Clinical Chemistry 68:9
1121–1127 (2022)

Q&A

Direct-to-Consumer Testing for Routine Purposes

Moderators: Michelle Stoffel [a,b,*] and Dina N. Greene [c,d]; Experts: Stacy G. Beal,[e,f] Peter Foley,[g] Anthony A. Killeen,[h] Hedyeh Shafi,[i] and Enrique Terrazas[j]

Direct-to-consumer (DTC) laboratory testing for routine clinical conditions, such as chronic disease monitoring and sexually transmitted infection (STI) screening, is a rapidly growing market sector. While many of the ethical and logistical issues surrounding genomic DTC testing have previously been discussed in the medical literature, there has been less focus on how routine care DTC testing presents its own opportunities to impact healthcare as well as unique challenges that must be addressed.

The quality and regulatory landscape of DTC testing is complex. DTC testing laboratories are not all equal, nor are all types of medical testing appropriate for DTC marketing. Within the United States, nonmedical wellness and other DTC tests may not be reviewed by the Food and Drug Administration, and consumers may not understand the distinctions between medical and nonmedical tests. Laboratories providing medical-grade DTC testing are subject to CLIA regulations, but some DTC laboratories may not be transparent about CLIA compliance. State-level regulations as to whether DTC testing is permitted and the degree of oversight for laboratories vary as well, adding to the complexity presented to the DTC consumer.

DTC testing is initiated by the consumer rather than the provider. However, DTC test companies often utilize a clinical team to peripherally approve the consumer-initiated orders. This DTC model along with provider-initiated home-collected testing has the potential to disrupt the conventional care paradigm, and creates a need for evidence-based approaches to new models of care. Healthcare providers presented with actionable DTC results at patient visits need guidance on how to evaluate DTC testing, and systems must decide whether to incorporate and document DTC tests into clinical practice. DTC companies may have treatment pathways built into their services, minimizing the need for external providers in some cases. Impacts of DTC testing on healthcare utilization should also be considered. For example, how might practice and costs of care change if patients shift to ordering many of their own tests?

In addition to DTC companies utilizing test collection sites, there are a growing number of self-collection options for tests. The need for asynchronous or virtually guided self-collection is driving innovations in collection devices and analysis methods (e.g., dried blood spot analysis technology), communication tools, and marketing approaches. These tools may evolve to shape patient and provider expectations for the entire laboratory testing landscape in the near future.

DTC testing also has the potential to benefit underserved populations, including the uninsured, the underinsured, those unable to miss work for medical appointments, and those hesitant to pursue testing due to social stigma or language/cultural barriers. Purposeful DTC testing design could increase healthcare access using self-ordered diagnostic tests to initiate clinical care and connect patients with appropriate resources. Ideally, DTC testing would complement traditional medical care and reduce existing barriers to testing access.

[a]Assistant Professor, Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN, USA; [b]Associate CMIO for Laboratory Medicine and Pathology, MHealth Fairview, Minneapolis, MN, USA; [c]Clinical Associate Professor, Department of Laboratory Medicine and Pathology, UW Medicine, Seattle, WA, USA; [d]Associate Laboratory Director, LetsGetChecked Laboratories, Monrovia, CA, USA; [e]Laboratory Director, LetsGetChecked, Monrovia, CA, USA; [f]Associate Professor, Department of Pathology, Immunology, and Laboratory Medicine, University of Florida College of Medicine, Gainesville, FL, USA; [g]Founder and Chief Executive Officer, LetsGetChecked Laboratories, Dublin, Ireland; [h]Ellis S. Benson Professor and Vice-Chair, Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, MN, USA; [i]Medical Director, Clinical Laboratory, Kaiser-Permanente, Los Angeles Medical Center, Los Angeles, CA, USA; [j]Senior Medical Director, Medical Quality, Quest Diagnostics, West Hills, CA, USA.
*Address correspondence to this author at: Department of Laboratory Medicine and Pathology, University of Minnesota, Twin Cities Campus, Mayo Mail Code 609, 420 Delaware St. SE, Minneapolis, MN 55455-0385, USA. Fax: 612-626-2696, E-mail stoff129@umn.edu.
Received May 24, 2022; accepted June 8, 2022.
https://doi.org/10.1093/clinchem/hvac106

What are good use cases for DTC services for routine laboratory testing and/or scenarios where DTC testing should not be used?

