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# After Theranos: Using point-of-care testing to advance measures of health biomarkers in human biology research

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## Abstract

**Objectives:** The rise and fall of the health technology startup Theranos is emblematic of the promise and peril of point-of-care testing (POCT). Instruments that deliver immediate results from minimally invasive samples at the location of collection can provide powerful tools to deliver health data in clinical and public health contexts. Yet, POCT availability is driven largely by market interests, which limits the development of inexpensive tests for diverse health conditions that can be used in resource-limited settings. These constraints, combined with complex regulatory hurdles and substantial ethical challenges, have contributed to the underutilization of POCT in human biology research.

**Methods:** We evaluate current POCT capabilities and limitations, discuss promising applications for POCT devices in resource-limited settings, and discuss the future of POCT.

**Results:** As evidenced by publication trends, POCT platforms have rapidly advanced in recent years, gaining traction among clinicians and health researchers. We highlight POCT devices of potential interest to population-based researchers and present specific examples of POCT applications in human biology research.

**Conclusions:** Several barriers can limit POCT applications, including cost, lack of regulatory approval for non-clinical use, requirements for expensive equipment, and the dearth of validation in remote field conditions. Despite these issues, we see immense potential for emerging POCT technology capable of analyzing new sample types and used in conjunction with increasingly common technology (e.g., smart phones). We argue that the fallout from Theranos may ultimately provide an opportunity to advance POCT, leading to more ethical data collection and novel opportunities in human biology research.

## 1 | INTRODUCTION: POINT OF CARE TESTING IN THE AFTERMATH OF THERANOS

Elizabeth Holmes, founder and CEO of the health technology startup Theranos, became a billionaire and media darling after convincing influential investors that her company had developed revolutionary healthcare devices. These portable, point-of-care testing (POCT) devices could allegedly run hundreds of medical tests using only a few drops of capillary blood, eliminating the need for needles and expensive clinical laboratory

analyses (Holmes et al., 2009). Instead, patients could, in theory, visit wellness centers conveniently located in their local pharmacy or grocery store and receive a rapid, painless set of diagnoses from one machine. An innovative and potentially lucrative idea, the company raised hundreds of millions of dollars (SEC, 2018). However, the devices that Theranos produced never came close to delivering on Holmes' promises and internal whistleblowers revealed widespread fraud, faulty science, and manufactured test results. As a result of these revelations, the company famously imploded in 2015 (Carreyrou, 2019).

The story of Theranos serves as a useful case study, highlighting several issues relevant to the development of POCT today. First, the ability of Theranos to defraud investors for so long illustrates the strong market-driven interests associated with POCT technology. Additionally, the same ethical concerns regarding the accuracy of POCT results and the reliable use of these data to inform medical care decisions exist today. While the Theranos case is likely the most widely known, other cautionary tales of medical technology fraud have emerged in the years since the company collapsed, including the recent allegations of fraud against the microbiome sequencing startup uBiome at the time of this writing (USAO – Northern California, 2021). Still, despite these well publicized cases, the allure of having one device capable of rapidly performing multiple tests from a small amount of biological sample continues to grow in the healthcare field (Bergenstal et al., 2018; Chen et al., 2017; Paknikar et al., 2016; Waltz, 2017).

The focus of several companies (e.g., NanoEntek, Abbott, Quidel Corporation, Abaxis, Roche, Samsung) is still on the development and sale of multi-analyte POCT devices, marketing new "lab-on-a-chip" platforms to care providers and researchers interested in moving away from centralized core laboratories (Jung et al., 2015; Mejía-Salazar et al., 2020; Nguyen et al., 2018; St John & Price, 2014; Waltz, 2017). The goal of lab-on-a-chip technology is to analyze extremely small sample volumes (on the order of picoliters or less) at the location of care, decrease test time and cost, and increase analysis sensitivity (Nguyen et al., 2018). However, the application of these complex POCT devices remains somewhat limited. None are able to operate at the scale envisioned by Theranos and many are not easily portable, still requiring an electrical outlet, technician training, and temperature-controlled environments, which have limited their utility outside of clinical settings (Waltz, 2017).

Despite there not being any "universal" device capable of measuring hundreds of analytes from a small blood sample, there are currently numerous commercially available devices that utilize a range of technological platforms (from paper-based tests to complex self-powered chips) and different sample types (e.g., blood, urine, saliva, etc.) (Jung et al., 2015; Murray & Mace, 2020). Some of these devices are relatively simple and analyze a single biomarker, while others are capable of measuring several different biomarkers. While a great deal of literature focuses on the medical applications of POCT devices (Drain et al., 2014; Engel & Krumeich, 2020; Gous et al., 2018; Herd & Musaad, 2021; Khan et al., 2019; Matthews et al., 2020), the development of high-quality devices is relevant not only for medical providers, but also for human biologists and others studying human health.

Validated POCT devices are useful for collecting repeat measures from a single individual, allowing researchers to more effectively monitor chronic conditions like type 2 diabetes and cardiovascular disease (Bergenstal et al., 2018; Chen et al., 2017; Paknikar et al., 2016). Additionally, POCT facilitates data collection from a large number of individuals at a relatively low cost, thereby supporting population-based health research (Land et al., 2019). The continued development of user-friendly, portable devices to collect health metrics in remote settings with limited medical and laboratory infrastructure therefore has enormous implications for research questions human biologists can ask and the collaborative community partnerships they can form (Madimenos et al., in preparation).

This article is intended to serve as a resource for human biologists, researchers in related disciplines, and healthcare providers interested in better understanding how current (and incipient) POCT is developed and can be used to ethically enhance their work. We focus in particular on the potential uses of POCT in human health research and medical care, particularly in low-resource and remote settings. To that end, we evaluate current POCT capabilities, discuss promising applications for POCT devices for both healthcare providers and human biologists, review the methodology behind POCT development, while also considering the current state of the field and the need for additional POCT validation in non-clinical settings. Importantly, this article addresses a critical gap in the literature by reviewing a wide range of currently available POCT devices, highlighting how this technology has been applied in the field of human biology. We conclude by examining relevant ethical and scientific issues that must be considered by those interested in using POCT during data collection, while also exploring current barriers and opportunities in POCT development. We argue that the fallout from Theranos serves as a call to action, highlighting the necessity of increased POCT oversight and regulation, as well as the need for POCT devices not controlled solely by market interests. The lessons learned from Theranos may consequently

move the field forward in a positive direction, leading to more ethical clinical decisions and human biological research.

## 1.1 | An overview of POCT devices

As the name implies, a POCT device is designed to deliver results at the location where the sample is collected from the individual, providing rapid medically-actionable data that can be used to monitor health patterns and disseminate important information to patients or research study participants (Bissonnette & Bergeron, 2017; Deng & Jiang, 2019; Engel & Krumeich, 2020; Gous et al., 2018). An overarching goal of POCT development is to create simple, portable tests that can be used to measure biomarkers contained within complex samples such as whole blood (Pandey et al., 2018). A diverse range of POCT types exist, including heel ultrasonometry, spirometry, oximeters, blood pressure and heart rate monitors, and physical activity monitors (e.g., increasingly common wearable smart watches and step counters). However, these devices are beyond the scope of this review; instead, we focus on more commonly used biological sample types (e.g., stool, saliva, urine), with a particular emphasis on blood since it is the preferred sample type used to measure many analytes (Larsson et al., 2015; St John & Price, 2014).

Driven largely by the healthcare market, POCT began to take off in the early 1960s with the development of a rapid blood glucose concentration measurement device (Clark Jr & Lyons, 1962; Drain et al., 2014). The development of POCT expanded in the 1970s with the marketing of rapid instrument-free pregnancy tests (Doshi, 1986; Drain et al., 2014), and the field continued to grow through the 1990s with the adoption of POCT clinical analyzers in emergency departments to measure several different electrolytes (Drain et al., 2014; Erickson & Wilding, 1993; Woo et al., 1993). However, POCT development continues to be driven primarily by market demands in high-income countries, incentivizing the creation of profitable POCT designed to address common conditions in these settings (e.g., chronic conditions like diabetes) while neglecting health concerns more common in low-resource areas (e.g., infectious disease, including many parasitic diseases) (Christodouleas et al., 2018; Engel & Krumeich, 2020; Liu et al., 2019). Point of care tests for analytes of interest may consequently not be available to healthcare providers and human biologists working in low-resource communities.

Still, in recent years POCT technology has rapidly advanced, allowing medical providers and health researchers to measure a wide range of biomarkers—associated with both infectious and chronic conditions—using various technological platforms and biological sample types (Bissonnette & Bergeron, 2017; Drain et al., 2014; Jung et al., 2015; Kozel & Burnham-Marusich, 2017; Malekjahani et al., 2019; Mejía-Salazar et al., 2020; Zarei, 2017a, 2017b). Point of care testing can generally be divided into analyses using small, durable devices and equipment-free rapid tests (e.g., paper test strips). Beyond this division, POCT devices can be further sorted into two groups: easily portable handheld devices and slightly larger—but still easily movable—benchtop devices that are essentially miniaturized versions of standard equipment found in core lab facilities (Pandey et al., 2018). Handheld devices offer more mobility and potential applications in remote settings, while benchtop devices are less portable but generally allow researchers more precise calibration and improved quality control (Larsson et al., 2015; Pandey et al., 2018). Larger benchtop devices are also often capable of running more complex diagnostic tests, allowing researchers to run more analyses on a single device (Larsson et al., 2015).

