Post-Pandemic, Patients Becoming More Powerful Stakeholders in Infectious Disease Testing

Jul 26, 2023 | Madeleine Johnson

A woman administers an at-home, COVID-19 antigen test.

NEW YORK – Before the COVID-19 pandemic, ordinary citizens were basically clueless about the meaning of terms like PCR and rapid antigen testing.

Instead, it was left to laboratorians and caregivers to decide what kinds of tests would best serve patients who came down with an illness.

But after three years of having swabs stuck up their noses and figuring out when a molecular assay might be more appropriate than an antigen test, patients are more knowledgeable than ever about infectious disease testing. Armed with a newfound wisdom, they are also seeking even more information and access to diagnostics and providing input into decisions about the healthcare they receive.

"Up until COVID, patients weren't all that interested in lab testing," said Romney Humphries, medical director of the Microbiology Laboratory at Vanderbilt University Medical Center. But it turns out, "Patients are actually incredibly savvy and intelligent about lab testing, and if you provide them with the information, they're able to make really informed decisions for their own health or the health of their own family members," she said.

Although COVID-19 is now becoming manageable, other infectious diseases are regaining the attention of the healthcare space and the public's interest. And with that, the patient's role in diagnosing and treating such diseases may need to change.

Sepsis, for example, kills 739 people in the US every single day and cost the healthcare system about $58 billion in 2022 — estimated to be the highest cost in the world — with delays in administering appropriate antibiotics known to increase the risk of death.

Antimicrobial resistant (AMR) infection rates are also creeping upward and threatening to set healthcare back to a pre-antibiotic era, even as the US Centers for Disease Control and Prevention estimates that as much as half of all antibiotic use is unnecessary or inappropriate. A report from the United Nations calculates that by 2050 "superbugs" will cause 10 million deaths worldwide per year, up from approximately 1.3 million deaths directly attributable to AMR in 2019, and rivaling annual cancer mortality globally.

Against this backdrop, patients more than ever want a voice in decisions about what they are being tested for, how the test will be administered, and how the results will be interpreted. Meanwhile, patient advocates like Nile's Project founder Carole Moss and Diane Shader Smith are acutely aware of the power of diagnostics and are working to educate and empower others as well.

In terms of education, patients are now more frequently encountering the core concepts of lab testing on the internet and have access to their own test results through online portals. A recent study in *The Journal of the American Medical Association* found that 96 percent of patients want their own lab test results made available to them immediately, even before physicians review them.

Patient awareness of diagnostics happens to be "expanding simultaneously with a rapid increase in the complexity and capabilities of diagnostic tests," said Michael Pulia, director of the Emergency Care for Infectious Diseases research program at the University of Wisconsin-Madison School of Medicine and Public Health. As a result, providers have a duty "to empower patients to have a strong voice in initiating discussions about our diagnostic process," he said.

Kimberly Claeys, an associate professor at the University of Maryland School of Pharmacy and a diagnostics researcher, said that in addition to improved patient knowledge of diagnostics, there is also an increasing recognition among providers that patient engagement can improve the quality of care.

"We're seeing more focus on patient-centered outcomes and how our decisions impact patient well-being," she said, as well as an uptick in patient advocates being included in diagnostic and antimicrobial research studies.

Laboratorians are also playing an expanded role in patient engagement. They became public faces during the pandemic and now have a vibrant and visible community on social media — and their communication of labs' challenges had the collateral benefit of educating the public about what labs do.

Omai Garner, director of Clinical Microbiology at UCLA Health Center, found himself in an outreach role during the pandemic. "I ended up on television and doing a lot of patient education because diagnostic testing was at the forefront of our discussions," he said. The lab community learned that these could be useful conversations that "help people better understand the tests that are being performed, what the results mean, and how the labs work," he said.

However, the impact of patients' new knowledge about lab-based, or even inpatient, testing is unclear, as is the point at which input from them may actually hurt their own care.

Historically, patient advocacy in infectious diseases has led to laws mandating infection prevention and reporting in hospitals, and new sepsis protocols. But, although an educated and motivated public can be a powerful agent for change in healthcare, there is also some danger that consumers can be misled in the diagnostics space, and misplaced zeal combined with patient-initiated diagnostics could lead some patients to seek testing for medically unsubstantiated conditions.

