supposed to take effect on March 15, 2021 that would have ensured at least four years of Medicare coverage for new medical products cleared by the Food and Drug Administration (FDA) as breakthrough devices under Section 510(k). Unlike many Trump administration regulations, the breakthrough device coverage rule may still come to fruition. But CMS is currently studying the rule and will not make a final decision sooner than May 15. Here is a look at the rule and its prospects of actually taking effect.

The Final Rule

Medicare covers only medical services and products that are "reasonable and necessary." *The Social Security Act* (Section 1862((a)(1)(A), to be precise) gives the Department of Health

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Telemedicine: Americans Like Telehealth Visits and Want More

After a year in pandemic lockdown, Americans' perception of visiting their doctors virtually rather than in-person has changed dramatically. The vast majority likes having a telemedicine option and want it to continue. So concludes a new survey by Sykes that polled 2,000 Americans in March on how their opinions on virtual care have changed within the past year.

What a Difference a Pandemic Makes

Before COVID-19, virtual care was more of a concept than a reality,

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Reimbursement: CMS Mulls Automatic Medicare Coverage of MCIT Breakthrough Devices, *from page 1*

and Human Services (HHS) Secretary authority to determine whether a particular service or product meets the standard. However, HHS has never established a formal regulation to define "reasonable and necessary." The rule, which was finalized on Jan. 12, creates such a definition, one that would enable breakthrough devices to qualify as reasonable and necessary.

Specifically, the rule would grant national Medicare coverage of breakthrough devices for a four-year period starting on the date of FDA market authorization. Once the period ends, CMS would then re-evaluate the device based on clinical and real world evidence of improved health outcomes to determine whether to make Medicare coverage permanent.

The policy behind the rule is to give Medicare beneficiaries better access to new medical technologies. Technically, the rule applies only to devices that pass through the Medicare Coverage of Innovative Technology (MCIT) pathway, which does not include laboratory developed tests (LDTs). However, CMS had made it clear that the MCIT rule would serve as a template that could be extended to breakthrough diagnostics, drugs and/or biologics that are not currently in the MCIT pathway.

The Biden Brake

Immediately upon taking office, the Biden administration signaled its suspicion and skepticism of the health care policies of its predecessor and imposed a blanket freeze on new regulations adopted in the regime's final days. (To find out about the other regulations affected, see G2 Blog, How the Transition from Trump to Biden Will Affect Federal Regulation and Reimbursement," Feb. 19, 2021). In addition, critics have attacked the rule for throttling CMS' clinical scrutiny and opening the door scientifically unproven devices as part of the Trump administration's supposed disdain for science and regulation. This criticism was bound to resonate with the new President who has expressed similar views on Trump policy.

Takeaway

Although the delay in implementation comes as no surprise, the final rule's ultimate demise is by no means a forgone conclusion. On the contrary, lack of a clear Medicare coverage definition of "reasonable and necessary" has been a problem for decades, serving not only as a thorn in the side of the medical device and lab industry but also in blocking the access of Medicare patients. The attempt to address the problem also enjoys bipartisan support in Congress.

But the Biden administration refuses to be rushed. In announcing the final rule's delay, CMS initiated a new 30-day comment period to gather public feedback on operational issues, overlapping rules, breakthrough device volume, patient protection and commercial insurance. And if the final rule does make it through, the door will be opened to extending it to LDTs. So, stay tuned.

DTET

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FDA WATCH

Agency Streamlines Authorization of COVID-19 Molecular Test Pooling for Screening Programs

Last July, in an effort to meet the desperate need for high throughput COVID-19 testing, the U.S. Food and Drug Administration (FDA) issued the first clearance for use of a previously authorized test on pooled samples to Quest Diagnostics' SARS-CoV-2 RNA test (See DTET, Sept. 8, 2020). More than two dozen other COVID-19 tests have received Emergency Use Authorization (EUA) since then. Now the agency has doubled down by promulgating new rules making it easier for makers of previously authorized molecular tests to get expanded EUA for pooling.

COVID-19 Test Pooling

Pooling is a technique that enables laboratories to expand throughput by testing a batch of combined specimens at once. If the pool tests negative, it becomes unnecessary to test the constituent samples. The tradeoff is that the pooled samples must be diluted, which makes the nucleic acids produced by the SARS-CoV-2 virus more difficult to detect thus increasing the risk of false negatives. The other downside is that pooling can backfire and consume more testing time and resources when the sample comes back positive because the samples then need to be tested individually to detect the source(s) of the positive result.