Stacy Beal: DTC services should meet certain criteria. First, consumers must be able to obtain their own specimen (if using a self-collected option), and the specimen must be stable during transportation from the home/collection site to the laboratory. For most routine tests, self-collection is a straightforward finger stick for capillary blood. Other specimen types that consumers can self-collect include urine, saliva, and stool. DTC would not be well suited for samples that require an invasive procedure, such as collection of spinal or pleural fluid. However, consumers who want to take charge of their testing and are willing to follow detailed collection instructions are likely able to collect specimens that require certain timing, fasting, storage at a certain temperature, or other specifics. Second, the test results must be relatively easy to interpret. At this time, DTC shouldn't be used for complex diagnoses and couldn't be used for acute care diagnoses (e.g., myocardial infarction).

Anthony Killeen: In most US states, it's legal for people to order their own laboratory testing. Culturally, we place a premium on individual autonomy, and DTC testing is consistent with that principle. Although you asked about routine testing, it's important to be aware that there are DTC testing companies that have received Food and Drug Administration approval for *BRCA1/BRCA2* genetic mutations and for gene variants that determine the rates of metabolism for many drugs. DTC testing in routine clinical chemistry and hematology, such as measurements of cholesterol, glucose, hemoglobin A_{1c} (Hb A_{1c}), and hemoglobin, are commonly available—so too are tests for STIs such as chlamydia, gonorrhea, and human HIV-1. Recently, it became possible for people to have severe acute respiratory syndrome coronavirus 2 testing done on their own initiative, using kits designed for home testing. This was widely adopted by the public; in fact, a few months ago, there were national shortages of such kits. There are a lot of people who are interested in their health and well-being who would like to know their lipid composition, for example, without the wait for a physician office visit. For those people, DTC testing may offer convenience and useful information and is empowering.

Where the role of DTC testing gets less clear is if a test result requires medical follow-up. For example, if a consumer has a positive HIV-1 screen or a positive result for a STI, they need to seek medical attention for treatment. Does the consumer understand the significance of the result they're getting? Does the DTC laboratory or the laboratory director have any responsibility in this matter? These are questions that are important.

Hedyeh Shafi: The coronavirus disease 2019 (COVID-19) pandemic confirms the feasibility and utility of direct-access infectious disease testing in situations in which face-to-face services are limited. In the case of STI testing, a web-based interactive test menu should explain the clinical indication and triage the consumer to the best test. A few pretest questions, such as age and risk factors for testing, can markedly improve pretest probability and test performance. Interpretive results are generally straightforward (e.g., in the case of chlamydia, gonorrhea, and trichomoniasis, positive results require treatment; negative results don't). Provided that additional test information, including real-time consultation if needed, is easily accessible on the DTC testing website, these tests seem safe, effective, and likely beneficial.

Clearly, DTC testing can address many of the obstacles associated with traditional STI testing, such as access, privacy, and the sense of stigma often associated with STI-specific care. Unlike chlamydia, however, some STI tests (e.g., syphilis) often require clinical and medical history for correct interpretation and management, necessitating enhanced decision support and likely more personalized consultation. Organisms for which we have no screening or diagnostic recommendations (e.g., *Ureaplasma* species and *M. hominis*) should not be offered or included in an STI screening panel.

Guidance to ensure an appropriate testing frequency is also important—monthly human papillomavirus testing makes no sense. Although the mathematics of probabilistic diagnostic reasoning (pretest probability, predictive values, likelihood

ratios) can be incorporated into DTC testing decision support, designing functional algorithms that can essentially replace a healthcare professional remain elusive. Until the necessary decision support is available, DTC testing should not be used in situations where the number and significance of pretest variables undermine the automated performance of risk assessment, test selection, and interpretation.