Home-use diagnostics

Infectious disease diagnostics were long considered so complex to appropriately order, perform, and interpret, that, aside from one at-home, over-the-counter HIV infection assay, only healthcare providers and laboratorians were authorized to use them.

But the past three years revealed a real need for different approaches to infectious disease diagnostic testing, according to UCLA's Garner. "There were some communities that couldn't get COVID testing at all, and those communities were also hit the hardest," he said in an interview.

Emergency Use Authorization from the FDA combined with massive federal and public support has since produced 35 authorized COVID-19 tests for use at home. Numerous non-COVID at-home assays — for flu, Strep A, and sexually transmitted infections — are now in development.

"Healthcare has been pulled, not pushed, by patients into the home," said Tim Stenzel, director of the FDA's office of *in vitro* diagnostics. For its part, the FDA has lowered barriers for developers, for example, by allowing simulated environments for studies rather than evaluations in homes.

The FDA is currently seeking comments from the public on home-use tests as part of its strategy to advance health equity, and its outreach effort hopes to uncover whether patients think the system is working and what more they want or need. Increased access to diagnostics is expected to help break down barriers to healthcare caused by racial inequities, geography, and disability.

Stenzel highlighted the Fastep COVID-19 Antigen Pen Home test from Azure Biotech, which was designed to be especially easy to manipulate and run. The test is a graduate of the Independent Test Assessment Program led by the National Institutes of Health Rapid Acceleration of Diagnostics (RADx) Tech division, he said, and "was a direct result of NIH and FDA working together to better meet patients' needs, particularly those with physical challenges."

Similarly, an at-home test for visually impaired people from Ellume exemplifies a technology whose increased adoption has been inspired in part by patient advocacy.

Home-use testing outreach to patients can also take the form of direct-to-consumer advertising of diagnostics.

Mike Nassif, head of Point of Care Diagnostics at Siemens Healthineers, said his company's first forays into DTC marketing to patients were with a campaign called Moments That Matter for its Clintest rapid COVID tests. The experience taught his team "about the shifts in tone and visual branding and advertising channels necessary to reach patients versus the professional healthcare community." Siemens plans to expand on this as they develop more consumer-focused, point-of care-products, he said.

Abbott, meanwhile, began offering consumer-facing education and an online locator for its over-the-counter BinaxNOW COVID-19 rapid antigen self-test, according to Paige Jones, the firm's manager of public affairs for rapid diagnostics.

Patient advocates have also played a role in the rise of at-home infectious disease testing.

Nile's Project's Moss serves on the Clinical Laboratory Improvement Advisory Committee alongside FDA's Stenzel and representatives from the CDC and the US Centers for Medicare & Medicaid Services. A long-time proponent of home testing — whose efforts resulted in a law requiring universal methicillin-resistant *Staphylococcus aureus* (MRSA) screening in California hospitals — Moss said that early in the pandemic she strongly advocated during CLIAC meetings for over-the-counter options and found the messaging from the advocacy group Rapid Tests particularly inspiring.

The most pressing need in at-home testing now, according to Moss, is a rapid test to distinguish a viral from a bacterial infection, akin to the FebriDx test from Lumos Diagnostics which received FDA clearance earlier this month for use by healthcare professionals. This type of rapid testing could save lives from sepsis and help stave off the AMR crisis, she suggested, because a patient could come to the hospital with a crucial diagnostic result in hand that would likely accelerate their appropriate treatment.

A low cost for at-home tests is essential as well, according to Garner. "You can't make a home test for $80," he said. "That's not increasing equity or accessibility."

Besides choosing among cleared at-home tests or advocating for more, from Garner's perspective patient voices should also be included early in the development of at-home testing, to ensure that

assays are tailored to the people using them. Humphries agreed, adding, "More and more in medicine we're talking about how important it is having the end user or the end beneficiary included — and their preferences and perspectives considered."

Point-of-care molecular testing and self-collected samples

Some diagnostics developers are now reinforcing and building upon new connections with patients to market point-of-care molecular infectious disease testing directly to the public.