For these reasons, the FDA has been historically reluctant to allow pooling. But with COVID-19 testing resources stretched so thin, the agency issued its first ever guidelines to help molecular test makers secure EUA for pooling. On April 20, the agency issued an amended version of those guidelines to facilitate authorization for pooling. **The punchline:** Molecular COVID-19 tests that have received EUA can be used with pooled samples performed to screen asymptomatic people as part of a "serial testing program," such as in a school or workplace setting as long as the test developer self-certifies that it has validated the test for pooling.

"If a test developer has self-certified it has validated its test for pooling, FDA will add that test to a list of tests that can be used for pooling nasal specimens as part of a serial testing program," noted the FDA's device center director, Jeffrey Shuren, in a statement, describing the policy as a way to help schools, workplaces and others establish routine testing programs.

The New Pooling Protocols

The amendment applies only to pooling of anterior nasal respiratory specimens and tests being used at least once per week as part of a serial testing program. To qualify for use of a test on a pool of more than three

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FDA Watch: Agency Streamlines Authorization of COVID-19 Molecular Test Pooling for Screening Programs, *from page 3*

specimens without first going through agency review, test makers must provide the FDA notification along with their validation data and the pooling procedures to be used, after which the test will be listed on the FDA website as allowed for pooling and updated labeling will be posted with the test's EUA. They can place up to three samples in the same transport vial, the amended guidelines explain, including self-performed swabs and swabs collected by a healthcare professional, without additional validation, as long as the analysis is performed in certified CLIA laboratories.

Here are some of the key new FDA EUAs and clearances announced in April:

New FDA Emergency Use Authorizations (EUAs) & Approvals

Manufacturer(s)	Product
Enzo Biochem	EUA for Ampicollect Sample Collection kit
Synergy Diagnostic Laboratory	EUA for SynergyDx SARS-CoV-2 RNA Test + SynergyDx SARS-CoV-2 RNA Test DTC, an over-the-counter version of test
Celltrion	EUA for DiaTrust COVID-19 Ag Rapid Test
LGC Biosearch Technologies	EUA for Biosearch Technologies SARS-CoV-2 Real-Time and End-Point RT-PCR Test
Yale School of Public Health	EUA for SalivaDirect At-Home Collection Kit
Clinical Enterprise	EUA for Clinical Enterprise SARS-CoV-2 RT-PCR Assay
Qorvo Biotechnologies	EUA for Omnia SARS-CoV-2 Antigen Test
Thermo Fisher Scientific	EUA for use of its Amplitude Solution with TaqPath COVID-19 High-Throughput Combo Kit
Lucira Health	EUA for Lucira Check It test kit for SARS-CoV-2 for over-the-counter use at home
Symbiotica	EUA for COVID-19 Self-Collected Antibody Test System, first antibody test authorized for use with home collected dried blood spot samples
Gold Standard Diagnostics	Clearance for *B. burgdorferi* IgG/IgM VlsE-OspC EIA test
DiaSorin	EUA for Liaison SARS-CoV-2 Ag SARS-CoV-2 antigen test
Bluestar Genomics	Breakthrough Device Designation for pancreatic cancer liquid biopsy assay in patients with new-onset diabetes
Quidel	EUA for QuickVue At-Home OTC COVID-19 Test
Abbott	EUA for BinaxNOW COVID-19 Ag Self Test for over-the-counter use by children as young as 2

Manufacturer(s)	Product
Becton Dickinson	EUA for BD Veritor Plus System for Rapid Detection of SARS-CoV-2
Becton Dickinson	EUA for BD Veritor System for Rapid Detection of SARS-CoV-2 & Flu A+B
Binx Health	CLIA waiver for Binx Health io CT/NG Assay rapid point-of-care assay for detection of chlamydia and gonorrhea
NeuMoDx Molecular	EUA for NeuMoDx Flu A-B/RSV/SARS-CoV-2 Vantage Assay
Twist Bioscience	EUA for SARS-CoV-2 Next-Generation Sequencing assay
Beckman Coulter	EUA for Access SARS-CoV-2 IgG II rapid antibody test
Color Health	EUA for Color SARS-CoV-2 RT-LAMP Diagnostic Assay
Color Health	EUA for DTC version of Color COVID-19 Self-Swab Collection Kit

Testing Strategy: CDC/NIH Team with Local Health Authorities to Promote, Evaluate Home COVID-19 Testing

As the COVID-19 crisis drags on, the primary focus of the federal government's testing strategy continues to shift from medical diagnosis and treatment to broad testing of the asymptomatic for purposes of screening. The U.S. Centers for Disease Control and Prevention's (CDC) new "Say Yes! COVID Test" initiative is an innovative program designed to enlist local public health authorities to promote screening at the community level.

