Geospatial Hotspots Need Point-of-Care Strategies to Stop Highly Infectious Outbreaks

Ebola and Coronavirus

Gerald J. Kost, MD, PhD, MS

Context.—Point-of-care testing (POCT), diagnostic testing at or near the site of patient care, is inherently spatial, that is, performed at points of need, and also intrinsically temporal, because it produces fast actionable results. Outbreaks generate geospatial “hotspots.” POC strategies help control hotspots, detect spread, and speed treatment of highly infectious diseases.

Objectives.—To stop outbreaks, accelerate detection, facilitate emergency response for epidemics, mobilize public health practitioners, enhance community resilience, and improve crisis standards of care.

Data Sources.—PubMed, World-Wide Web, newssprint, and others were searched until Coronavirus infectious disease-19 was declared a pandemic, the United States, a national emergency, and Europe, the epicenter. Coverage comprised interviews in Asia, email to/from Wuhan, papers, articles, chapters, documents, maps, flowcharts, schematics, and geospatial-associated concepts. EndNote X9.1 (Clarivate Analytics) consolidated literature as abstracts, ULRs, and PDFs, recovering 136 hotspot articles.

More than 500 geospatial science articles were assessed for relevance to POCT.

Conclusions.—POCT can interrupt spirals of dysfunction and delay by enhancing disease detection, decision-making, contagion containment, and safe spacing, thereby softening outbreak surges and diminishing risk before human, economic, and cultural losses mount. POCT results identify where infected individuals spread Coronavirus infectious disease-19, where delays cause death, and how to deploy resources. Results in national cloud databases help optimize outbreak control, mitigation, emergency response, and community resilience. The Coronavirus infectious disease-19 pandemic demonstrates unequivocally that governments must support POCT and multidisciplinary healthcare personnel must learn its principles, then adopt POC geospatial strategies, so that onsite diagnostic testing can ramp up to meet needs in times of crisis.

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The goals of this study were as follows: (1) to understand point-of-care (POC) geospatial strategies and concepts needed to stop outbreaks of highly infectious diseases from spreading; (2) to rapidly detect stealth transmission, accelerate response, and control epidemics in time, place, and space; (3) to facilitate diagnostic support, preparedness, and emergency/critical care in healthcare small-world networks; (4) to introduce public health practitioners to POC principles and practice, mobilize them in the use of POC testing, and thereby, enhance manpower, diagnostic access, and community resilience; and (5) to improve crisis standards of care worldwide.

CHALLENGES

Increasingly, we observe the adverse personal, societal, economic, and cultural impact of outbreaks, such as Coronavirus infectious disease-19 (COVID-19; Figure 1), antimicrobial resistance, disasters, and other world crises. This article chronicles POC strategies,1–21 such as drive-up/in/through testing in healthcare small-world networks (Figure 2), and concepts22–40 that decrease risk and reduce harm. It evaluates the most expeditious paths to diagnostic testing (Figure 3). It concludes with a recommended global framework supported by national point-of-care testing (POCT) policy and guidelines and shared financial burden.

COVID-19 is generating huge loss of life and resources and redefining human existence, exacerbated by inadequate diagnostic testing, lack of trained field personnel, and limited knowledge of temperature and humidity effects in volatile settings where devices are used and testing performed. The number of cases in the United States overtook those (81 340) in China on March 26, and then at the time of writing, totaled 1 312 496 with 72 636 deaths worldwide; 349 992 and 10 327 in the United States; and 130 689 and 4758 in New York, respectively.41 Please find the latest tallies at “Worldometer” (https://www.worldometers.info/coronavirus/).
Historically, Asian Influenza first appeared at the University of California, Davis in 1957. With an attack rate of 89%, it spread explosively. The first community transmission of severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) occurred a few miles west from Davis in Vacaville (Figure 4). The patient was transported 36 miles east to the University Medical Center. No diagnostic testing for SARS-CoV-2 was available. Drive-up/in/through sites (Figure 2) allow personnel to obtain specimens safely outside hospitals. Testing may be performed there too. Research laboratories must establish acceptable environmental temperature and humidity limits and standards for this type of field implementation.