In addition to variation in device size, a range of POCT types are available, varying in degree of complexity. Some of the simplest POCT are paper-based technologies, which have the benefit of being inexpensive and easy to use in remote locations with limited electricity or cold chain capabilities (Jung et al., 2015; Murray & Mace, 2020). There is a long history of using paper-based POCT. In the past, this technology typically relied on an interaction between a target biomarker and a chromogenic probe, leading to chemical reactions (e.g., color changes) visible to the naked eye in relatively few steps (Murray & Mace, 2020; Suntornsuk & Suntornsuk, 2020). More recently, paper POCT has also been paired with electrodes, resulting in electrogenerated chemiluminescence and the ability to detect a much wider array of analytes present at low concentrations (Chinnadayyala et al., 2019). However, many recent POCT devices rely on microfluidics, technology based on very small fluid volumes (on the order of $10^{-9}$–$10^{-18}$ L) (Chen et al., 2019; Jung et al., 2015; Kozel & Burnham-Marusich, 2017; Mejía-Salazar et al., 2020; Nasseri et al., 2018; Pandey et al., 2018; Sri et al., 2019). Microfluidics allows samples and reagents to be moved (e.g., through capillary action), mixed, and reacted in designated microchambers in a highly precise and controlled way (Chen et al., 2019). This technique is used by many of the current lab-on-a-chip POCT devices.

While the proliferation of POCT types has increased the testing options available to researchers and medical providers, the wide array of devices may also make it difficult to select the best test to meet a particular need, especially in limited-resource settings (Kosack et al., 2017).

Given these difficulties, the WHO has developed the ASSURED criteria to help identify appropriate tests for use in non-clinical settings (Kosack et al., 2017). According to this benchmark (Bissonnette & Bergeron, 2017; Chen et al., 2019; Kozel & Burnham-Marusich, 2017; Land et al., 2019; Suntornsuk & Suntornsuk, 2020), POCT should be:

1. Affordable—test prices should not preclude their use in low-resource areas.
2. Sensitive—tests should minimize false negative rates (i.e., the condition or analyte is present, but the test wrongly indicates it is absent), especially when POCT is used in disease screening.
3. Specific—tests should have low false positive rates (i.e., the condition or analyte is absent, but the test wrongly indicates it is present), particularly in cases where disease treatment is expensive or associated with harmful side effects.
4. User-friendly—the test should be easy to perform by minimally trained users and require only a few steps.
5. Rapid and robust—results should be available quickly (e.g., within 30 min) and test accuracy should not be significantly affected by external conditions (e.g., temperature, humidity, lack of refrigeration).
6. Equipment-free—test does not require any specialized or expensive equipment to use effectively. However, it may be more accurate to say "equipment-minimal," since POCT often requires some basic equipment.
7. Deliverable to end-users—tests should be easily accessible to those using them in low-resource settings. Data produced should be standardized and be readily interpretable to care providers and patients.

Adherence to this set of criteria may help inform the design and successful implementation of POCT across diverse settings, helping POCT applications reach their full potential in healthcare and research.

## 1.2 | Applications of POCT

The development and implementation of POCT has the potential to improve research and clinical outcomes at different scales, from individualized medical care to nationally representative population studies.

### 1.2.1 | Clinical uses and healthcare equity

The implementation of POCT within the medical field has the potential to improve healthcare in several ways, including enhancing access to needed medical tests (especially in low-resource regions) and rapidly providing actionable results. The speed of POCT is especially important within the medical field, where the ability to quickly access information needed to make a treatment plan may save lives. Thus, even if a POCT device is slightly less accurate than standard laboratory test, the rapid generation of results may outweigh this limitation. For instance, according to one estimate, a POCT device for malaria with sensitivity and specificity levels of 90% but no laboratory analysis component saves 22% more lives than a standard laboratory test with a 95% sensitivity and specificity level (Kozel & Burnham-Marusich, 2017; Malekjahani et al., 2019).

Additionally, POCT in low-resource areas may improve patient care and save lives through reducing barriers for patients who live far from healthcare providers and/or lack reliable transportation; this allows medical tests to be administered, results to be reviewed, and treatment plans to be decided in a single visit (Bissonnette & Bergeron, 2017; Kozel & Burnham-Marusich, 2017; Larsson et al., 2015). The widespread use of POCT is also expected to increase access to preventive care, such as cancer screening procedures (DeLouize et al., 2021). Finally, widespread POCT access may also help personalize medical care plans, facilitating the collection of several samples from a single individual that can be used to tailor treatment and drive improvements in health (Pandey et al., 2018). For instance, continuous glucose monitoring and recent advances in HbA1c measures have helped providers and diabetic patients more effectively manage this chronic condition (Bergenstal et al., 2018; Chen et al., 2017; Paknikar et al., 2016). But the benefits of POCT use are not limited to medical providers; health research across diverse settings could also be strengthened by POCT use.

### 1.2.2 | Uses within human biology and health research

Standard laboratory biomarker measurement techniques (e.g., enzyme-linked immunosorbent assays, flow cytometry, automated chemistry, and automated hematology performed on traditional samples) generally involve a substantial time and labor investment and rely on specialized equipment. Similarly, certain sampling techniques within human biological research are not applicable in all situations. For example, dried blood spot (DBS) samples represent a useful minimally-invasive sample type, but DBS sample analysis typically requires that existing protocols be adapted and validated for DBS use in a laboratory setting and can only be used so long as the required components remain on the market

(McDade, 2014; Snodgrass et al., in preparation). Biomarker detection reliant on certain sample types and laboratory facilities is consequently of limited use at the location of care, especially in lower-income regions with limited clinical infrastructure (Suntornsuk & Suntornsuk, 2020). Thus, the ability to immediately process collected samples with POCT allows researchers to work more efficiently in remote areas where the storage and shipment of samples may not be possible (Madimenos et al., in preparation). The utilization of POCT can standardize data collection and analysis methods across diverse settings, thereby producing data that can be more reliably compared between sampling sites and among researchers.

Further, since POCT generally rely on biological samples collected using minimally-invasive techniques, researchers may be able to recruit participants who might be hesitant to participate in studies using more invasive sampling techniques (e.g., venous blood draw or tissue sampling). Minimally-invasive sampling techniques also facilitate the collection of data from vulnerable populations (e.g., infants, children, or older adults). For example, one recent study successfully used a Hemocue POCT device to measure hemoglobin in 1650 Indigenous Ecuadorian Shuar of all ages, allowing researchers to assess anemia patterns across all life stages (DeLouize et al., 2021). The ability to quickly produce and share health data may also help researchers build community trust and collaboratively develop interventions through the rapid results dissemination; this combined with more affordable testing methods may lead to increased study sample sizes. Moreover, relatively simple POCT use may facilitate the collection of longitudinal data, allowing researchers to better identify key lifestyle or environmental factors contributing to the development of common health conditions within particular settings. The collection and rapid dissemination of study results is also enhanced through strong collaborations between researchers and participant communities.

### 1.2.3 | Benefits of partnering with participant communities

Population-based POCT studies in the field of human biology are strengthened by partnering with participant communities to ensure that study focus and design align with community priorities and interests (Madimenos et al., in preparation). Simple and rapid POCT should not be used in human health research simply because it is available and low cost; these tests should, instead, be intentionally chosen to address study hypotheses informed by participant feedback, and to help remedy data gaps in health information. Additionally, POCT can offer an opportunity to provide health information directly to communities and, when appropriate, can be shared with individuals, often in conjunction with local health providers or promoters (Broesch et al., 2020). The use of POCT by human biologists consequently offers an important opportunity to enhance ethical data sharing practices, by enabling researchers to rapidly share study results with participants, who have the right to oversee the dissemination of these data.

However, care must be taken to ensure any data shared are interpretable to community members. This too can be addressed through community partnerships. Working with community leaders and local healthcare providers can ensure that information is returned using culturally relevant language and explanations. It is consequently important to seek community feedback from the outset of the project, prior to data collection. This early communication will help researchers develop culturally appropriate methodologies and dissemination strategies designed to address issues of concern identified by community members (Broesch et al., 2020). Additionally, steps can be taken at this stage to establish a plan for how to support participants if their POCT results indicate a potential health concern (e.g., by arranging additional low- or no-cost testing or treatment options with local healthcare providers). The need to offer further testing and care to potentially at-risk participants is especially important in surveillance studies tracking emerging health concerns.

### 1.2.4 | Chronic and infectious disease surveillance

Importantly, standardized POCT methods can be used to address a range of important health issues, including both chronic and infectious global health concerns (Land et al., 2019; Liebert et al., 2013; Mejía-Salazar et al., 2020; Zarei, 2018). For instance, the world is currently experiencing a rapid aging transition that is expected to increase medical testing demands for aging-related health conditions and strain medical care systems, especially in the context of growing socioeconomic inequality (Henderson et al., 2017; Higo & Khan, 2015). This demographic trend, combined with growing healthcare costs in many countries, necessitates the development of more effective methods to diagnose and monitor health conditions associated with aging (e.g., diabetes, cardiovascular disease, cancer) (Bissonnette & Bergeron, 2017; Pandey et al., 2018; D. Xu et al., 2018). Accurate, cost-effective, and simple POCT devices may help address this need, improving the management of age-related chronic conditions while reducing financial and care provider burdens.

Reliable POCT can also play a vital role in the surveillance of infectious diseases. Specifically, POCT can be used in response to public health emergencies (e.g., disease outbreaks), especially in remote areas where traditional medical and lab tests are not possible and that may be especially hard hit by emerging infectious diseases (Bissonnette & Bergeron, 2017; Chen et al., 2019; Kaushik & Mujawar, 2018; Sri et al., 2019). Effective POCT reduces the threat of disease spread to others (e.g., by eliminating the need for multiple patient visits to be tested and receive results), while also allowing care providers to start treatment immediately and reduce transmission (Kozel & Burnham-Marusich, 2017). To take one recent example, the rapid tracking of the SARS-CoV-2 virus was crucial in public health efforts to contain the COVID-19 pandemic, and the development of novel POCT aided in this endeavor (Dinnes et al., 2020). The ongoing pandemic clearly demonstrates the need for novel disease surveillance strategies, as an enhanced ability to track dangerous pathogens will be crucial for preventing another global pandemic. By drawing on a range of diagnostic technologies, POCT may help with these efforts.