The Diagnostic Challenge

Regrettably, COVID-19 infection remains a threat and frequent testing will be essential to make the return to work, school and society as safe as possible. According to the National Institutes of Health (NIH), along with social distancing, vaccination, wearing a mask and regular hand washing, frequent testing offers the best chance of containing the threat posed by the "silent spread" of COVID-19 that occurs when people are infected but do not yet exhibit symptoms.

Although it is accurate, polymerase chain reaction (PCR) molecular testing performed by an offsite laboratory is not suited for such purposes. What is required are rapid tests that can provide reliable results at the point of care, including at home. In a recent study conducted by the NIH RADx initiative, researchers found that rapid antigen testing at least three times per week achieves a viral detection level on par with PCR-based COVID-19 testing processed in a laboratory.

The other major challenges are logistics, test distribution and education. These obstacles will have to be confronted and solved at the local level.

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Testing Strategy: CDC/NIH Team with Local Health Authorities to Promote, Evaluate Home COVID-19 Testing, *from page 5*

Although the federal government can provide general leadership and support, engagement of local public health authorities and government laboratories will be utterly crucial.

The CDC Say Yes! Program

With these principles in mind, the new Say Yes! COVID Test program (Program) is a first of its kind collaboration between the CDC and state and local public health departments, starting in Pitt County, North Carolina, and then Chattanooga, Tennessee. These locations were selected based on local infection rates, public availability of accurate COVID-19 tracking data, existing community relationships through the NIH Rapid Acceleration of Diagnostics Underserved Populations (RADx-UP)(link is external) and local infrastructure to support the Program.

As many as 160,000 residents across the two communities will have access to Quidel's QuickVue At-Home COVID-19 rapid antigen test kits provided by NIH free of charge. The prime targets are individuals who have not yet received the COVID-19 vaccine and/or who are highest risk for exposure to COVID-19, such as those who work or go to school outside the home. Participants may order their test kits online for home delivery or pick them up at a local distribution site.

The Quidel QuickVue At-Home COVID-19 Rapid Antigen Test Kit

The Quidel QuickVue At-Home COVID-19 test used by the Program is a rapid, antigen test that received Emergency Use Authorization from the Food and Drug Administration on March 1. It uses a lateral flow format that individuals can use to rapidly collect their samples at home without having to send them to a laboratory for analysis. The test is authorized for prescription home use with self-collected anterior nasal swabs from individuals 14 years or older and individuals as young as 8 years old with swabs collected by an adult. Quidel claims that the test can return results in 10 minutes and that it showed positive results that agreed with PCR testing 84.8 percent of the time and negative results that agreed with PCR results 99.1 percent of the time. Each kit supports frequent testing of two household members.

Tests require samples from a swab inside each nostril, and results can be read in 10 minutes. Participants can administer the test themselves at home three times a week for one month. A free online tool that is also available as a phone app will be offered to provide testing instructions, information to help understand test results and text message reminders about testing. with each kit supporting frequent home testing for two household members.

End Game: Determine If Frequent Home Testing Reduces Infection

Participants in the Program will also have the option to volunteer in an NIH-supported research study that will collect additional data through surveys. The survey questions are designed to determine whether frequent

self-administered testing has made a difference in behavior, knowledge on preventing spread of the virus and thoughts about COVID-19 vaccination. NIH will use the data to determine whether frequent self-administered COVID-19 testing helps residents reduce community transmission of SARS-CoV-2.

Researchers at NIH-supported University of North Carolina at Chapel Hill, and Duke University and the Duke Clinical Research Institute, both in Durham, North Carolina, will work with the CDC and NIH to use publicly available COVID-19 case surveillance data on test positivity rates, COVID-19-related illness and hospitalizations and measurements of viral particles in sewage wastewater to evaluate viral transmission in the community. At the same time, publicly available data will be reviewed from other communities of similar size that have not received widespread self-administered tests to evaluate the impact of frequent self-administered testing.

Takeaway

The Program is a test balloon that may lay the groundwork for much more widespread federal intervention. If self-testing is shown to be effective in reducing COVIDO19 spread in the selected communities, the expectation is that the CDC and other federal agencies will initiate further projects to ensure wider distribution and acceptance of frequent home testing across the country in the hopes of ultimately providing an easy and accessible new means of stemming the spread of the virus.