However significant the benefits of POC technologies become during this crisis, the scale of investment needed to properly prepare hospitals to respond demands an integrated global response. Sustainable POCT business models are badly needed, so commercial development of POCT for pandemics, disasters, and complex crises becomes viable long term. Financial incentives, such as the $20 million prize of the Antimicrobial Resistance Diagnostic Challenge for POC inventions to combat that burgeoning problem, and recent federal and state stopgap emergency measures intended to slow the COVID-19 pandemic, will save money downstream.

Financial losses from COVID-19 are expected to total ~$4 trillion with approximately 5% reduction in global gross domestic product. Much more than that will be spent to offset financial set-backs in the light of market crashes, business failures, and widespread unemployment. Obviously, the return on investment in new POCT technologies, environmental safeguards, and geospatial strategies and concepts will be highly favorable, provided the current quick start is sustained long term. Grim forecasts predict the pandemic will last more than 1 year until access to vaccines occurs. Vaccines are as yet unproven and COVID-19 may become seasonal for years to come.

NOMENCLATURE

Coronavirus

SARS-CoV-2 is the virus, and COVID-19 the disease it causes. The virus name reflects genetic relationship with the Coronavirus responsible for the SARS outbreak in 2003.

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However, the two viruses differ. Virus names based on genetic structure facilitate development of diagnostic tests, vaccines, and medicines. Disease nomenclature enables analysis of prevention, spread, transmissibility, severity, and treatment.

The World Health Organization (WHO) is responsible for human disease preparedness, response, and nomenclature in the International Classification of Diseases. China called the outbreak, "Novel Coronavirus Pneumonia," based on its primary clinical manifestation diagnosed by chest X-ray and computed tomography scan because reliable and accurate diagnostic testing was not available in Wuhan initially.

Hotspots

A “hotspot” is a topographic area or region of unusual danger to personal or public health. People in the community may be at extreme risk during an outbreak of a highly infectious disease that spreads quickly, as we are witnessing with the COVID-19 pandemic. Additionally, dangerous situations, such as civil strife and war, or belligerent political attitudes, may complicate the control of hotspots, rendering them even more difficult to address medically, quell socially, and stop quickly.

Point-of-Care Testing

POCT, defined as diagnostic testing at or near the site of patient care, is inherently spatial, that is, performed at points of need, and also intrinsically temporal, because it produces fast actionable results. This definition does not depend on the size or format of the handheld, portable, or transportable instrument, test module (e.g., for a smartphone), or assay design. POCT encompasses near-patient testing, rapid diagnostic tests (such as lateral flow), disposable test strips, and in situ, ex vivo, in vivo, and on vivo monitoring (e.g., pulse oximeters, wearables, and remote temperature monitoring).

The “Cape Cod” group codified this definition, which first appeared in standard dictionaries of the English language years ago. The Point-of-care Testing Center for Teaching and Research (POCT/CCTR) wrote the original Wikipedia article. Historic terms include alternate site testing, testing outside the clinical laboratory, point-of-need testing, rapid diagnostic test, and others, now mostly abandoned in favor of the simplified concept above that professionals, laypersons, and politicians alike recognize, especially now during the pandemic.
METHODS

Research Scope

This article assesses the importance of geospatial science as it pertains specifically to highly infectious diseases and POCT. Numerous sources identified through PubMed dealt with the general area of geographic information systems in healthcare. The majority addressed geographic information systems for tracking, monitoring, and managing common endemic infectious diseases, such as malaria and HIV. Only those geospatially oriented publications explicitly discussing or integrating POCT, closely related mobile technologies, or conceptually relevant concepts are presented here.

Data Sources

PubMed, the World-Wide Web, numerous local, regional, and international newspapers, Asia television broadcasts, and other timely sources were gathered and assessed, including onsite interviews in Asia, email to/from a professorial colleague in Wuhan, key updates, papers, articles, chapters, documents, maps, flowcharts, schematics, and geospatial concepts associated with POCT and outbreaks. Several articles discussed, introduced, and/or summarized POC/rapid tests for the detection and differential diagnosis of COVID-19. 47–53

EndNote X9.1 (Clarivate Analytics, https://clarivate.com/) was used to consolidate literature entries and retrieve abstracts, ULRs, and PDFs automatically. PubMed driven EndNote recovered 136 geospatial hotspot articles. More than 500 geospatial science articles were assessed previously for geospatial relevance to POCT and closely related mobile technologies. 54 Molecular diagnostics for highly infectious threats can be found in a book chapter 4 and comprehensive analysis. 4,14,15,55