## 2 | BASIC DIAGNOSTIC PLATFORM TYPES

While a range of POCT technologies exist, we focus on those that rely on methods drawn from four standard classes of medical diagnostic tests: (a) immunoassays; (b) general chemistry; (c) DNA and RNA assays; and (d) hematology. We concentrate primarily on the potential applications of these test types within population-based health and disease surveillance programs, especially work done in resource-limited settings using minimally-invasive biological sample types such as capillary blood, saliva, and urine.

### 2.1 | Immunoassays

Immunoassays (e.g., enzyme-linked immunosorbent assays and radioimmunoassays) rely on interactions between antibodies and specific antigens if they are present in a biological sample (Jung et al., 2015; Kozel & Burnham-Marusich, 2017; Sun et al., 2014; Suntornsuk & Suntornsuk, 2020). The antibodies used in the analysis are chemically linked to some type of label (e.g., radioactive isotopes or enzymes), which produces a measurable signal (e.g., color change or fluorescence) upon binding with the antigen of interest; this signal can then be measured and the strength of the signal used to determine the concentration of analyte present in the sample (Sri et al., 2019; Suntornsuk & Suntornsuk, 2020). Strengths of immunoassays include high sensitivity and specificity, producing reliable results (Jung et al., 2015; Kozel & Burnham-Marusich, 2017; Suntornsuk & Suntornsuk, 2020). However, running these analyses can be complex and expensive, requiring many steps (e.g., washes and incubation periods) and it may be hours until results are available (Sun et al., 2014).

Still, despite these limitations, the principles behind immunoassays have been successfully used to develop several POCT devices, most commonly using a lateral flow immunoassay (LFIA) platform (Kozel & Burnham-Marusich, 2017; St John & Price, 2014; Sun et al., 2014). Rapid diagnostic tests based on LFIA are very simple, allowing instrument-free analysis—with results visible to the naked eye—and have been used extensively for commercially-available pregnancy tests (Kozel & Burnham-Marusich, 2017; Sun et al., 2014). Due to their simplicity, LFIA tests have been developed for many conditions (e.g., influenza, *Helicobacter pylori*, HIV, Lyme disease, syphilis, hepatitis C, etc.) (Kozel & Burnham-Marusich, 2017). Still, the sensitivity of LFIA tests is generally lower than that of standard clinical immunoassay tests, although efforts are underway to improve test sensitivity (Sun et al., 2014). More complex immunoassays that rely on chip-based electrochemical sensors are also being developed; these assays measure electron flow caused by an enzymatic reaction between the analyte of interest and the detection antibodies coating the sensor surface (Waltz, 2017). However, these more sophisticated assays typically require controlled binding and wash steps, making them difficult to develop and use in low-resource settings (Waltz, 2017).

### 2.2 | General chemistry

Unlike immunoassays, general chemistry tests do not rely on binding between select antigens and antibodies; rather, these tests rely on other chemical principles (e.g., alterations in electrical signals to light absorbance levels). These tests are widely used by clinicians to measure electrolytes (e.g., potassium, chloride, sodium), metabolites (e.g., glucose levels and glycosylated hemoglobin to monitor diabetes), enzymes (e.g., aspartate aminotransferase or alanine aminotransferase indicative of liver function), and proteins (e.g., creatinine indicative of kidney function) (Chen et al., 2017; Martin, 2010; Waltz, 2017). The development of general chemistry POCT is therefore critical to support health testing in low-resource areas.

General chemistry POCT devices that use cartridges designed to perform a select test or group of tests are currently available. For instance, basic general chemistry tests to measure individual electrolytes, urea, and creatinine are performed using test cartridges that are essentially miniaturized versions of the standard electrode technology used in clinical laboratories (Martin, 2010). Limits to this technology include the need for user training to ensure samples are correctly collected and added to the test cartridge. Also, regular quality control checks must be performed to ensure accurate device performance (Martin, 2010). The need for regular quality checks may pose a burden to busy researchers and medical staff, especially since multiple checks may be required to account for a wide range of tests performed on a single device. Still, the ability to perform general chemistry tests outside of a lab setting has enhanced the ability of clinical providers and researchers to identify and treat medical conditions, and also assess population-level health patterns (Liu et al., 2019; Shrivastava et al., 2020; St John & Price, 2014).

## 2.3 | DNA and RNA assays

Given that nucleic acids are present in all pathogens, the detection of these molecules is a very sensitive and specific way to identify specific diseases (Jung et al., 2015; Kozel & Burnham-Marusich, 2017). Genomic technology has advanced, allowing researchers and clinicians to amplify isolated nucleic acid segments for use in diagnosis. However, standard clinical nucleic acid detection methods are very complicated, requiring expertly trained lab technicians, expensive equipment, and several time-consuming steps (Jung et al., 2015; Suntornsuk & Suntornsuk, 2020).

In response to these challenges, promising POCT technology using microfluidics is being developed that miniaturizes and integrates complex steps (i.e., cell lysis, purification, amplification, and nucleic acid detection) within a single chip (Jung et al., 2015; Kozel & Burnham-Marusich, 2017). Many of these emerging POCT technologies also use special techniques (e.g., loop-mediated isothermal amplification) that greatly simplify the testing process (e.g., by removing the need for thermocycling and stabilizing reagents) (Jung et al., 2015; Kozel & Burnham-Marusich, 2017). However, additional work is needed. Nucleic acid POCT platforms still require more extensive personnel training, a greater number of reagents, and longer test times than other POCT methods (Jung et al., 2015). In addition, these devices have high power requirements and must be designed with extensive computing capabilities to process the raw data and produce interpretable results (Jung et al., 2015). Nucleic acid POCT may therefore be difficult to transport and reliably use in low-resource settings. Still, progress has been made in the development of non-clinical POCT devices, leading to the availability of more sensitive diagnostic tests based on novel technologies (e.g., CRISPR) and panels capable of running several tests simultaneously (Kozel & Burnham-Marusich, 2017; van Dongen et al., 2020; Xu et al., 2020).

## 2.4 | Hematology

Hematological tests can be used to explore the causes, prognosis, and treatment of blood-related disorders such as anemia. The commercialization of hematological tests dates to the 1940s with the development of the spectrophotometer. This device functions by sending beams of light through a blood sample and determining how much light is absorbed by the sample, allowing the concentration of molecules (e.g., hemoglobin or glucose) in the sample to be inferred from the amount of light absorption (Vembadi et al., 2019). Another hematological technique, called cytometry, is also commonly used. Cytometry is based on counting blood cells, often by measuring sample electrical conductivity: the greater the number of cells, the lower the conductivity (Vembadi et al., 2019; Waltz, 2017). Like general chemistry tests, hematological tests—such as complete blood counts to determine the proportion of different blood cells present in a sample—are commonly ordered by medical providers. Expanding access to these important tests with POCT is consequently needed (Bransky et al., 2021; U. Hassan et al., 2015; Jung et al., 2015).

A strength of hematology POCT is that it generally requires a smaller blood sample and can use less invasive collection techniques (e.g., finger or heel pricks) (Larsson et al., 2015). These devices have been successfully used in a variety of settings. For example, POCT devices capable of measuring hemoglobin levels have allowed researchers and healthcare providers to better test for anemia in both low-resource settings (where nutritional deficiencies may be prevalent) and high-income countries (e.g., during blood donation screenings) (Nass et al., 2020). Still, many available POCT devices are not capable of measuring all relevant parameters (e.g., quantities of different blood cell types), while more powerful benchtop hematology POCT devices typically require extensive maintenance and frequent calibration by trained technicians (Bransky et al., 2021). This limits benchtop POCT utility and has led to efforts to develop portable devices capable of running more complex hematological tests, including complete blood counts (Bransky et al., 2021). While some

progress has been made on this front, additional work is needed to ensure emerging hematological techniques can be reliably used in non-clinical settings.

## 3 | TRENDS IN POCT APPLICATIONS

Building upon standard medical diagnostic testing technology, POCT platforms have rapidly advanced in recent years, gaining more traction in the medical field and among health researchers. For example, a recent Web of Science search using the search terms "point of care test" and "point of care device" indicated that 2896 articles written in English have been published between 2000 and 2020, with a steady increase in the number of publications per year (Figure 1). Interestingly, the funding sources of the studies identified in this Web of Science search varied greatly (Figure 2). Most studies appear to have been funded by American and Chinese institutions, although some studies were also supported by European funders. Despite this publication attention, the emergence of novel POCT technologies has raised questions about how these devices should be regulated for use by medical professionals and health researchers working outside of a clinical setting.

### 3.1 | The challenges of POCT regulation

Since POCT are intended to produce clinically accurate, actionable medical results, they are often regulated at the national level in high-income countries. The regulation of POCT is dependent on several factors, including country and setting of intended use. For example, in the United States, regulation is generally determined by whether the test is performed in a lab. In 1988, Congress passed the Clinical Laboratory Improvement Amendments (CLIA) program, which dictates that the Centers for Medicare & Medicaid Services (CMS) should regulate all in-house laboratory diagnostic testing performed on humans to ensure reliable and accurate diagnostic results (Camacho-Ryan & Bertholf, 2016; CMS, 2021). Labs performing these tests are required to obtain CLIA certification—demonstrating their adherence to the guidelines laid out by the CLIA program—and remain CLIA compliant to continue their work (CMS, 2021). These CLIA compliant labs may develop and perform diagnostic tests in-house, but these tests may not be commercially sold or used in other laboratories (CMS, 2021).