Enrique Terrazas: The COVID-19 pandemic was a landmark moment for consumer testing because it accelerated patients' adoption of virtually enabled healthcare. Due to the pandemic, people were more likely to delay preventive care even with signs of disease, due to fear of COVID-19 illness and difficulty scheduling appointments. Consumer-initiated testing is a great option because it allows individuals to engage the healthcare system with comfort and convenience. Additionally, consumer-initiated testing is a good option for those who want to view and understand their test results before engaging their healthcare practitioner.

There are DTC companies that offer the tests and biometric screenings that a physician would typically order as part of a routine annual physical, such as a complete blood count, comprehensive metabolic panel, urinalysis, and cardiovascular and diabetes risk assessment.

Consumer-initiated testing should not be used in emergency situations. For example, if someone is experiencing rectal bleeding, they should see a healthcare practitioner vs ordering a colorectal screening test.

What are consumer indicators of high-quality DTC testing services to ensure reliable results and support appropriate clinical follow-up?

Stacy Beal: A quality DTC service should be a CLIA-certified and College of American Pathologists or equivalent-accredited laboratory. Consumers should expect results within the time stated and be given the opportunity to discuss their results with the laboratory's medical team. Additional challenges that need to be addressed to ensure the quality of testing include cost, equity of access, and timely communication. Delayed communication of reportable conditions to public health agencies may delay treatment and lead to missed opportunities for partner services, surveillance, and prevention of community transmission.

Peter Foley: Many DTC companies contract laboratories to perform their testing. The DTC company itself is responsible for the consumer interface, but all laboratory testing is overseen by various client laboratories. Assessing for transparency in the performing laboratory is important. Does the DTC company disclose who the performing laboratory is? Does that laboratory specialize in that specimen and testing type? For example, a laboratory that specializes in evaluating capillary specimens would have workflows and validation protocols specifically designed to process such samples. The more a laboratory's overall business model aligns with the DTC company's is an indicator of a well-designed system where all parties are working together to ensure quality is seamless. This model also allows for clinical inquiries to be properly routed to the nursing or clinical laboratory professionals, as appropriate.

Anthony Killeen: I would argue that most consumers don't have the ability to assess the quality of a clinical laboratory's results. It's a US requirement that all laboratory testing for clinical purposes be performed in a CLIA-certified laboratory. So that sets a basic standard. Things I would look for are the turnaround time, the ease of sample collection, mechanism of sample collection (i.e., at home or elsewhere), the presentation of the report, the availability of interpretive comments, and response to consumer questions about result interpretation. Can results be transmitted to the consumer's healthcare provider? Is the test being performed within a larger healthcare system? Does the laboratory have a solid reputation? Is there a feeling that the laboratory is just selling whatever testing it can do with no regard to its medical necessity? I'd feel better going to a DTC laboratory that discouraged unnecessary or wasteful testing.

Enrique Terrazas: Consumers should look for tests that are the same high-quality validated solution offered to providers. They should look for laboratories that are regulated under CLIA. Patients can also look for solutions that offer physician oversight and connection to care, whether that is through a physician consult or access to prescription therapies, when appropriate. As consumer-initiated testing becomes more mainstream, regulators will continue to carefully monitor for quality.

How should healthcare providers approach routine DTC testing when caring for patients with recent and actionable results?

Stacy Beal: Healthcare providers should make sure that the laboratory that provided the test result is legitimate. An easy way is to look for CLIA certification and College of American Pathologists (or equivalent) accreditation. Clinicians can review data surrounding the laboratory result itself. Is the name of the analyte tested clearly stated? Is a reference interval provided? Does the report include at least 2 patient identifiers?

Laboratory results—DTC or not—should always be interpreted in the context of the patient's history and other findings. If a result appears out of place, it is certainly reasonable to repeat the test. One should never make a serious decision based on a single data point, no matter what the origin. However, repeating a full set of tests due to distrust of the DTC system is not necessary. Numerous high-quality laboratories provide DTC services, and some states even require it.

Healthcare providers should applaud patients who take control and responsibility for their healthcare. Patient questions about results should be answered in detail by their providers, and the patient and healthcare provider should work together for decision-making. Outcomes will be best if the patient and provider function as a team.