Geospatial Science

Geospatial science identifies and leverages the power of location data. 56 Location data embody a geographic dimension. Location intelligence is the process of turning geographic (spatial) data into insights for decision making. POCT is pivotal to quick decision making, triage, and quarantine. A spatial care path is the most efficient route taken by the patient when receiving definitive care in a small-world network. A geospatial care path adds in geographic and topographic coordinates, physical sites, and quantitative metrics to the healthcare small-world network.

TIMELINE AND IMPACT ANALYSIS

This article analyzes the COVID-19 outbreak from the sentinel case (see Figure 1), presumed to have appeared in Hubei Province, China, in November, 2019, up until March 2020. Figure 3. Pathways to diagnosis and care in the Coronavirus infectious disease-19 outbreak. Caught off guard like many other countries, the United States sat for weeks on the critical path (CP—the slowest route, on the right). Optimized provider services moved more swiftly in locations that implemented geospatial care paths (left), such as South Korea, and early adopter locations, such as Stanford University, both of which responded quickly with creative diagnostic testing. In the future, the United States should redesign healthcare strategies for readiness at points of care.
11 when the WHO finally declared COVID-19 a pandemic (118,000 cases, 110 countries), the United States declared a national emergency, the epicenter shifted to Europe with both suppression and mitigation underway, and the number of cases in the United States surpassed that in China. Analysis of COVID-19, POC technologies, and social learning curves is in part modeled after previous assessments of evolving molecular diagnostics during the 2014 to 2016 Ebola epidemic.4,14,15,55 Despite prior warnings of need during the 2014 to 2016 Ebola crisis,4,14,15,55 POC diagnostics production capacity for highly infectious diseases was not properly strategized. By the third week of March, a Wall Street Journal front page headline read, “America Needed Tests. The Government Failed.”57 Drastic changes are in order to bring the replication rate under 1 (R₀ < 1). In fact, the scale of the solution is much broader than just fixing government failures. It demands reinvention and overhaul of the future practice of public health.39,58,59

Table 1 highlights the early impact of COVID-19 as contagion mushroomed spatially and temporally to panepidemics then pandemic, collectively termed “newdemic.”40 Fear, panic, and lifestyle changes ensued as COVID-19 stress-tested healthcare providers, reality of the world crisis set in, and compulsory orders under harsh governmental decrees upset daily life. Next, economic markets crashed and community culture suffered. The pandemic is morphing into an economic recession unlikely to spare any nation for at least the next decade.

**POINT-OF-CARE GEOSPATIAL STRATEGIES AND CONCEPTS**

The general principle of geoscience is that “everything is related to everything else, but near things are more related than distant things.”56 The exception is the spread of an outbreak where distant sites effectively become time and space near neighbors, because asymptomatic carriers rapidly spread disease. So, we can modify the basic principle as, “everything is related to everything else, and mobility compresses spatial things.” Hence, the need for safe spacing (i.e., social distancing, physical distancing, or physical separation) in the United States is critically dependent on the extent to which both ruling out COVID-19 and
Table 1. Outbreaks of Highly Infectious Diseases and their Geospatial Impact