"Reliable and widely available testing is a critical part of our efforts to stop the spread of COVID-19. Regular screening with at-home COVID-19 tests can strengthen our prevention efforts," said CDC Director Rochelle P. Walensky, M.D., M.P.H in a news release *. "Combined with efforts to increase vaccinations, this important initiative will help us understand how best to utilize these new at-home tests to reduce viral transmission rates in communities."*

Genetic Testing: New Study Supports Use of Liquid Biopsy Technology to Bolster MRI Accuracy in Cancer Treatment

Important new evidence has emerged supporting the capabilities of liquid biopsy to enhance the accuracy of magnetic resonance imaging (MRI) for cancer diagnosis and treatment. That evidence comes from a new report revealed at the annual American Association for Cancer Research (AACR) showing that adding liquid biopsy to MRI may improve the ability to gauge breast cancer treatment response. Here is an overview of the report and what it may portend.

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Genetic Testing: New Study Supports Use of Liquid Biopsy Technology to Bolster MRI Accuracy in Cancer Treatment, *from page 7*

The Diagnostic Challenge

Liquid biopsy is a noninvasive diagnostic approach involving isolation of circulating tumor markers such as cell-free nucleic acids and circulating tumor cells from peripheral blood. The tumor microenvironment hosts growing and apoptotic cancer cells that release biomarkers into the circulation, that can subsequently be collected for use in analyzing tumor biology.

Can the capabilities of liquid biopsy to measure plasma cell-free DNA (cfDNA) non-invasively and at relatively low cost be used to enhance the accuracy of MRI? This question has become an important focus of cancer research in recent years.

The AACR Report

The AACR report comes from a retrospective study sponsored by the University of Genoa and other organizations in Italy. The study focuses on cancer patients after they receive chemotherapy and before surgery. Under current methods, MRI is used to measure cfDNA in patients treated for localized breast cancer. However, as the study indicates, use of MRI alone for this application yields results of "suboptimal accuracy."

Current methods of post-chemotherapy and pre-surgery assessment of axillary node response are also invasive to the extent that they typically involve performing sentinel lymph node biopsy followed by lymph node dissection in patients who do not have a complete response.

Given MRI's limitations as a presurgical guiding tool and the invasive nature of lymph node response, the researchers set out to explore whether cfDNA testing could aid in the assessment of pathological complete response in the crucial period between chemotherapy and surgery. To find out, the researchers analyzed blood from breast cancer patients who had undergone neoadjuvant anthracycline/taxane chemotherapy. They profiled samples available from the time of diagnosis and after treatment based on histopathological analysis and created a DNA integrity index to measure the degree of fragmentation of cells in the blood of responders and non-responders.

The Study Findings

The researchers used their cfDNA integrity index to evaluate 38 patients, of whom 11 had a pathological complete response after neoadjuvant chemotherapy treatment. They applied the cfDNA integrity to assess both the accuracy of MRI and cfDNA integrity indexing performed alone and MRI performed together with cfDNA when the results were in agreement. **Result:** Agreement of MRI and cfDNA results yielded a positive predictive value of 87.5 percent and a negative predictive value of 94.7 percent.

Accuracy in Predicting Pathological Response after Chemotherapy

MRI alone	cfDNA Integrity Index	MRI + cfDNA (when in agreement)
77.1 percent accuracy	81.6 percent accuracy	92.6 percent accuracy

The researchers are planning a study to build on their findings. First, they plan to evaluate the value of the cfDNA integrity measure and MRI in assessing complete pathological response in a larger sample of similar breast cancer patients. If that phase proves successful, they will carry out a follow-up study of the clinical utility of the MRI/cfDNA integrity index for assessing complete response, replacing sentinel lymph node biopsy with ultrasound to measure the local rate of relapse.

Takeaway

While there is still more research to do, these preliminary findings suggest that when used together with MRI, liquid biopsy does have the potential to improve accuracy and spare patients the need for sentinel lymph node biopsy. This study reinforces earlier research supporting the potential of liquid biopsy and ctDNA testing to improve cancer diagnosis and treatment when combined with MRI.

