The post-Theranos world

Advances in technology and changes to healthcare during the pandemic may finally realize the vision of patient-centric blood testing espoused by disgraced Theranos CEO Elizabeth Holmes.

On 10 January, Elizabeth Holmes was found guilty of defrauding investors out of hundreds of millions of dollars. The conviction is the culmination of a meteoric fall from grace — just six years ago, she was the iconic CEO heading blood-testing company Theranos, with a >$9 billion valuation and partnerships with the Cleveland Clinic and pharmacy chain Walgreens. Holmes's unique mix of charisma, chutzpah and hucksterism allowed her to intimidate employees, hound whistleblowers, captivate investors, bamboozle executives, beguile journalists, hoodwink legislators, and worst of all mislead patients. But the idea behind her venture remains alluring: bringing medical tests to the masses with just a finger prick of blood.

Of course, Holmes and Theranos never delivered. She habitually lied about the company's Edison miniaturized blood analyzer, which was supposedly running ~240 tests on a disposable cartridge containing 10 µL of blood. And she went to great lengths to conceal the inaccuracy of those tests, all but 12 of which were running on other manufacturers' machines modified to work on diluted samples.

But four years after Theranos's lights went out, advances in blood analysis — including volumetric adsorptive microsampling (VAM), integrated point-of-care (POC) devices, wearables and telemedicine — are reaching an inflection point that could make Holmes's fantasy attainable. And, with the COVID-19 pandemic forcing healthcare providers to adopt a more patient-centric model, the centralized laboratory testing market appears ripe for disruption.

That global market is currently valued at ~$208 billion, with an expected combined annual growth rate of 10%. In the United States, blood tests can cost hundreds of dollars, depending on the state, clinical center or insurer. And for ambulatory testing, it can take days to receive results, delaying changes to treatment plans and forcing patients to make multiple trips to their doctor. As a result, nearly a third of patients getting blood drawn in a doctor's office never follow up on their test results — not to mention the many who cannot afford to travel or miss work for clinical checkups.

This is what motivated Theranos — and motivates firms like Genaltye and Cepheid — to pursue integrated POC blood testing. It can transform acute care in neonatal units, emergency rooms and operating rooms; and it can be rapid, convenient and integrated into outpatient care. Cepheid's GeneXpert system (already in 25,000 locations worldwide) runs up to 20 tests, giving results in 20–120 min; Genalyte's Maverick photonic ring resonance system runs up to 26 tests on a blood drop in 30 mins — fast enough to have results back while the patient waits in the doctor's office.

Any new POC device requires extensive testing in large cohorts of patients under varied conditions to ensure the accuracy of measurements. Theranos egregiously failed to do this, but the entire POC field has struggled with reliability, reproducibility and validation. For wide adoption, devices need ease of use, durability (weeks or longer), portability, affordability and preferably self-calibrating capability.

The source of sample, size of sample, collection procedure and environmental conditions all affect measurements. For example, venous blood contains less oxygen and glucose than capillary blood; and capillary blood from a finger prick can be contaminated with interstitial fluid from damaged tissue. The volume of sample from venipuncture (~7 mL) allows testing of up to 10–100 analytes, whereas 10–250 µL of finger prick or upper-arm capillary blood allows measurement of tens of analytes (too little for certain clinical chemistry analyzers requiring ~100–300 µL samples). Some circulating blood markers are at such vanishingly small levels, they are undetectable; in this respect, liquid biopsy screening for early-stage cancer markers with a low mutant allele fraction remains controversial.

Many new startups — Drawbridge Health, Neoteryx, Tasso, Captainer, PanoHealth, HemaXis and On the Spot — are looking into VAM, a form of the dried blood spot, which is less invasive than a traditional vein draw and doesn't require cold-chain transportation. But this also has drawbacks: sample exposure to humidity and temperature swings can accelerate hemolysis, altering the content of lipids and other analytes and interfering with spectrophotometric assays. Some companies are seeking to overcome this by separating plasma from hematocrit before drying.

All these challenges notwithstanding, penetration of the testing market by POC devices has begun. In the United States, the Moving Health Home coalition, which includes Amazon Care and hospital systems, wants to "expand the services covered in a home-based setting." Continuous glucose monitoring devices for blood (for example, Care Touch and True Metrix) and interstitial fluid (such as Freestyle Libre and Dexcom G6) are being adopted for diabetes. Similarly, at-home testing for health monitoring is being pushed by firms like Thorne and Humanity.

Digital integration is also driving POC adoption. Many at-home systems (for example, LetsGetChecked, Everlywell and 1health) deliver lab results to smart phones; others (such as Ellume) use phone cameras to read and record tests, and some (such as Fulgent Genetics) incorporate telemedicine in follow-up. The secure integration of test data into physician and patient communication interfaces and apps will also help clinical practice integrate and analyze the longitudinal data from wearables.

A final major driver is the pandemic. COVID-19 has massively accelerated the adoption of telemedicine. The US Centers for Medicare & Medicaid Services has announced its Hospitals Without Walls and Acute Hospital Care At Home programs. In Britain, NHS England now recommends using video or a phone for 25% of outpatient appointments. In clinical research, SARS-CoV-2 testing is driving VAM home sampling, increasing remote collection and enabling research groups to conduct large, decentralized population studies — both with traditional clinical markers and increasingly with genomic, proteomic and metabolomic data. As clinical researchers and regulators explore real-world data, at-home blood testing inevitably will increase.

All of this means that at home testing is just too compelling to go away. The star of consumer-centered blood testing is rising just as Elizabeth Holmes's star finally went out. ❐

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