<table>
<thead>
<tr>
<th>Geospatial Hotspot</th>
<th>Threat/Outbreak</th>
<th>Highlights of Medical, Cultural, and Economic Impact*</th>
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</table>
| Wuhan, China; November 2019 to 2020, then worldwide (WHO declared pandemic March 11 2020) | COVID-19 (Coronavirus Infectious Disease 2019, WHO) (aka “2019-nCoV”—CDC initial abbreviation; and “Novel Coronavirus Pneumonia [NCP]”—China nomenclature) | Contagion in live animal/seafood Wuhan market, dense city of 11 million, Hubei Province  
Not prepared—no SARS-CoV-2 POCT in China; viral sequence known in January  
Poor test reliability changes diagnostic criteria to CXR/CT; next, test confirmation  
Infected sick people leave Wuhan to seek help in, but spread virus to, larger cities  
Many walk out over Yangtze bridge to Jiangxi Province, deaths reach thousands  
Person-to-person transmission by asymptomatic carriers, incubate virus 1–14 days >1000 healthcare workers in China infected, several die, ER staff/patients panic  
CDC/WHO confuse face mask use, panic N95 buying, health worker supply short  
Central Chinese borders close; Beijing orders labs to destroy test samples, will not cooperate with probe into virus origin  
Finally, takes draconian steps to abate epidemic, international/Hubei borders close  
Widespread lock-down traps 60 million++, transportation ceases, mail delayed  
Schools closed, devastating effect on family and New Year cultural celebrations  
Work stoppages, material shortages, exports cuts, GDP deceleration inevitable  
WHO declares global emergency belatedly, spreads worldwide, cases >100 000  
United States, Thailand, Japan, South Korea, and other countries evacuate citizens from Wuhan  
Thai first person-to-person January 31, 2020, so telemedicine robots rolled out to decrease risk  
Hong Kong, others cancel flights, screen/spray travelers; mutations anticipated  
Cruise ships stranded, people cannot disembark, industry devastated economically  
California hangs quarantine, first community transmission; Australia, Christmas Island  
Italy locks down whole country, fatality rate soars to 7%, panepidemic growing  
Reminiscent of MERS-CoV, South Korea stock market plummets 6% with first case  
AISEAN discusses cooperation to enhance detection, control clusters, and stop spread  
More new cases outside China than inside, February 27; tertiary spread rampant  
International supply chains interrupted; NYSE takes hit; IMF, economic setbacks  
Cash injection, debt-tax-wage-rent relief, governments try to offset slowdown  
WHO public enemy #1 demands global cooperation; vaccine unlikely for >1 yr  
3416 cases, 2237 deaths, and 65.5% mortality; 5% of cases healthcare workers  
Second largest outbreak ever recorded since Ebola discovered in DRC in 1976  
Many received rVSV-ZEBOV-GP, Ad26.ZEBOV/MVA-BN-Filo vaccines  
War zone strife with several healthcare workers killed by militants  
Value life lost $17 761 539 (to 5/19); 45%–49% borne by children <9, adults 15–59 yrs  
11 treatment and 25 transit centers in North Kivu, South Kivu, and Ituri provinces  
Untold social and cultural disruption with regional spread  
11 316 deaths and 28 639 suspected, probable, and confirmed cases  
Guinea, Liberia, and Sierra Leone lost $2.2 billion in 2015 GDP  
United States, United Kingdom, and Germany donated >$3.611 billion by December 2015  
Liberia lost 8% of its doctors, nurses, and midwives; Sierra Leone and Guinea lost 7% and 1% of their healthcare workers, respectively  
Guinea, Liberia, and Sierra Leone estimate >17 300 children orphaned  
Vast cultural impact yet to be completely restored  
Limited spread to other countries, including the United States |

| Democratic Republic of the Congo (DRC), 2018-now | Ebola virus disease | 
|-------------------------------------------------|---------------------|--------------------------------------------------|

|-------------------------|---------------------|--------------------------------------------------|

Abbreviations: ASEAN, Association of Southeast Asian Nations; CDC, Centers for Disease Control and Prevention; COVID-19, Coronavirus infectious disease-19; CT, computed tomography; CXR, chest X-ray; ER, emergency room; GDP, gross domestic product; IMF, International Monetary Fund; MD, medical doctor; MERS-CoV, Middle East respiratory syndrome coronavirus; NYSE, New York Stock Exchange; POCT, point-of-care testing; SARS-CoV-2, severe acute respiratory syndrome-coronavirus-2; WHO, World Health Organization.