Emerging Tests: Blood Test to Detect Early-Stage Lung Cancer Inches Closer to Reality

Maybe one day, medical science will find a way to eradicate lung cancer from the face of the earth. Until then, improving diagnosis of lung cancer at the early stages will remain an urgent priority. To save lives, the diagnostic would have to be not only accurate and highly sensitive, but relatively inexpensive, simple and easy to use. Something like a blood test. Of course, laboratories and research scientists around the world are working toward that goal. And now comes word of a promising project taking place north of the border.

The Diagnostic Challenge

Few forms of cancer are as deadly as lung cancer. One reason for that is the absence of clinical symptoms in its early stages. Adding to the problem is that CT screening, the primary method of diagnosing lung cancer, is a costly procedure that physicians are highly unlikely to order for patients without symptoms.

As a result, lung cancer is most often diagnosed in the later stages. By then, the cancer has advanced enough to do damage and make treatment outcomes poor. Thus, approximately half of all lung cancer cases are

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Emerging Tests: Blood Test to Detect Early-Stage Lung Cancer Inches Closer to Reality, *from page 9*

likely to be diagnosed at stage 4 when the patient's three-year survival rate can be as low as 5 percent. Early detection increases survival rates dramatically. If the cancer is detected at stage 1, survival rates rise 66 percent.

Early Detection Blood Testing

Once dismissed as nothing but a pipe dream, new evidence has emerged to suggest that it may be feasible to develop a simple blood test that is capable of detecting early-stage lung cancer. Of course, liquid biopsy type blood tests have long been used to assess the genetic characteristics of tumors to inform patient treatment at the late stages. But a 2018 breakthrough study from the American Society of Clinical Oncology in 2018 was among the first to conclude that these tests might also be able to actually detect the condition at an early stage.

The TMIC Project

Having established its feasibility, laboratories and researchers now face the challenge of actually coming up with an actual early-stage lung cancer detection blood test. One of the more promising projects is being carried out in British Columbia by Dr. David Wishart, head of The Metabolics Innovation Centre (TMIC). Dr. Wishart and his TMIC team were recently able to secure funding via a Sparks Grant from the Canadian Cancer Society to support development of a liquid biopsy test to detect and measure lung cancer-specific metabolites for use in early screening.

"We are coming up with a whole variety of novel, cheap and easy ways to detect early-stage cancer using only metabolites found in blood or urine," Dr. Wishart noted.

Telemedicine: Americans Like Telehealth Visits and Want More, *from page 1*

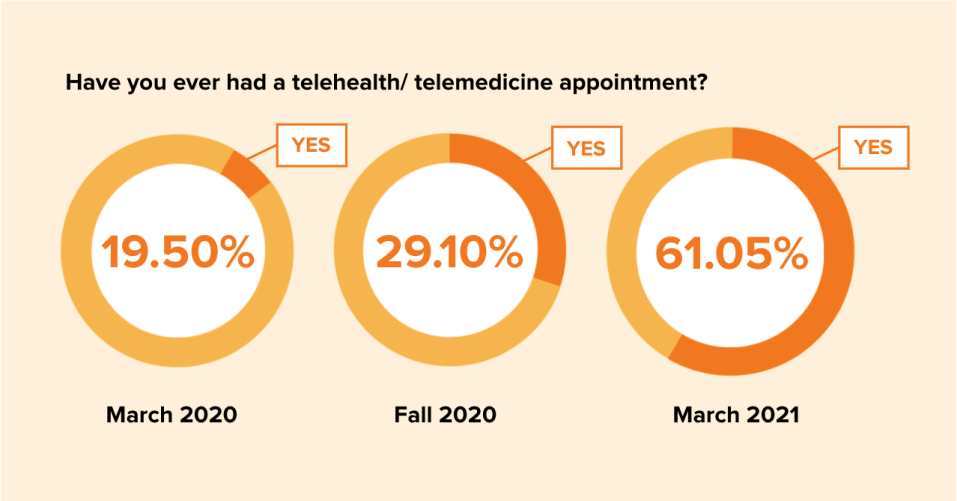
one hampered by regulatory and insurance requirements. An earlier Sykes Survey from March 2020 found that fewer than 20 percent had ever had a telemedicine appointment. COVID-19, however, proved a game changer as the government and insurers temporarily lifted previous restrictions so that homebound patients could seek medical care and advice safely from a distance. Thus, in the Sykes survey from March 2021, 61 percent of respondents reported having had a telehealth visit.