For its ID Now rapid point-of-care molecular system, Abbott encouraged pharmacies and clinics to opt into a healthcare professional locator tool in the second half 2021, Jones said. The firm then built a consumer-facing webpage, which it made public early last year.

The site educates patients on the difference between rapid molecular and lab-based PCR testing. It also has a test locator map. Currently, consumers can select from a menu of COVID-19, flu A/B, respiratory syncytial virus, and Strep A assays, enter their zip code, and quickly find a clinic or pharmacy offering for the test they want.

"Our market research shows that both accurate test results and the convenience of getting testing and treatment in a single clinical visit are very important to consumers," Jones said, adding that Abbott has seen both awareness and use of the map growing since it launched.

Pharmacy chain store Walgreens increased its offering of Abbott ID Now testing to include the flu A/B assays in more than 5,000 stores nationwide in December, according to Anita Patel, Walgreens' VP of pharmacy services development. "This expands on our broader efforts to relieve the burden on traditional providers," she said, and provides convenient options for patients to both reduce viral spread and get faster treatment.

Similarly, patients are increasingly seeking point-of-care molecular options for sexually transmitted diseases, where patient engagement through direct-to-consumer marketing may also make sense.

Charlotte Gaydos, an expert in point-of-care STI testing and emeritus professor at Johns Hopkins University, said in an interview that she knows of only two FDA-cleared and CLIA-waived rapid molecular point-of-care STI test systems — from Binx and Visby Medical — and neither has yet tried any large-scale DTC campaigns, to her knowledge.

To Alex Nowak, an analyst at investment bank Craig-Hallum, DTC marketing overall is part of the increasing consumerization of healthcare. "The pandemic maybe even accelerated that in a meaningful way within the diagnostic landscape," he said in an interview.

As with at-home testing, companies with cleared devices are allowed to advertise directly to patients, as long as they stay within authorized claims, according to FDA's Stenzel. "Knowledge is power to the patient and the consumer," he said.

Stenzel pointed out that another way patients have become more involved in their own diagnostic testing is through home sample collection. This strategy was pioneered for human papillomavirus testing in cervical cancer screening but became more widely adopted with lockdowns and the rise of telemedicine.

Nathan Ledeboer, who oversees clinical microbiology and diagnostics at the Medical College of Wisconsin, said the self-sampling trend has also been expanding to STI testing and seems likely to grow in the future. "We're really seeing a lot of movement to diversify the settings where care is delivered and how it's delivered," he said, adding that the adoption of self-collection more broadly may be slow-going because it requires an eye to patient safety as well as test sensitivity.

However, Stenzel emphasized that important work was done during the pandemic by developers on self-collection in order to determine that "patients can do this, they can do it well, and we can include them very upfront in our thinking."

Overall, Zach Rothstein, executive director of the industry advocacy group AdvaMedDx, said that the role of patients is set to become even more central to diagnostic device development and utilization in the years to come, particularly for the in-home and point-of-care spaces. The future will likely also include more patient involvement in designing and participating in clinical trials and contributing to real-world data.

"Patients are becoming integral to shaping more effective, personalized diagnostic solutions," Rothstein said.

Patient-initiated lab testing

While the expanded role of the patient in at-home, point-of-care, and self-collected samples is a welcome, even encouraged outcome of the pandemic, direct-to-consumer, or patient-initiated, lab testing seems to be viewed more skeptically.

Patients are increasingly able to order their own lab tests and can locate local testing sites using websites like Lab Finder and Any Lab Test Now. Quest Diagnostics, meanwhile, now offers a menu of more than 75 assays directly to consumers.

Laboratorians were generally positive about routine DTC testing last year in a *Clinical Chemistry* Q&A. In a related American Association of Clinical Chemistry (now called the Association for Diagnostics & Laboratory Medicine) podcast, author Michelle Stoffel noted that "consumers today really want to have autonomy over their healthcare processes."

This push for autonomy is related to a desire to know more about lab testing and health, and a desire to "have shared decision-making with their medical providers," Stoffel said, and DTC testing satisfies these patient desires, as well as patients' interest in having more control over how and when they experience lab testing.