*Record reflects sentinel case, beginning of outbreak, until approximately >100 000 cases worldwide and pandemic declared by WHO on March 11.  
Numerous regional and global news sources gathered while the author was in southeastern Asia during the initial outbreak, including the Bangkok Post, BBC, Channel New Asia, CDC, CNN Live, Japan Times, New York Times International, Time Asia, Viet Nam News, Wall Street Journal, and WHO.
<table>
<thead>
<tr>
<th>Strategy 1</th>
<th>Geospatial Science Tool, Title of Paper(s), Synopsis, and Impact Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A. Spatial and Geospatial Care Paths</strong></td>
<td></td>
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<tr>
<td>Kost¹ <em>Amer J Dis Med</em> 2015</td>
<td>Strategic planning for epidemics</td>
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<tr>
<td><strong>Kost² <em>Point of Care</em> 2015</strong></td>
<td>Reenergizing vision</td>
</tr>
<tr>
<td>Kost³ <em>Tri•Con Symposium</em> 2019</td>
<td>Hualien County, Taiwan; Palawan, the Philippines; Isaan, Thailand; and Central Vietnam</td>
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<tr>
<td><strong>B. FAST•POC, POCT•POD, and Other Safe Spacing</strong></td>
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<tr>
<td>Kost⁴ In: <em>A Practical Guide to Global POC</em> 2016</td>
<td>Biosafety and environmental conditions control</td>
</tr>
<tr>
<td>Thomas⁵ <em>Health Management, Policy &amp; Innovation</em> 2020</td>
<td>Stanford University, Palo Alto, California</td>
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<th>Strategy 2</th>
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<tr>
<td>Grusky⁶ <em>Behav Med</em> 2010</td>
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**Table 2. Geospatial Strategies Using Point-of-Care Testing (POCT)**