Peter Foley: Clinicians need to trust their laboratory results, which relies on the clinician trusting their laboratory. Trust is something that must be earned, and it's unsurprising that providers may be wary of results from laboratories, DTC or otherwise, outside of their routine services. Similarly, all laboratories are fallible, and all laboratories have, at some point, reported erroneous results. Clinicians should review the results as they would results transferred from an outside care provider in context of the specific pathology. For example, diagnosis of hypogonadism in cisgender males requires 2 collections with concentrations of testosterone below the reference interval. If a patient brought a previous DTC result to a provider indicating low testosterone, the provider is following guidelines to repeat the testing, but the initial DTC screen was what motivated the patient to seek care. Each case will be different, but the patient should be given the dignity of their experience, and work with the clinician to interpret the results, the need for repeat or additional testing, and the appropriate treatment strategy.

Anthony Killeen: This is a subject of concern. Considering the *BRCA1*/*BRCA2* or the pharmacogenetic test, if a patient comes to their physician with a positive result, does the physician know what to do with it? A negative *BRCA1* result does not exclude the possibility of pathological mutations that weren't tested for in the panel. Would a negative result lead a patient to think they are not going to get breast cancer and therefore don't need regular screening? That would be a bad outcome. So, healthcare providers may need to interpret the test result for a patient, and some of these tests may be outside their area of expertise.

DTC results should, in principle, be treated the same way that results from provider-ordered tests should be treated. A problem I foresee is that DTC results may not be available in the patient's medical record if the test was performed outside of the healthcare system. Documentation of results that inform a treatment decision or lead to further workup is important for medical reasons and possibly to justify further workup. A provider may well decide to repeat the test, not just to verify the result, but also to get a result into the patient's record. I think that providers should also ask why the patient decided to do a DTC test. Are there symptoms or signs that may be relevant to the test that was ordered or may point in an entirely different direction for workup than the route the patient chose in ordering a DTC?

Hedyeh Shafi: If presented with recent, actionable results, one should either initiate treatment (if the diagnosis is straightforward) or pursue repeat and/or additional testing (to confirm the recent DTC test result). Clinical context guides test interpretation and patient management. The popularity of direct access to testing services continues to rise, as does consumer acceptance of placing online orders, using self-collection kits, and viewing online test results. Positive user experience and high rates of follow-up are common. If designed correctly, direct access testing can potentially increase efficiency and perhaps even lower the workload in primary care. It would seem wise for healthcare providers to become familiar with the benefits and limitations of DTC testing services. If queried by patients, one should consider offering a list of high-quality DTC services and appropriate DTC tests (e.g., as recommended by public health or clinical guidelines). Approached together, DTC testing may prove valuable to both patient and provider.

What are ways DTC testing for routine indications could impact the cost of healthcare?

Stacy Beal: DTC laboratory tests are extremely transparent in their cost. Consumers pay up front and know exactly what they are paying for. Unfortunately, the same cannot be said for many other healthcare services.

My academic hospital laboratory accepts home-collected sputum for acid fast bacilli cultures. Samples collected at home are of excellent quality, which has lowered the rate of "quantity not sufficient" rejections. This

means less time spent recollecting poor samples and traveling to and waiting at laboratory collection sites, which likely translates to better value for patients. Although acid fast bacilli cultures are not DTC, this highlights the benefits of at-home collection and giving patients control of their sample collection.

Giving consumers easier access to laboratory tests may improve time to diagnosis for certain diseases. Laboratory testing via DTC can help a patient narrow down a broad differential, allowing a patient to connect with healthcare providers that would be most helpful. I believe that DTC laboratory testing has the power to reduce unnecessary clinic visits and laboratory testing, which leads to savings on overall healthcare costs.

Peter Foley: In European countries, publicly sponsored screening programs have been effective in improving quality-adjusted life years. DTC companies are developing operational systems that can process large volumes of home-collected samples. Marrying these 2 initiatives—widespread population screening and at-home testing—is a powerful way to improve public health initiatives. In the United States, the impact of increased access to screening tests would be dependent on the type of healthcare coverage a person has. For insured patients, this means a decreased cost to insurers. DTC companies can assist healthcare organizations in meeting the screening requirements for Medicare and Medicaid patients. For uninsured and underinsured patients, DTC testing is often more economical than clinic-based testing because the business model for DTC testing differs from conventional healthcare. Thus, the mark-up cost for a particular laboratory test will be derived differently.