Yuri Fesko, VP of Medical Affairs at Quest, said in an interview that the pandemic "greatly accelerated consumer-centric healthcare" as patients became used to virtual doctor visits and scrolling on smartphones for health services.

At Quest, patient-initiated testing for infectious diseases requires an order by an authorized healthcare professional who, along with the patient, receives the results, Fesko said. The patient can also opt to consult this physician in addition to their own personal physician. Quest is currently seeing an uptick of patient-initiated comprehensive health panels, he said, which patients say is due in part to delays in scheduling appointments with their own providers.

"Quest has invested in its consumer-initiated test service … largely because we recognized that the dynamics introduced by the pandemic are not going to end," Fesko said.

But not everyone is convinced it's a good idea for patients to order their own lab tests. Some clinical laboratorians and infectious disease doctors voiced concerns that desperate patients can be easily misled. These experts cited the case of patient advocacy for chronic Lyme disease, which soured some in the clinical space on the public's involvement in diagnostics.

Robin Colgrove, an infectious disease physician and professor of medicine at Harvard Medical School, said he has a few patients each week arrive with reams of self-initiated tick-borne infection test results they want interpreted.

Colgrove, who is also chair of the diagnostics committee at the Infectious Disease Society of America, said patients so desperately want to find something that is treatable that they likely misattribute vague symptoms like prolonged fatigue and difficulty concentrating to a prior tick-borne infection. "I'm sympathetic because these people don't feel good, they have honest-to-God, real symptoms," Colgrove said, but their conclusion that what they have is chronic active Lyme disease is not supported by medical data.

These patients go "through a lot of trouble and expense to [obtain results from] labs that almost certainly don't really explain why they don't feel well," Colgrove said. Educating them on pretest probability and the differences between IgG and IgM, or digging into the meaning of the fuzzy lines in western blots takes time and resources "that the medical system just does not have."

That said, not all patient advocacy in Lyme disease is troublesome, as ULCA's Garner has seen another side, too. He's active in Lyme disease research and noted that funders like the Cohen Foundation enable scientists and advocates to work together "to push forward new, clinically approved, validated, accurate diagnostics."

In the hospital

Where self-initiated chronic Lyme testing offers a cautionary tale, the pandemic demonstrates the accelerated pace at which people can get up to speed and start seeking out crucial, potentially lifesaving diagnostics.

But how much can, or should, patients know about the lab-based testing that is used in hospitals? Should makers of highly complex rapid molecular tests for sepsis or AMR advertise directly to patients, or offer them test locator maps akin to Abbott's for the ID Now?

Patient input would be a net win for healthcare, according to some experts, while others think decision-making about testing inside the lab is a line that patients should not cross.

Developers of lab-based tests are increasingly putting their brands in front of patients — through campaigns for cancer screening or disease awareness. For example, Hologic last year became sponsor of the Women's Tennis Association, and Jane Mazur, Hologic's VP of global communications said at the time this was part of a larger campaign to combat pandemic-related shortfalls in women's health that included health equity messaging and celebrity and influencer collaborations.

But novel, and potentially lifesaving, rapid molecular technologies for infectious diseases have a much lower public profile than cancer screening tests, even with efforts at the federal level to spur their adoption.

The FDA's Breakthrough Devices program is meant to bring novel, possibly lifesaving products to market sooner, while the CMS New Technologies Add-on Payment program can reduce the cost of testing for hospitals and labs that adopt these systems. A CMS spokesperson said that as of March 2023 there have been 112 devices and drugs awarded NTAP, a list that includes a rapid molecular sepsis test from T2 Biosystems.

And legislation called Transitional Coverage for Emerging Technologies (TCET) is currently striving to increase coverage for breakthrough technologies and further encourage uptake and outcomes studies.

Nevertheless, adoption of new rapid technologies for sepsis and AMR has been slow, and these diagnostics seem to have struggled to supplant status quo testing in part because of a lack of clinical utility data, which in turn hinges on and reinforces the lack of uptake.

Could patient advocacy be the missing ingredient that breaks this cycle? Is the public ready to know about — and seek out — things like rapid sepsis diagnostics, syndromic meningitis panels, or rapid genetic or phenotypic antimicrobial resistance testing?