In order for POCT to be used clinically outside of a CLIA certified lab, additional approvals must be obtained. Specifically, device manufacturers must seek clearance from the Food and Drug Administration (FDA), which regulates health testing devices sold and used outside of a CLIA certified lab under the Federal Food, Drug, and Cosmetic Act (FFDCA) to ensure that the devices are safe and effective (CMS, 2021). To obtain a CLIA waiver, POCT devices must be simple and accurate (i.e., with minimal risk of an incorrect result) (CMS, 2019; Kozel & Burnham-Marusich, 2017). Test complexity is key in determining whether it can be waived from CLIA restrictions, such that tests the FDA deems to be moderately or highly complex are restricted to laboratory use (CDC, 2018; Kozel & Burnham-Marusich, 2017).

Complexity classification is based on the degree of expertise required to perform the test (including level of test output interpretation required), how numerous and challenging the test steps are, the need for reagent preparation and quality control, and how difficult it is to calibrate and maintain testing equipment (CDC, 2018;

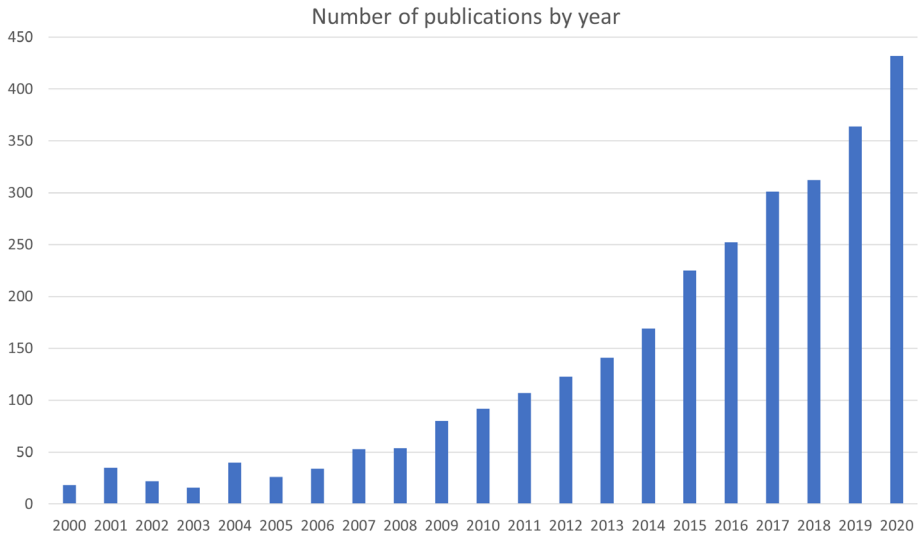



**FIGURE 1** The number of published articles written in English per year (2000–2020) based on a Web of Science Core Collection search using the topic search terms "point of care test" and "point of care device." The search was performed on May 8th, 2021 ($n = 2896$)

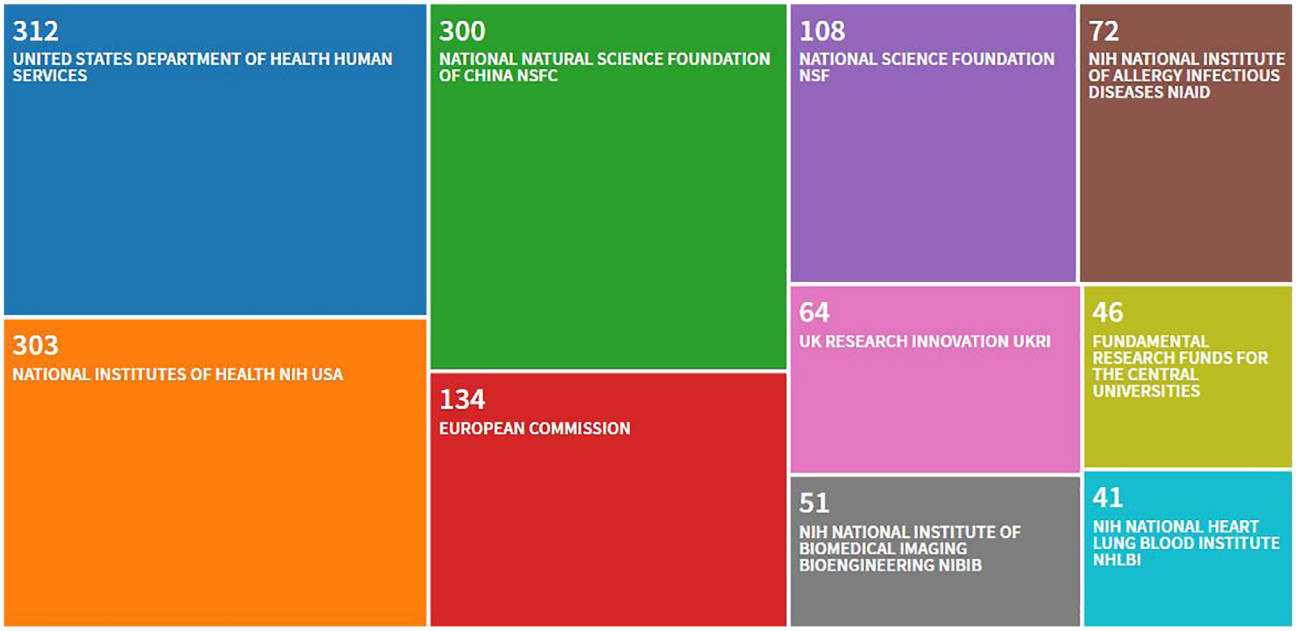



**FIGURE 2** The top 10 funding sources for 2896 articles on point of care tests/devices published between 2000 and 2020. The number of articles listing the funding source is indicated in the top left corner of each box. Image created using Web of Science search results analysis capabilities on May 8th, 2021

Kozel & Burnham-Marusich, 2017). Based on these criteria, several simple POCT devices have received a CLIA-waiver, including devices cleared by the FDA for home use (e.g., to help diabetic patients monitor blood glucose levels) (Bissonnette & Bergeron, 2017; FDA, 2021). These CLIA-waived devices are also useful to human biologists, allowing them to measure a range of biomarkers (e.g., measures of cardiometabolic health) in the field.

A similar regulatory system exists in the European Union. In accordance with the Medical Devices Directive (93/42/EEC) or In Vitro Diagnostic Devices Directive (98/79/EC), manufacturers seeking approval for POCT devices must demonstrate that the device meets EU standards related to test performance, accuracy, and safety (Bissonnette & Bergeron, 2017; Larsson et al., 2015). Devices meeting EU regulatory requirements receive a CE marking, allowing for the commercialization of the test across all EU member countries (Bissonnette & Bergeron, 2017). Importantly, POCT classification is not always consistent between the United States and EU, allowing for the sale and use of devices in the EU that have not been cleared for use by the FDA, partly due to the cost, time, and high level of regulation associated with test approval in the United States (Genzen, 2019). Clear regulatory guidelines are not evident in many other countries (Khan et al., 2019), although international laboratories may apply for CLIA certification in some cases (CMS, 2020a). Efforts are also underway in some low-resource care facilities to develop regulatory standards based on recommendations from organizations like Joint Commission International (Khan et al., 2019).

### 3.2 | Select examples of POCT currently available or in advanced stages of development

Many POCT platforms are commercially available or are very close to entering the market (Table 1), although test availability sometimes varies by region. These tests draw on the standard classes of medical diagnostic techniques discussed above, and some have combined multiple diagnostic types using novel technologies. It should be noted that the devices presented in Table 1 represent only a fraction of the POCT in development or currently available.

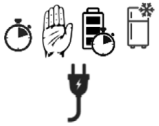
## 4 | POINT OF CARE DEVICES WITHIN HUMAN BIOLOGY: AN UNMET NEED

Despite the wide array of devices available, the application of this emerging technology has yet to be fully realized in the field of human biology. To examine how POCT has been used by human biologists, literature searches of the terms "point of care," "rapid test," and

**TABLE 1** Examples of a small fraction of point-of-care devices either currently available (not underlined) or in advanced stages of development (underlined) at the time of publication

| Device name | Company | Sample type | Diagnostic type(s) | Cost[a] | Field friendly[b] | Key analytes | ASSURED criteria[c] |
|---|---|---|---|---|---|---|---|
| i-STAT*†❖ | Abbot | 17–65 µl whole blood | Immunoassay, General Chemistry, Hematology | Device: $$$-$$$$ Cartridge: $$-$$$ |  | Hemoglobin, glucose, creatinine, electrolytes (sodium, potassium, chloride), cardiac markers (troponin I, BNP, CK-MB), blood gases (pH, $sO_2$, $PO_2$) | **S**URED |
| rHEALTH | DMI | 5–10 µl whole blood | General Chemistry, Hematology | |  | Currently developing testing for: vital signs | |
| Maverick Detection System | Genalyte | 5 µl serum or 10 µl whole blood | Immunoassay | |  | Antinuclear antibodies, SARS-CoV-2 antigens, MERS antigens, influenza antigens | |
| Minicare I-20❖ | Philips | Drop of capillary blood | Immunoassay | Device: $$$$ |  | Troponin I | **S**U**R** |
| Owlstone ReCIVA Breath Sampler❖ | Owlstone | Exhaled breath | General Chemistry | |  | Lung cancer, respiratory disease, and liver disease detection, metabolism markers, environmental exposures | U |
| Spartan Cube❖ | Spartan Bioscience | Saliva, nasal swab, water | DNA/RNA Assay | Device: $$$$ |  | Legionella bacteria in water, CYP2c19 mutation, and SARS-CoV-2 | **S**UD |
| LightDeck Analyzer | LightDeck Diagnostics | Capillary volumes of whole blood, serum, plasma | Immunoassay, Hematology | |  | Currently developing: SARS-CoV-2 Ag/Ab, hormones (thyroid, male and female reproductive hormones), Immune factors (markers of infection), cardiac markers related to heart attacks, veterinary diagnostics, water testing (toxins associated with algae bloom) | **S**U**R**D |
| Biosensia Rapiplex System | Kypha | Whole blood, serum, plasma, milk, urine, saliva (20–100 µl) | Immunoassay | |  | Currently developing: Cardiac markers (C-reactive protein [CRP] and myoglobin), drug screening (cocaine and amphetamines), inflammatory proteins | URE |
| LiDia-SEQ | DNA Electronics | 10 mL vacutainer with whole blood | DNA/RNA Assay | | | Bloodstream infection and antibacterial resistance to aid in sepsis diagnosis | |