Anthony Killeen: I see a risk here in that companies that offer DTC testing and self-testing kits could generate unnecessary worry in the minds of many people that they need to have a test performed or to have a test performed much more frequently than is medically necessary. This could certainly drive up the costs of healthcare, at least in laboratory testing. On the other hand, if a DTC test result leads to earlier diagnosis and treatment, then perhaps there is a cost benefit. I'm not aware of many studies that address the overall financial impact of DTC testing, but it seems like an interesting area for health economists to investigate.

Enrique Terrazas: Right now, most consumer-initiated tests are available out of pocket. This may change over time. However, consumer-initiated testing is designed to meet the needs of individuals who want more visibility into their own health data and access to preventive care at their convenience. This kind of access helps people keep up with preventive care and prevent, delay, or manage chronic diseases that contribute a large cost to the healthcare system.

How will the technology driving DTC services for routine laboratory testing shape the overall laboratory landscape?

Stacy Beal: DTC laboratory tests offer consumers access to laboratory tests and control over their laboratory tests. I foresee that DTC laboratory testing is going to couple well with telehealth visits. Together, patients and clinicians will be able to make evidence- and data-based decisions about treatment or courses of action. I believe that patients will no longer spend a half day going to their physician's office and then waiting for their laboratory draw, and then visiting the clinic again a month later to review results.

Anthony Killeen: The underlying technology for DTC testing in clinical laboratories is no different from that used for traditional patient testing. If the kind of self-testing that we saw during the peaks of the COVID-19 pandemic were to become more common, then there is likely to be an overall increase in laboratory testing, with a growing fraction of it done outside the traditional laboratory setting, such as at home. The kind of technology that would enable this is currently available with kits for continuous glucose monitoring, Hb A_{1c}, cholesterol, and pregnancy. In those cases, the consumer is being supplied with the testing materials themselves, so that's different from a laboratory-based DTC test. Self-testing necessitates simple test methods that can be performed on a drop of blood or a urine sample by users with varying health literacy. Technology that is user-friendly, fast, inexpensive, and can produce reliable results is needed.

Hedyeh Shafi: Internet connectivity has enabled the rapid expansion of online DTC testing services, and miniaturization through microfluids, microelectronics, and nucleic acid amplification technology has made possible numerous self-testing devices. The demand for DTC testing will continue to drive development of noninvasive self-testing and self-collection kits, with the potential to increase testing rates around the globe. Self-collection kits and remote testing have been shown to be highly effective for cervical cancer and colorectal carcinoma screening. DTC testing services should champion the expansion of internet access, and DTC testing web portals should provide reliable health information to improve health literacy. In the future, DTC testing will benefit from analytical harmonization and information technology interoperability, delivering seamless connectivity between electronic health records, DTC testing services, home testing, and wearable monitors.

How can DTC testing for routine indications be leveraged to improve health outcomes?

Stacy Beal: One major advantage to DTC testing is that consumers are in the driver's seat. Health outcomes can certainly be improved by having more patients diagnosed and treated, especially for public health concerns such as respiratory viruses and STIs. Some patients may feel more comfortable revealing their medical and social history to a DTC testing laboratory compared with their usual healthcare provider (or worse, no one at all). Furthermore, consumers decide when and where to obtain the sample for the test. Those who may have otherwise been uncomfortable with certain specimen collections may be much more likely to provide a sample from their own homes. Although one might assume this only applies to genital sites, many patients also dislike the idea of collecting saliva or handing a cup of urine to staff at a laboratory draw station. Being able to be discreet in collecting the sample, packaging it, and mailing it to a laboratory offers comfort. Home-collected samples also allow for repeated sample collections if indicated at certain times (e.g., Hb A_{1c} every 3 months) without requiring the patients to leave their homes. Lower barriers lead to increased adherence, which ultimately leads to better outcomes.