Test makers in this space have not yet made patient-facing maps of their installed base, but it is not out of the question. Vanderbilt's Humphries served as chief scientific officer at Accelerate Diagnostics prior to the pandemic and said that offering consumer-facing information on the availability of the firm's rapid phenotypic antimicrobial susceptibility testing was something her team discussed. They ultimately decided against this strategy because at the time it didn't seem that patients had enough understanding about diagnostics.

Oliver Schacht, CEO of rapid molecular diagnostic and AMR detection firm OpGen, said that disclosing his installed base to patients would have the disadvantage of informing competing companies, too. Furthermore, unlike the simple yes/no answers available with rapid at-home tests, rapid molecular sepsis and AMR assays produce complex results that can be challenging to interpret, he said, even for some clinicians.

UCLA's Garner highlighted that rapid diagnostics are only one of the interventions deployed for time-critical infectious diseases. "They don't necessarily affect downstream clinical care like you think they would," he said, though antimicrobial stewardship efforts are starting to make a difference here.

This is partly because, as Humphries said, physicians treating very sick people are often reluctant to de-escalate empiric broad-spectrum antibiotic therapies even when rapid test results indicate they should. "They want to see that the patient is turning the corner first," she said.

Colgrove and Ledeboer further added that patients choosing to go to hospitals using rapid lab-based testing would not be an unalloyed benefit, as oftentimes the old-school, culture-based phenotypic tests, while slower, provide more definitive information about antimicrobial susceptibility.

Craig-Hallum analyst Nowak further said that while DTC marketing in the cancer screening space can be a positive on the ledger for companies like Exact Sciences — and investors do track the return on investment for these campaigns — to his mind, direct marketing of high-complexity lab testing doesn't make sense.

"Let's say you do have sepsis and you are being rushed to the emergency room — you're not going to pull out your phone and see who has an Accelerate system," he said. Nevertheless, "If I were a patient, I would want to go to a lab that had Accelerate Diagnostics. I would want to go where the lab has T2, just because they do offer what would appear to be, on paper, a much better, quicker, faster solution," Nowak added.

Other experts, however, said informing patients about rapid lab-based testing availability could be beneficial.

"Directing patients to places where more advanced tests are offered is a good concept," said David Perlin, chief scientific officer and executive VP at Hackensack Meridian Health Center for Discovery and Innovation.

Perlin also strongly favors providing detailed diagnostic reports to patients, but added, "Patients need to understand the value of the test they are taking, and the potential action implied by a result, and a qualified physician should be engaged at all stages."

U of Wisconsin's Pulia also said a DTC marketing approach for lab-based tests seems generally reasonable. "I do not see any issue with a hospital advertising that they are using advanced diagnostic

technology," he said. But he questioned the quality of any technology that would need to be advertised to patients in order to drive uptake.

"A truly groundbreaking technology that has excellent performance, is feasible to implement, and has been shown to improve outcomes does not need to do any advertising. The medical community would demand it be made available immediately," Pulia said. "I am not aware of any new technology in the ID space that checks all those boxes at present."

Betsy Wonderly Trainor, leader of the diagnostics program at the AMR advocacy group CARB-X, said that patients should be aware of their diagnostic options when seeking care, and should consider the speed, accuracy, and cost of tests that are available to them. That said, the usefulness of a lab-based test locator would probably vary across the different syndromic areas within AMR, she said.

Noting there is no prohibition on DTC advertising for high-complexity tests, FDA's Stenzel said it is judicious for consumers and patients to have more knowledge, education, and information in order to better make decisions. Assuming patients work collaboratively with their physicians and understand that no test is perfect, being able to find out that a particular location has a test that could be really useful to their care is to the patient's benefit.

"Why not know that information?" Stenzel asked.

For patient advocates like Moss and Shader Smith, patients seeking out specific lab-based testing brands may be a long way off — and is predicated on a rising level of outreach and patient education — but it is not impossible.

Shader Smith, whose daughter Mallory died at age 25 of a resistant infection, has addressed AMR issues in presentations to Congress, the White House, and NATO, and she now plans to focus on diagnostics when she speaks to the World AMR Congress in September. She is also joining CARB-X and others in generating support for the PASTEUR Act, newly reintroduced legislation that includes recommendations for improving AMR diagnostics.