**TABLE 1** (Continued)

| Device name | Company | Sample type | Diagnostic type(s) | Cost[a] | Field friendly[b] | Key analytes | ASSURED criteria[c] |
|---|---|---|---|---|---|---|---|
| FREND System❖ | NanoEntek | 35–70 µl of plasma or serum and nasopharyngeal swab | Immunoassay | Device: $$$$ Cartridge: $$ |  | Testosterone, vitamin D, FLU A&B, thyroid hormones (TSH, free T4, total T3), COVID-19 (total Ab, IgG/IgM duo, Ag) | SSUD |
| i-CHROMA II❖ | Boditech Med INC | Whole blood, serum, plasma, nasopharyngeal swab, nasal swab | Immunoassay | Device: $$$ |  | HbA1c, thyroid hormones (TSH, T3, T4), reproductive hormones (FSH, progesterone, LH, testosterone), immune (CRP, HIV Ag/Ab, strep A, influenza A + B), ferritin, vitamin D, cortisol | SSUED |
| Immunocard STAT! *❖† | Meridian Bioscience | Whole blood, serum, plasma, stool, urine, throat swab, nasal swab, nasopharyngeal swab | Immunoassay | Device: $$-$$$ |  | *Cryptosporidium parvum*, *Giardia lamblia*; *Helicobacter pylori*, *Campylobacter*, *E. coli*, mononucleosis, rotavirus, strep A, hCG | ASSUED |
| Triage MeterPro*❖† | Quidel | Plasma or whole blood in EDTA | Immunoassay | Device: $$$ Cartridge: $$-$$$ |  | Creatine kinase MB, myoglobin, troponin I, B-type natriuretic peptide (BNP) | SSUED |
| cobas Liat PCR System*❖ | Roche Diagnostics | Nasopharyngeal swab, throat swab and stool | DNA/RNA Assay | Device: $$$$ Cartridge: $$$ |  | SARS-CoV-2, influenza A + B, Respiratory Syncytial Virus (RSV), strep A, *C. difficile* | SSUD |
| RapiDx | Sandia National Laboratories | One drop of blood or saliva | Immunoassay | |  | Protein signatures of various pathogens and toxins. | |
| nanoFluidic Processor & Molecular Diagnostic (MolDx) product | Midiagnostics | Small sample of whole blood or nasal swab | DNA/RNA Assay | |  | Currently developing testing for: respiratory infections, chemo drug monitoring, and antimicrobial resistance | |
| Siemens DCA Vantage Analyzer*❖ | Siemens Healthineers | Whole blood (1 µl) and urine (40 µl) | Immunoassay | Device: $$$ Cartridge: $$ |  | HbA1c, microalbumin/creatinine ratio | SSUD |
| Piccolo Xpress*❖ | Abbott | Whole blood, serum or plasma | General Chemistry | Device: $$$$ Cartridge: $$ |  | Blood lipids (total cholesterol, HDL, triglycerides, LDL, VLDL, total chol/HDL ratio), metabolic (creatinine, calcium, sodium, potassium, glucose) | SSUED |
| LABGEO❖ | Samsung Corporation | Whole blood, or plasma (70-500 µl) | Immunoassay | Device: $$$$ |  | Troponin I, TSH, beta-hCG, D-dimer, procalcitonin, NT-proBNP | SSUED |

(Continues)

TABLE 1 (Continued)

| Device name | Company | Sample type | Diagnostic type(s) | Cost[a] | Field friendly[b] | Key analytes | ASSURED criteria[c] |
|---|---|---|---|---|---|---|---|
| GeneXpert® Omni Cepheid | Cepheid | Sputum or nasopharyngeal swab | DNA/RNA Assay | Device: $$$-$$$$ Cartridge: $$ |  | *Mycobacterium tuberculosis*/ rifampicin, SARS-CoV-2 | SUD |
| BD MAX System*† | BD | Stool, nasal swab, vaginal swab, urine | DNA/RNA Assay | Device: $$$$ Cartridge: $$-$$$ |  | SARS-CoV-2, enteric bacteria (*Salmonella*, *Shigella*, *Campylobacter*, *Shigella dysenteriae*), women's health (*Trichomonas vaginalis*, bacterial vaginosis, vulvovaginal candidiasis, Group B Streptococcus), STI (*Chlamydia trachomatis*, *Neisseria gonorrhoeae*, and *Trichomonas vaginalis*), enteric parasites (giardia, cryptosporidium, and *Entamoeba histolytica*), enteric viruses (norovirus GI & GII, rotavirus A, adenovirus F40/41, sapovirus, human astrovirus) *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Staphylococcus aureus* | SS |
| ID Now (formally Alere i platform)* | Abbott | Nasal, nasopharyngeal and throat swabs | DNA/RNA Assay | Device: $$$$ Cartridge: $$ $ |  | Influenza A + B, strep A, RSV, SARS-CoV-2 | SSURD |
| CardioChek*❖ | PTS Diagnostics | Fingerstick sampling and small sample size (40 µl) | Hematology | Device: $$-$$$ Cartridge: $-$$ |  | Blood lipids (total cholesterol, HDL cholesterol, triglyceride levels, LDL cholesterol), glucose | ASSURED |
| Hemocue Hb 201+*❖ | HemoCue | Capillary, venous or arterial whole blood (10 µl) | Hematology | Device: $$ Cartridge: $$ |  | Total hemoglobin | ASSURED |
| A1CNOW*❖ | PTS Diagnostics | 5 µl of whole blood | Immunoassay, General Chemistry | Device: $ Cartridge: $ |  | HbA1C | ASSURED |
| CHOLESTECH LDX ANALYZER*❖ | Abbott | Fingerstick sampling and small sample size (40 µl) | Immunoassay, General Chemistry | Device: $$-$$$ Cartridge: $-$$ |  | Blood lipids (total cholesterol, HDL cholesterol, triglyceride levels, LDL cholesterol), glucose | ASSURED |

**TABLE 1** (Continued)

| Device name | Company | Sample type | Diagnostic type(s) | Cost[a] | Field friendly[b] | Key analytes | ASSURED criteria[c] |
|---|---|---|---|---|---|---|---|
| ASSURE readers❖ | MP Biomedicals LLC | Serum, plasma, whole blood, whole blood (capillary or venous) | Immunoassay | |  | Dengue Ab/Ag, HCV antibody, HIV Rapid, HAV IgM Rapid, HEV IgM, *H. pylori*, tuberculosis | SSUR |
| Sofia*†❖ | Quidel | Whole blood, serum, urine, throat swab, nasal swab, nasopharyngeal aspirate/wash or swab | Immunoassay | Device: $$$ Cartridge: $$ |  | Strep A, SARS antigen, *S. pneumoniae*, RSV, *Legionella*, influenza A + B, hCG, Lyme, Lyme +, flu+SARS, vitamin D | SSURED |

*Note*: The devices listed here are capable of running several test types (although not the hundreds of tests envisioned by Theranos) or are single analyte tests of particular interest to human biologists. Regulatory approval is indicated by symbol: * = CLIA-waived, † = regulated by CLIA, ❖ = test has EU CE mark (note that some multi-analyte devices have more than one designation).

[a]Cost (based on available information) is broken into two categories: Approximate device cost and relative cost per test/cartridge. $ = $0–$99, $$ = $100–$999, $$$ = $1000–$4999, $$$$ = $5000+.

[b]Field friendliness of the POCT is indicated by icons:  indicates refrigeration is required (e.g., for the sample or test cartridge);  indicates the test is performed in 30 minutes or less;  indicates the device is handheld or easily portable;  indicates electrical outlets are required to run the device;  indicates the device is fully battery powered;  indicates the device may be run on battery power for a short period of time.  indicates the device is very durable (e.g., to travel, heat, humidity, cold).

[c]ASSURED criteria met by each device are indicated, based on published device information. Blank entries indicate that the POCT either did not meet ASSURED specifications or there was not enough information available to determine whether the criteria were met. To distinguish between "sensitive" (the first "S" in the acronym) and "specific" (the second "S"), an unbolded single "S" stands for "sensitive," while a bolded single "S" stands for "specific." A cutoff point of 85% was used to classify tests as sensitive or specific.

"rapid diagnostic test" were performed. Additional searches were performed for the terms "capillary," "finger prick," and "portable device"; articles including these terms were examined to ensure they were relevant to POCT. Literature searches were performed using Google Scholar, PubMed, Embase, and CINAHL and were restricted to the years 2000–2021. Many relevant articles were identified, but it should be noted that some pertinent POCT devices may not have been included in these databases, including recently developed technology that has not yet undergone the peer-review process for publication.