Attitudes have Changed

Given the opportunity and impetus to try out virtual health, most seem to have liked the experience and want to keep doing it. A year ago, roughly 65 percent of Americans said they felt hesitant or doubtful about the quality of telemedicine, and 56 percent did not believe it was possible to receive

the same level of care as compared to in-person appointments. One year later, almost 88 percent want to continue using telehealth for nonurgent consultations after COVID-19 has passed, while almost 80 percent say that it is possible to receive quality care virtually.

Furthermore, the pandemic increased the willingness of Americans to try telehealth.



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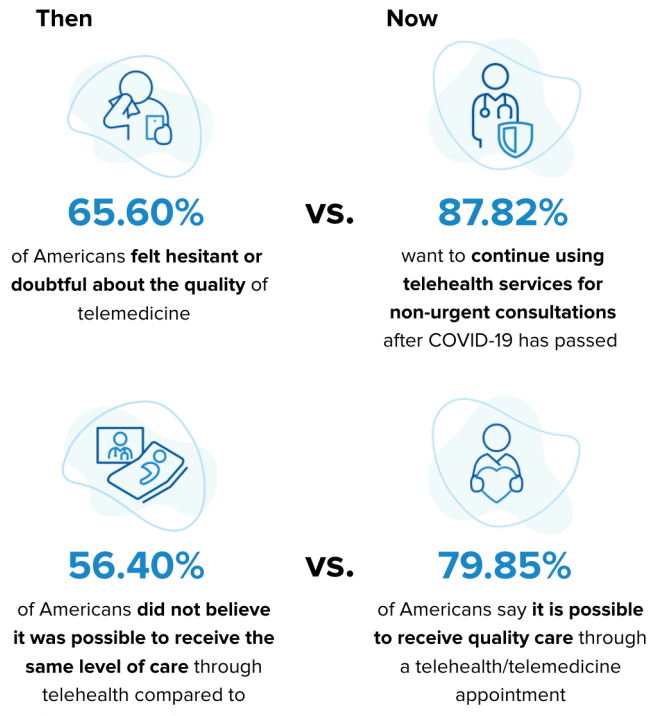

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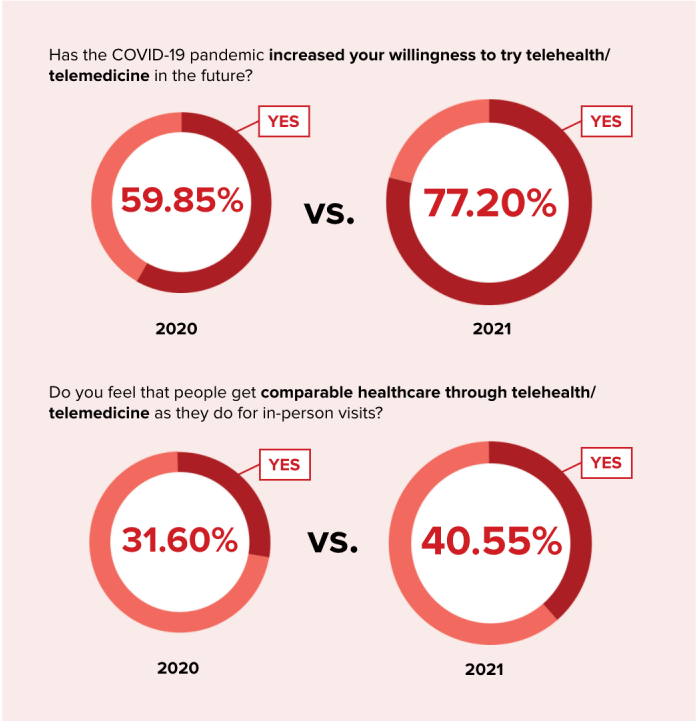

Source: Sykes

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Telemedicine: Americans Like Telehealth Visits and Want More, *from page 11*

Over 85 percent of surveyed respondents agreed that telehealth has made it easier to get needed health care and over 64 percent said that going forward, they would like to have at least part of their annual exams done via telehealth. Another 74 percent said they would be willing to share data collected on a fitness tracker or smart medical devise with their physicians. Among the perceived benefits of telehealth is the convenience and ease of not having to commute to a doctor's office, and not having to wait in a doctor's waiting room around other sick patients.

Takeaway

According to Sykes, the telehealth/telemedicine industry is poised to expand at compound annual growth rates as high as 21.4 percent by 2025. "As more and more patients come to experience telehealth, many are already discovering and enjoying the numerous benefits that come with digitally distant care. And given all that telemedicine has to offer, it's a safe bet that the next waiting room you enter will require a username and password."