To Moss, whose son Nile was 15 when he died from a hospital-acquired MRSA infection, increased sepsis education will drive patients to demand rapid testing.

"That is the only way that you're going to get people asking, 'Don't you have one of those fast tests like they have for COVID?' or, 'Why do we have to wait 12 hours for that result? I'm a parent and I'm watching my child and it's obvious this child cannot breathe — what's causing this respiratory problem?'"

Hospitals are not going to stockpile new technologies without a demand, Moss said, so patients need to start demanding them.

What the world needs now

Guiding newly curious and energized patients will be the responsibility of labs, physicians, advocates, the diagnostics industry, and the media. And there are still many questions, such as, what do patients actually want in diagnostics.

Their desires are sometimes inferred, Humphries said, but not always accurately. For example, clinical studies often presume death is the worst possible disease outcome, but, she said, some research shows that patients care more about paralysis or living in a vegetative state.

Patient satisfaction with infectious disease diagnostics is also understudied, although makers of multiplex syndromic PCR panels often cite patient satisfaction with pathogen identification as a

collateral benefit of including targets for certain uncommon viruses for which there is no specific treatment.

Indeed, "In my experience talking to patients about this, they do have some benefit," Harvard's Colgrove said. Physicians also benefit, he said, because pathogen ID can allow them to conclude the diagnostic workup.

Humphries added that the public's desire for ID is particularly evident in pediatrics. "When parents come in with a severely ill infant, they're not satisfied with just, 'It's not flu.' They want a full respiratory viral panel because now they're familiar with the kind of testing that can be done for their child," she said.

This satisfaction isn't free, however, and several experts said that patients need to be told how much a pathogen ID test that doesn't necessarily impact care will cost them, so that they can make an informed decision.

Patients could also have an increased say in diagnostics if they were considered a stakeholder when clinical labs develop their annual strategic plans, Humphries said.

There is perhaps room for more patient voices in professional societies, too. Colgrove said that while patients are consulted for controversial guidelines like those for Lyme, the IDSA diagnostics committee doesn't routinely include patient perspectives. "Maybe we should, but we haven't historically," he said.

That said, patient-led efforts don't necessarily lead to medically justifiable outcomes, Colgrove again cautioned. In Massachusetts, chronic Lyme advocates won a lobbying effort in 2016 to get long-term antibiotic treatment covered by insurance, despite efforts from IDSA and others against such a plan, he said, adding universal MRSA screening has also failed to show clinical benefit in numerous studies.

Whatever the answer to these questions, going forward Siemens' Nassif said that medtech and diagnostic companies will have to focus more on "measuring and adapting to patient behavior and demand," and then partner with providers — their more traditional customer base — to develop solutions that empower patients to take charge of their healthcare.

Finally, everyone seems to agree that diagnostics education is key to best direct this new patient energy.

"We need to shine a light on the stewardship team, we need to shine a light on what laboratories do, and we need to shine a light on how important the information that labs provide is to the decisions that our clinical colleagues ultimately make," said Ledeboer.

Federal agencies are another source of educational information. CMS consistently engages patients and families in its work, according to a spokesperson, and provides public information on hospital-acquired infections and hospital quality through its Care Compare site and Hospital Star ratings. CDC, meanwhile, supports patient engagement and offers information online about the benefits of patient education and healthcare literacy.

Patient advocates have also taken on education to a remarkable degree — organizing peer support networks, social media outreach, gala balls, concerts, and educational websites — and all assert that public messaging must be both simple and engaging.

OpGen's Schacht quoted a recent GlaxoSmithKline social media post saying that while COVID was a tsunami, AMR is more like global sea level rise due to climate change. Generating interest and energy for action among the public will take compelling messaging, he said, but, "We haven't yet come up with our Greta Thunberg of infectious disease."

Moss concurred, yet also emphasized that strong federal action is still required in order to educate people on sepsis and AMR, akin to what was done during the COVID-19 pandemic.

The public needs to start pounding on doors, she said, and insisting, "This is all preventable. Why aren't you educating us? Who has to die at the top to make this a federal issue?"