These literature searches focused on anthropological journals (e.g., *American Journal of Human Biology*, *Annals of Human Biology*, *American Journal of Physical Anthropology*, *Human Biology*, *Journal of Human Evolution*, and *Evolutionary Anthropology*), global and public health journals (e.g., *The Lancet*, *Annals of Global Health*, *Journal of Global Health*, *Public Health*), and additional journals publishing articles from a broad range of disciplines (e.g., *PLoS ONE*, *Nutrients*, *Breastfeeding Medicine*, and *Point of Care*). The articles identified by these searches shared some common themes, indicating certain devices are favored by anthropologists and health researchers within specific study contexts (Table 2).

Still, despite the growing use of certain POCT by human biologists, more work is needed to establish the utility of these tests in non-clinical contexts (Ceponis & Robins, 2021). For instance, we are aware of very few published results of formal testing under field conditions. The development of POCT devices occurs in biomedical laboratories, with validation tests occurring in these very controlled settings. It is consequently unclear how many of these tests perform in a non-clinical, field setting. Human biology fieldwork often occurs in settings where ambient temperature and humidity levels vary unpredictably from lab settings. This may require researchers to modify data collection protocols in response to local conditions (e.g., keeping test strips and cartridges in their original packaging and carefully stored until the time of immediate use to protect them from humidity and extreme temperatures). Samples to be analyzed in labs are also often shipped from the collection site and may experience temperature fluctuations associated with storage during transport. More work is consequently needed to assess how well commercially available POCT perform in field settings in comparison to use in controlled laboratory testing environments.

Relevant factors that should be considered by human biologists interested in using POCT devices in the field include regulatory approval status, power source, whether refrigeration is needed, test speed, device portability (e.g., size) and durability (e.g., resistance to extreme temperatures, humidity, and travel), test result accuracy, cost of the device and each individual test, and any special test requirements or recommendations (e.g., requiring special equipment like a vortex mixer to process the sample for analysis). Another consideration is instrument type. Companies continually produce novel POCT devices and phase out old models, potentially leading to confusion when ordering compatible test cartridges. It can also be unclear whether the performance of different device models differs significantly, especially in a field setting. Overall, additional work assessing POCT utility in field conditions and publishing these findings will advance the field, helping other researchers determine whether these data collection methods can be reliably used at their particular field site. Without further testing under relevant non-clinical conditions, the potential benefits of these devices in human biology research cannot be realized.

Beyond testing existing POCT in field conditions, many biomarkers of interest to human biologists have not yet been developed or are not commercially available to researchers without a medical license or CLIA certified laboratory. More work is therefore needed to develop POCT directly applicable to central questions in human biology, including tests designed to measure not only disease markers but that can also provide reliable data on individual health and underlying physiology (e.g., biomarkers of reproductive function). The development of POCT occurs not only at for-profit companies, but also occasionally within academic laboratories (Heidt et al., 2020; Nguyen et al., 2020). The advancement of tests relevant to human biological research could therefore be enhanced by stronger collaborations between human biologists and researchers in other fields working to develop needed POCT.

Still, promising POCT often does not make it beyond preliminary inception and testing due to weak connections between academia and industry, leading to insufficient investment, inadequate marketing, and poor supply chain management (Heidt et al., 2020; Nguyen et al., 2020). Multidisciplinary teams are consequently needed from the outset of development to successfully commercialize novel POCT (Heidt et al., 2020). Recognizing these gaps, efforts have recently been made to fund innovative POCT research and successfully bring tests to market, including new funding streams available from the NIH RADX program to support COVID-19 rapid test creation (NIH, 2020). Cumulatively, the continued development of POCT measuring novel analytes will support future human biology research exploring how lifestyle and environmental conditions shape health patterns in diverse populations and understudied contexts (e.g., low-resource areas). The use of POCT can also increase the

**TABLE 2** Selected applications of commercially available POCT in human biology research. A description of the study focus, sample type collected, device/test used, analyte(s) measured, and relevant references are provided

| POCT device | Sample type | Analytes measured | Research application | References |
|---|---|---|---|---|
| Hemocue Hb 201+ | Capillary blood | Hemoglobin | Hemoglobin and anemia assessment and treatment | Bai et al., 2018; *Christensen et al., 2014*; *DeLouize et al., 2021*; **Demirchyan et al., 2016**; **Didzun et al., 2019**; *Dorsey & Thompson, 2020*; Ernawati et al., 2021; *Goetz & Valeggia, 2017*; **Hailu et al., 2019**; **Kejo et al., 2018**; *Mattison et al., 2015*; *McDade, 2014*; **Mendes et al., 2020**; *Stibbard-Hawkes et al., 2020*; *Wander et al., 2017* |
| HemoCue B-Glucose 201+ | Capillary blood | Fasting glucose | Cardiovascular health and metabolic disease assessment | *Christensen et al., 2014*; Duboz et al., 2017; **Lee et al., 2021**; **Msemo et al., 2018**; **Mwanri et al., 2014**; *Tavares et al., 2003* |
| CardioChek | Capillary blood | Blood lipids (total cholesterol, HDL cholesterol, triglyceride levels, LDL cholesterol), glucose | Cardiovascular health and metabolic disease assessment | *Cepon-Robins, 2021*; *Kuzawa et al., 2019*; *Lagranja et al., 2015*; **Lartey et al., 2018**; *Liebert et al., 2013*; *McClure et al., 2010*; *McDade, 2014*; **Pengpid & Peltzer, 2020**; *Raichlen et al., 2017*; *Sanchez-Samaniego et al., 2021*; **Zhang et al., 2015** |
| sAA Biosensor Prototype | Saliva | Salivary α-amylase | Physiological and psychological stress response | *DeCaro, 2016*; *Robles et al., 2013*; Shetty et al., 2011 |
| MIRIS Human Milk Analyzer (HMA) | Breast milk | Milk concentration of fat, lactose, and protein | Breast milk composition, infant energy in-take | Be'er et al., 2020; **Bruun et al., 2018**; Bzikowska-Jura et al., 2018; **de Fluiter et al., 2021**; **Dritsakou et al., 2017**; **He et al., 2014**; **Miller et al., 2013**; **Petrullo et al., 2019**; Sahin et al., 2020; Thakkar et al., 2019 |
| i-STAT | Whole blood and capillary blood | Hemoglobin, glucose, electrolytes, cardiac markers, blood gases | Emergency response health assessments and treatment, clinical trials | **Dainton et al., 2018** ; **Marr et al., 2021**; Shephard et al., 2011; Shephard et al., 2014; **Vanholder et al., 2010**; **Wesson et al., 2019** |

(Continues)

**TABLE 2** (Continued)

| POCT device | Sample type | Analytes measured | Research application | References |
|---|---|---|---|---|
| iChroma II | Whole blood, serum, plasma, and stool | Thyroid hormones(TSH, T3, T4), reproductive hormones (P4, testosterone, LH, FSH, immune markers (CRP), cortisol, ferritin, vitamin D | Emergency medicine assessment, tuberculosis screening, health assessment for people with pre-existing conditions | **Al-asady & Al-dulaimy, 2019** ; **Daag et al., 2021**; **Deng et al., 2018**; **Manikandan et al., 2019**; **Yoon et al., 2017** |
| Cholestech LDX Analyzer | Capillary blood | Blood lipids (total cholesterol, HDL cholesterol, triglyceride levels, LDL cholesterol), glucose | Cardiovascular health and metabolic disease assessment, lifestyle intervention assessment | **Brogan et al., 2014** ; *Buchan et al., 2017*; *Duncan et al., 2013*; **Farag et al., 2010**; *Horwitz et al., 2009*; Jen et al., 2017; **Marrero et al., 2016**; *Martins et al., 2013*; *McDade, 2014*; *Mota et al., 2013*; Shephard et al., 2006 |
| Immunocard STAT | Whole blood, serum, plasma, stool, urine, nasal, throat and nasopharyngeal swab | *H. pylori*, *Campylobacter*, rotavirus, *E. coli*, cryptosporidium, giardia, mononucleosis, strep A, flu A + B, hCG | Parasite, toxin and bacteria testing and treatment, primate health assessments | **Dado et al., 2012** ; **Deankanob et al., 2006**; **Eassa et al., 2017**; **El-Malky et al., 2018**; **Hatchette, 2009**; **Helen et al., 2015**; **Kalema-Zikusoka et al., 2018**; **Mellingen et al., 2010**; **Nygård et al., 2006**; **Ope et al., 2017**; **Plants-Paris et al., 2019**; **van Zijll Langhout et al., 2010**; **Wong-McClure et al., 2012** |
| Cobas b101 | Capillary blood | HbA1c, blood lipids (total cholesterol, HDL cholesterol, triglyceride levels, LDL cholesterol), CRP | Metabolic disease assessment, lifestyle interventions | **Agbaria et al., 2020** ; **Martins et al., 2020**; **Sousa-Coelho et al., 2020** |
| Triage MeterPro | Whole blood in EDTA and plasma | Creatine kinase MB, myoglobin, troponin I, B-type natriuretic peptide (BNP), *placental growth factor* (*PIGF*)[a] | Pre-eclampsia testing and treatment | **Duhig et al., 2019** |
| cobas Liat PCR System | Nasopharyngeal swab, throat swab and stool | Influenza A + B, Respiratory Syncytial Virus (RSV), Strep A, *C. difficile* | Influenza testing, surveillance and treatment | **DeMuri & Wald, 2020** ; **Trombetta et al., 2018** |
| Siemens DCA Vantage Analyzer | Whole blood and urine | HbA1c, microalbumin/creatinine ratio | Diabetes testing and treatment | *Cepon-Robins, 2021*; **Handrinos et al., 2020**; **Høj et al., 2017**; **Mach et al., 2019**; **Marrero et al., 2016**; *McDade, 2014*; **Millard** |