Peter Foley: At-home DTC testing offers a new model for care that compliments current telehealth initiatives. This can be harnessed to improve medical services for specific patient populations. For example, virtual healthcare organizations that specialize in LGBTQ+ medical care would need to partner with a laboratory that can perform routine testing, such as STI screening and hormone analysis. Commercial laboratories have a difficult time creating operational systems that are inclusive for transgender people, and in some areas globally, LGBTQ+ people may be discriminated against in general. Combining services allows for marginalized populations to access medical care in a safe environment, regardless of their location, directly improving health outcomes in people who have been repeatedly underserved.

Anthony Killeen: I think that the use cases have to be clear. What conditions might benefit from testing that could be specifically offered as DTC? Disease screening, where early detection and intervention are beneficial, is a good use case for provider-initiated laboratory testing or DTC. That could include infectious diseases and some cancers. Again, here we get into questions of appropriate follow-up and whether consumers understand the test result and its implications. Another area is monitoring of biomarkers such as cholesterol in patients who are on cholesterol-lowering therapy and who want to monitor their response to treatment between physician office visits. Some people may be afraid that their test results may adversely affect their insurability or their employment and may seek a testing venue because it's not connected to their main healthcare system. Ideally, DTC would provide a service that complements what a healthcare provider does, without incurring unnecessary costs or wasteful testing.

Hedyeh Shafi: For patients receiving anticoagulation therapy, regular hemostasis monitoring is indicated. Some healthcare systems utilize DTC point-of-care testing to allow patients on such therapies to monitor their international normalized ratio values from home and follow preset algorithms for medication adjustments. One challenge that remains is incorporating the results into patients' medical records; advances in technology can significantly improve the continuity of care. Similarly, for other chronic conditions such as diabetes, glycemic control can be monitored by utilizing self-ordering services that can lessen the burden on primary care providers and increase accessibility and satisfaction to patients.

Enrique Terrazas: COVID-19 accelerated patients' adoption of virtually enabled healthcare. People want to interact with healthcare the same way they interact with other services in their life. Life is busy, and in some ways, healthcare is a chore. People want a frictionless experience. Consumer-initiated testing is a response to the need for more cost-effective, high-quality healthcare through expansions of its own offerings and partnerships. I envision DTC testing empowering people, with access to actionable insights from clinical-grade testing when, where, and how they want it. This kind of access helps individuals to maintain preventative care and prevent, delay, or manage chronic diseases.

Nonstandard Abbreviations: DTC, direct-to-consumer; STI, sexually transmitted infection; Hb A_{1c}, hemoglobin A_{1c}; COVID-19, coronavirus disease 2019.

Human Genes: *BRCA1, BRCA2.*

Author Contributions: *All authors confirmed they have contributed to the intellectual content of this paper and have met the following 4 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; (c) final approval of the published article; and (d) agreement to be accountable for all aspects of the article thus ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.*

Authors' Disclosures or Potential Conflicts of Interest: *Upon manuscript submission, all authors completed the author disclosure form. Disclosures and/or potential conflicts of interest:*

Employment or Leadership: M. Stoffel, Association for Pathology Informatics; D.N. Greene, *The Journal of Applied Laboratory Medicine* and EBLM committee, AACC, CAP; A.A. Killeen, ACLPS, AACC; E. Terrazas, Diagnostics Laboratory of Oklahoma LLC.

Consultant or Advisory Role: None declared.
Stock Ownership: P. Foley, LetsGetChecked; E. Terrazas, Quest Diagnostics.
Honoraria: D.N. Greene, Mayo Clinic, ASCP; A.A. Killeen, presentations at the AACC Annual Meeting.
Research Funding: M. Stoffel, University of Minnesota, MHealth Fairview Health System; P. Foley, LetsGetChecked; A.A. Killeen, NIH, CDC, Diasorin, gift to academic department of reagents from Roche for an NIH-funded study; E. Terrazas, Quest Diagnostics.
Expert Testimony: None declared.
Patents: None declared.
Other Remuneration: D.N. Greene, support for attending meetings and/or travel from AACC, ASCP, CAP; A.A. Killeen, royalties or licenses from Springer, Elsevier, support for attending meetings and/or travel from AACC, CAP.