**TABLE 2** (Continued)

| POCT device | Sample type | Analytes measured | Research application | References |
|---|---|---|---|---|
| | | | | **et al., 2017**; **Miškinytė & Litvinaitė, 2015**; **Owiti et al., 2017**; **Raisanen et al., 2014**; **Regnier et al., 2020**; **Saxton et al., 2018**; **Wade et al., 2021** |
| LABGEO IB10 | Whole blood and plasma | Troponin I, TSH, beta-hCG, D-dimer, procalcitonin, NT-proBNP | Metabolic syndrome evaluation | **Pezzuto et al., 2019** ; **Ryu et al., 2017** |
| Sofia 2 | Capillary blood, serum, urine, throat swab, nasal swab, and nasopharyngeal swab | Strep A antigens, Strep A, SARS-CoV-2 antigen, *S. pneumoniae*[a], RSV, *Legionella*[a], influenza A + B, hCG, Lyme, Lyme + flu + SARS[a], vitamin D | SARS-CoV-2 testing, respiratory illness surveillance | **Checovich et al., 2019** ; Peeling et al., 2021; **Reddy et al., 2018** |
| A1CNOW | Capillary blood | HbA1C | Diabetes testing and treatment | *Cepon-Robins, 2021*; **Hassan et al., 2021**; *McDade, 2014*; *Wander et al., 2017* |
| HemoCue WBC System | Capillary blood | White blood cell count | Bacterial infection | **Hildenwall et al., 2017** |

*Note*: Articles referencing each POCT device are formatted by topic: *Italic represents anthropological journals*; **Bold indicates global and public health journals**; Underlined indicates other journals publishing a broad range of articles.
[a]Test not available in the United States.

ability of researchers to immediately share study results with participants, directly involving community members in data collection and interpretation (Madimenos et al., in preparation).

## 5 | ETHICAL AND SCIENTIFIC CONSIDERATIONS

Beyond the need for further testing in low-resource settings, there are several ethical and scientific considerations that must be addressed to ensure that POCT technology provides actionable health data. Rigorous scientific design, thorough POCT validation, and the clear communication of test strengths and limitations are all needed.

### 5.1 | Device marketing and data transparency

One issue surrounding the current market for POCT technology is that tests are increasingly advertised and sold directly to consumers (e.g., at-home glucose or cholesterol monitoring devices), bypassing medical visits entirely. Yet, most consumers do not have the scientific or medical training to ensure consistent test administration or accurate interpretation of results, potentially leading to an inaccurate understanding of individual health. A related concern is that many POCT devices rely on proprietary technology that is not shared with healthcare providers, scientists, or patients, making it difficult to assess the accuracy of the test. This secrecy in POCT development may also allow faulty or fraudulent tests to avoid detection, as was the case for years with the devices being developed by Theranos (Carreyrou, 2019).

Consequently, it is important to balance company interests with regulatory oversight to ensure that POCT devices operate as advertised, and corners are not being cut during test development. The need for increased transparency is apparent in the POCT literature. For example, one review of published POCT validations found that only 41% of articles reviewed explicitly detailed how the test compared to the current gold standard diagnostic test, information needed to establish the health impact of the POCT (Malekjahani et al., 2019). Increased scrutiny of the POCT development process can also be viewed in a positive light. Greater transparency in

POCT validation and operation will help ensure test quality and allow end users to be confident in POCT results, enhancing the reputation of the POCT developer and trust in their products. Increased transparency about what POCT can and cannot do will also assist health researchers, allowing them to make informed methodological decisions appropriate for their study site, spend their grant money wisely, and more accurately interpret study findings.

### 5.2 | Scientific study design

An additional consideration is the continued need for rigorous scientific study designs as increasingly sophisticated POCT becomes commercially available; researchers should not rely blindly on well-validated tests simply because they are convenient. The ability to quickly measure multiple analytes with relative ease should not serve as a justification for lax experimental design. Researchers should still think critically about research questions and data collection techniques before POCT data collection begins, weighing the importance of obtaining descriptive health data and the goal of conducting rigorous, hypothesis-driven research. Scientists must also pay close attention to the quality of data produced by POCT, and carefully consider how best to interpret study findings (e.g., by accounting for the limitations associated with the performance of a particular test in a specific study setting).

Researchers should also consider whether health data can be provided to community members not involved in a particular research study, such as when a community member is not eligible for a particular study on scientific grounds (e.g., excluding pregnant women in a study of metabolism), yet they may have a greater need for access to health information. As discussed previously, a strong partnership between researchers and community members can help address these study design issues. A collaborative approach will not only foster ongoing partnerships between researchers and communities but will also improve community-scientist relations more generally and enhance data interpretation (e.g., by helping researchers understand relevant local factors that may influence POCT performance and test results).

### 5.3 | Quality control, regulation, and innovation

The regulation of POCT technology performance and quality is another important concern. For instance, most quality control protocols are developed by laboratory personnel with expertise in POCT technology, which may lead to the implementation of quality control measures that do not match end-user level of experience, with implications for the reliability of tests and accuracy of results. The training of end-users should consequently be considered during POCT development to ensure that they are able to accurately perform quality control checks; otherwise, POCT training should include background information on good laboratory practice and quality control measures (Engel & Krumeich, 2020; Herd & Musaad, 2021). Without this additional training, test results may be inaccurate and lead to missed diagnoses (false negatives), unneeded medical treatments (false positives), or wasted tests.

However, while POCT regulation and continuous quality control checks are important, it has been argued that excessive regulation may have unintended consequences. Not only can regulatory testing be expensive, but it may also impede scientific innovation, leading to missed opportunities in the development of more reliable, accessible, and low-cost POCT technologies (Genzen, 2019). Given the global need for innovative diagnostic techniques, striking the proper balance between regulation—to avoid another Theranos—and creative freedom is an important consideration. Further, due to the fact that market interests predominantly influence POCT development (Christodouleas et al., 2018; Engel & Krumeich, 2020; Liu et al., 2019), it is currently difficult or impossible for individual researchers to develop POCT devices within the existing expensive and complicated regulatory landscape. Professional societies, such as the Human Biology Association (HBA), may have a role to play too in advancing POCT technology development (e.g., by supporting efforts to disseminate POCT information and to develop novel tests of particular interest to human biologists). Overall, the rapid development of POCT in recent years indicates that the field is continuing to move forward in transformative ways.

## 6 | FUTURE OPPORTUNITIES AND CHALLENGES

Point-of-care technology has advanced tremendously in the last several years, with important implications for human biology research. Whenever possible, available POCT should be incorporated into human biology research design for scientific and ethical reasons, as these tests facilitate both the rapid collection of needed biological measures and, when used responsibly to provide reliable health feedback, can contribute to community wellbeing, especially in low-resource settings. Still, more work is needed to fully realize the potential applications

of these technologies in low-resource communities. In addition to accounting for the scientific and ethical considerations discussed above, researchers and healthcare providers interested in using these tests must carefully weigh the strengths and limitations of various devices to select the test best suited for their particular needs.

## 6.1 | Existing barriers and limitations

Several barriers exist that may make it difficult for researchers and healthcare providers to use POCT outside of a clinical laboratory, especially in low-resource settings. Many tests are only sold to CLIA-certified labs or licensed physicians, making it difficult for researchers or small clinics to use more complex POCT. It can also be difficult to order POCT equipment from certain regions, requiring researchers or healthcare providers working internationally to purchase the POCT devices and then personally carry or ship them to their final destination. Further, it may be difficult for human biologists to receive IRB approval for the use of complex POCT devices without a physician as part of the research team. Researchers could potentially circumvent this barrier by collecting data with regulated POCT but not sharing potentially diagnostic analysis results with individual participants (i.e., share data on general patterns observed at the community level), although a lack of individual data sharing may frustrate study participants and moreover, is an ethically inappropriate means of conducting participant-focused research. Finally, as previously mentioned, it is unclear how many tests perform reliably in field settings, especially in extreme temperatures or humidity. It can also be difficult to troubleshoot malfunctioning devices in remote areas without accessible laboratory support (Herd & Musaad, 2021).

Energy usage is also a concern. Although some devices have been designed to be powered by batteries and rapid diagnostic tests (such as paper-based tests) can be used in areas without reliable access to electricity, multianalyte cost-efficient tests generally require reliable electricity and outlet access (Bissonnette & Bergeron, 2017; Zarei, 2017a, 2018). While some studies have explored potential applications of POCT in low-resource clinics (Herd & Musaad, 2021; Khan et al., 2019), additional work is needed to test POCT under conditions replicating those of intended use (Malekjahani et al., 2019; Murray & Mace, 2020). The cultural appropriateness of each POCT within a given setting must also be considered by researchers and providers (Herd & Musaad, 2021). Further, while simple and inexpensive POCT may enable population health researchers to collect data from participants living in remote field settings lacking medical infrastructure, this also raises additional ethical considerations. Low-resource communities may not have the capacity to monitor local research projects, and individuals may feel pressured to take part in the study in order to receive needed health information (Regmi et al., 2017). Researchers must therefore consider how limited access to medical care and health information may influence individual decision making and take steps to ensure that the informed consent process is appropriately conducted (Regmi et al., 2017).

The tests themselves also have some important limitations. For instance, some biomarkers can be hard to detect and quantify because they may be present in a sample at low levels or they may be difficult to detect in complex biological samples containing many different molecule types (Bissonnette & Bergeron, 2017; Suntornsuk & Suntornsuk, 2020). This may lead to false negative POCT results, and a potentially dangerous situation where individuals do not receive needed medical care (Kozel & Burnham-Marusich, 2017). Given these limitations, a prudent approach in some situations is to view POCT results as preliminary—an initial screening used to determine next steps—rather than a definitive diagnostic medical or research tool. If a study participant shows results potentially indicating a medical issue, researchers can then help participants access follow-up testing and care.

In addition, some POCT are fairly complicated, requiring several steps, specialized equipment, and significant training or experience to perform properly (Engel & Krumeich, 2020; Murray & Mace, 2020). Training might therefore require researchers or care providers to learn about analysis quality control and device maintenance, beyond the steps involved in the test itself (Engel & Krumeich, 2020). Yet, paradoxically, simplifying POCT too much may also lead to poor test results. For example, test simplicity may lead POCT operators to be lax, miss device malfunctions, and misinterpret test results (Engel & Krumeich, 2020). Simple POCT may also have low throughput, leading to long wait times for patients or study participants when many samples are being processed at once (Engel & Krumeich, 2020).

A final barrier to the development of accessible POCT in low-resource communities is cost. The cost of individual tests may still be a barrier in many cases, such that the high cost of single tests may make it difficult for researchers or patients to afford useful POCT (Engel & Krumeich, 2020; Kozel & Burnham-Marusich, 2017; Nelson, 2020). Beyond test costs, the capitalistic interests inherent in medical technology also play an important role in driving the development and availability of POCT. As demonstrated by the hundreds of millions of

investment dollars raised by Theranos (SEC, 2018), POCT development is of great financial interest given its potential to disrupt the healthcare field. This disruption has enormous economic implications, given the substantial percentage of Gross Domestic Product (GDP) accounted for by national health expenditures in some countries (e.g., health expenses accounted for 17.7% of US GDP in 2019, a number expected to rise in coming years) (CMS, 2020b). Yet, as is the case with drug and vaccine development, POCT are most lucrative if they are repeatedly useful to end users in high-income nations, decreasing financial incentives to develop POCT for conditions that affect relatively few people or which are primarily found in lower income countries (Genzen, 2019). Still, the development of novel POCT technology, including the use of new sample types, may help make POCT more widely available.

## 6.2 | Emerging sample types, novel technologies, and creative design

While many POCT continue to rely on standard biological samples (e.g., saliva, urine, stool, or small amounts of blood), some tests are now being designed to analyze novel sample types, including tears, sweat, breath, and nose swabs (Christodouleas et al., 2018; Liu et al., 2019; Shrivastava et al., 2020). Novel sample types are already being used to measure participant electrolyte, glucose, and lactate levels and are typically collected by non-invasive methods, such as absorption pads or micro-capillary tubes at the site of fluid excretion (Shrivastava et al., 2020). As an added benefit, these sample types may help researchers avoid methods that may be objectionable in certain settings (e.g., collecting blood in cultures with blood taboos), thereby increasing study enrollment and sample size.

Despite their potential, only a limited number of analytes can currently be assayed using novel sample types (Liu et al., 2019). In addition, these minimally-invasive samples are not always easy to collect. For example, participant perspiration must occur to collect sweat samples and eye watering or crying must be elicited to obtain tears, which may be uncomfortable for some participants (Christodouleas et al., 2018). A second impediment is that, for each analyte, there is generally a need to determine the relationship between the novel sample type and the 'gold standard' traditional sample type (typically blood), a process that is time consuming and expensive. Most work to date has focused on military and sports applications for these POCT platforms (Christodouleas et al., 2018); additional work is consequently needed to develop tests able to measure analytes of interest to healthcare providers or human biologists working with diverse populations.

Besides developing tests using new sample types, efforts are ongoing to leverage existing technology to enhance POCT capabilities such as using 3D printing to create durable components for microfluidic POCT devices (Zarei, 2017a, 2017b). Researchers have also begun pairing existing technology with smartphones. Smartphones have become more prevalent globally and phone technology (e.g., sensors, cameras, and data storage and transfer capabilities) has advanced significantly. Phones could therefore be paired with emerging applications and accessories to facilitate POCT to meet the specific needs of the populations in areas with limited medical or laboratory infrastructure (Malekjahani et al., 2019; Nasseri et al., 2018; Xu et al., 2018; Zarei, 2017a, 2017b, 2018). Smartphones could also act as analyzers in some cases, quantifying color change that can be converted into analyte concentrations or reading electrochemical test strips using modules embedded inside the phone (Xu et al., 2018). Phones can also be used to power the dongles performing the test or read and interpret colorimetric changes to test strips through specially designed phone accessories (Xu et al., 2018).

The pairing of POCT with smartphones is a powerful combination, enabling the rapid collection and transfer of data. Indeed, smartphone companies are already marketing comprehensive fitness apps designed to track user health in real time (e.g., the Apple Health app on the iPhone) (Sawh, 2020). Smartphone health technology has several applications, from monitoring individual health over time (e.g., supporting the maintenance of easily accessible electronic health records), to tracking regional disease outbreaks (e.g., providing contemporaneous data needed to inform time-sensitive decisions) (Gous et al., 2018). The use of phones to quickly share health metrics can also allow real time monitoring of data quality and POCT functioning, facilitating the rapid identification of erroneous results (Gous et al., 2018). However, providers and researchers interested in using phone-based POCT must consider how to ensure participant data and privacy are protected (Gous et al., 2018; Kozel & Burnham-Marusich, 2017; Mejía-Salazar et al., 2020).

In addition to phone-based tests, development of handheld breath analyzers is currently underway, with the goal of identifying cancer, infections, and inflammatory conditions early in the course of disease, potentially saving thousands of lives and millions of dollars in healthcare costs (Sinclair & LaPlante, 2019). Eventually, POCT technologies using minimally-invasive samples may become ubiquitous, efficiently identifying physiological changes that serve as the first indications of poor health. These POCT devices may also be designed to

prompt individuals to seek appropriate treatment and/or adjust their behavior to address any underlying issues that can lead to future poor health (e.g., dietary adjustments in response to nutrient deficiencies) (Sinclair & LaPlante, 2019), ostensibly increasing individual autonomy over health outcomes.

The development and increased availability of "wearable" POCT will support efforts to monitor individuals for early signs of disease. Several wearable devices being developed rely on flexible substrates such as polymer films, flexible graphite, or textiles that can be used to measure analytes from body fluids (e.g., graphite devices placed on the skin measuring analytes in sweat) (Bissonnette & Bergeron, 2017; Zarei, 2017a, 2017b). Further, like smartphones, wearable technology can facilitate the rapid transmission of data to researchers or healthcare providers working in areas where POCT wearable devices can be connected reliably to the internet or paired with cell phones or computers using Bluetooth (Mejía-Salazar et al., 2020). While still new and limited by the availability of reliable Bluetooth devices, internet, and phone network coverage, these emerging technologies have the potential to revolutionize the use of POCT in low-resource settings.

## 7 | CONCLUSIONS

While POCT development has progressed tremendously in recent years, there is still more work to be done. Years after the fallout from Theranos, concerns over ethical test development and use remain. Moreover, the production of novel tests remains largely determined by market interests and investor priorities, curtailing the development of POCT designed for human biology research and limiting accessibility of health information in underserved high-need populations globally. Likewise, many existing POCT devices remain poorly tested in nonclinical settings and regulatory testing is largely performed by highly trained technicians; therefore, it is unclear how accurate many tests are in field settings of interest to human biologists. However, current events clearly demonstrate the importance of health monitoring in low-resource settings, a need that can be filled in part by reliable POCT. During the ongoing COVID-19 pandemic, the ability to track disease spread locally and globally has been crucial in efforts to contain the virus. Unfortunately, we can be reasonably certain that COVID-19 will not be the only public health challenge in coming years.

The development of novel POCT that meets the WHO's ASSURED standards is urgently needed to assist in the identification and management of emerging health crises, especially conditions disproportionately impacting low-resource communities with limited medical infrastructure and clinical testing capabilities. Access to well-validated POCT in these settings can support more accurate diagnosis and treatment of both chronic conditions (e.g., type 2 diabetes) and infectious diseases (e.g., SARS-CoV-2). There is consequently an ongoing demand for POCT technology, which Theranos tapped into. If this demand is coupled with streamlined regulatory processes and stronger connections between POCT developers and investors, we believe emerging POCT may make centralized medical testing in core facilities less common in the coming years.

Additionally, beyond aiding healthcare providers and public health researchers in tracking health patterns, the production of POCT will advance the field of human biology by expanding the methodological toolkit. The ability to measure a wide range of analytes using various sample types and testing platforms will allow human biologists to select the test most appropriate to their field site (i.e., accounting for relevant environmental constraints and the cultural context in which they are working), while also supporting collaborations and data sharing with participant communities (Madimenos et al., in preparation). Although a single portable device capable of quickly testing hundreds of analytes from a few drops of blood—as promised by Theranos—currently remains science fiction, well-regulated POCT designed for use in low-resource settings holds great promise in helping human biologists share basic epidemiological data with underserved populations and test important hypotheses related to human evolution, physiology, and health.

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## CONFLICT OF INTEREST

All authors have indicated no conflicts of interest.

## AUTHOR CONTRIBUTIONS

**Theresa E. Gildner:** Conceptualization (equal); writing – original draft (lead); writing – review and editing (lead). **Geeta N. Eick:** Conceptualization (lead); writing – original draft (lead); writing – review and editing (supporting). **Alaina L. Schneider:** Writing – original

draft (equal); writing – review and editing (equal). **Felicia C. Madimenos:** Writing – original draft (equal); writing – review and editing (equal). **J. Josh Snodgrass:** Conceptualization (lead); writing – original draft (equal); writing – review and editing (equal).

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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