<table>
<thead>
<tr>
<th>First Author, Journal/Y/Reference</th>
<th>Country, Setting, or Focus</th>
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<tr>
<td><strong>Strategy 1</strong></td>
<td></td>
<td><strong>Spatial Optimization of POCT</strong></td>
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<tr>
<td>A. Spatial and Geospatial Care Paths</td>
<td></td>
<td><strong>The Ebola Spatial Care Path: Accelerating point-of-care diagnosis, decision making, and community resilience in outbreaks</strong></td>
</tr>
<tr>
<td>Kost¹ <em>Amer J Dis Med</em> 2015</td>
<td></td>
<td>POCT is facilitating global health. Now, global health problems are elevating POCT to new levels of importance for accelerating diagnosis and evidence-based decision-making during disease outbreaks. The authors present a vision where POCT accelerates an Ebola SCP and future molecular diagnostics enable facilitated-access self-testing; design an alternate care facility for the SCP; innovate an Ebola diagnostic center; and propel rapid POCT to the frontline to create resilience that stops future outbreaks</td>
</tr>
<tr>
<td><strong>Kost² <em>Point of Care</em> 2015</strong></td>
<td></td>
<td><strong>Spatial Care Paths strengthen links in the chain of global resilience: disaster caches, prediabetes, Ebola virus disease, and the future of point of care</strong></td>
</tr>
<tr>
<td>Kost³ <em>Tri•Con Symposium</em> 2019</td>
<td>Hualien County, Taiwan; Palawan, the Philippines; Isaan, Thailand; and Central Vietnam</td>
<td>By identifying weak links in the chain of community resilience, SCPs upscale key unfulfilled needs, reveal new ideas for innovation-invention, bolster educational outreach, and improve patient access to evidence-based primary, emergency, and hospital care</td>
</tr>
<tr>
<td><strong>B. FAST•POC, POCT•POD, and Other Safe Spacing</strong></td>
<td></td>
<td><strong>Point-of-care cardiac biomarkers in Vietnam, the Philippines, Taiwan, and Thailand</strong></td>
</tr>
<tr>
<td>Kost⁴ In: <em>A Practical Guide to Global POC</em> 2016</td>
<td></td>
<td>The author invented FAST•POC (facilitated-access, self-testing at the point of care) where the patient performs self-testing with the help of a safely spaced facilitator and POCT•POD (POCT personal outbreak [outcome] detection[device]) where the patient in an isolation pod follows e-instructions for testing, then after exiting, the pod or sampling site begins a hygiene cycle of self-cleaning. Applications include walk-in/through, drive-up/in/through, triage near ERs, primary care, homes, pop-ups near factories, airports, disaster sites, telehealth, mobile labs, and any points of care</td>
</tr>
<tr>
<td>Thomas⁵ <em>Health Management, Policy &amp; Innovation</em> 2020</td>
<td>Stanford University, Palo Alto, California</td>
<td><strong>Integrating telemedicine triage and drive-through testing for COVID-19 rapid response</strong></td>
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<tr>
<td><strong>Strategy 2</strong></td>
<td></td>
<td><strong>Staff strategies for improving HIV detection using mobile HIV rapid testing</strong></td>
</tr>
<tr>
<td>Grusky⁶ <em>Behav Med</em> 2010</td>
<td>Los Angeles, California</td>
<td>The authors created maps using geographic GIS data on 9 3MTU locations and 2003 AIDS cases. MTU testing locations were clustered near high AIDS rate areas. Staff strategies that were used included keeping clients with them while rapid test results were being processed and adjusting to clients’ schedules when arranging for picking up test results. GIS findings and client risk data support the CDC policy of implementing MTUs and rapid testing in large urban communities with high AIDS rates</td>
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<tr>
<td>Goswami7 BMC Infect Dis 2011</td>
<td>Wake County, North Carolina</td>
<td>Feasibility and willingness-to-pay for integrated community-based TB testing. Integrated testing for TB, HIV, and syphilis was performed in neighborhoods identified using GIS-based disease mapping. TB testing included skin testing and interferon gamma release assays. Successful integrated testing programs in high-risk populations will likely require one-visit diagnostic testing and incentives.</td>
</tr>
<tr>
<td>Alegana8 Spatial Spatiotemp Epidem 2013</td>
<td>Northern Namibia</td>
<td>Estimation of malaria incidence in northern Namibia in 2009 using Bayesian conditional-autoregressive spatial-temporal models. A spatial-temporal model was used to identify constituencies with high malaria incidence to guide malaria control. Rapid diagnostic tests were used to examine blood samples from most patients at primary health facilities although a few, mostly at tertiary facilities, were examined using microscopy.</td>
</tr>
<tr>
<td>Yao9 Health Place 2014</td>
<td>Rural Mozambique</td>
<td>Spatial and social inequities in HIV testing utilization in the context of rapid scale-up of HIV/AIDS services in rural Mozambique. Applying GIS-based methods and multilevel regression analysis to unique longitudinal three-wave survey data from rural Mozambique, the authors investigated the impact of a rapid expansion of HIV-related services on access to and utilization of HIV testing. The results illustrate the declining importance of spatial barriers to utilization of HIV testing services as these services expanded.</td>
</tr>
<tr>
<td>Larroca10 Malaria J 2016</td>
<td>Districts with highest prevalence of malaria, Uganda</td>
<td>Malaria diagnosis and mapping with mHealth and GIS: evidence from Uganda. Affordable remote malaria diagnosis and mHealth can help to decongest health facilities, reducing costs and contagion. The authors discuss rapid diagnostic tests, their limitations, advantages, and impact in conjunction with mHealth. Mapping by means of GIS analysis could provide real-time and geolocalized data transmission, improving antimalarial strategies in Uganda.</td>
</tr>
<tr>
<td>Girdwood11 PloS One 2019</td>
<td>Zambia sample transportation network</td>
<td>Geospatial cost model for point of care instrument placement. VL monitoring programs are now facing the challenge of providing access to remote facilities. The authors used a combination of both on-site POCT and placement at facilities acting as POC hubs. A location allocation model was used to identify POCT hubs. For the hardest-to-reach facilities in Zambia, the authors compared the cost of placing POCT VL instruments at or near facilities with the cost of an expanded sample transportation network to deliver samples to centralized laboratories. ArcGIS 10.5 (ESRI) was used to run different algorithms to identify candidate POCT facilities, select facilities for POC placement, and model the different scenarios. An optimal combination of both on-site placement and the use of POC hubs can reduce the cost per test by 6%–35% by reducing transport costs and increasing instrument utilization.</td>
</tr>
<tr>
<td>Kuupiel12 BMC Public Health 2019</td>
<td>Ghana</td>
<td>Geographic accessibility to public health facilities providing tuberculosis testing services at point-of-care in the upper east region, Ghana. There is poor geographic accessibility to public health facilities providing TB testing services at the POC in the upper east region of Ghana. The authors assembled detailed spatial data on all 10 health facilities providing TB testing services at the POC, and landscape features influencing journeys. These data were used in a geospatial model to estimate actual distance and travel time from the residential areas to health facilities providing TB testing services.</td>
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<td>Strategy 3</td>
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<tr>
<td>Hill13 Lab Med 2014</td>
<td>Emory University, Atlanta, Georgia</td>
<td>Laboratory test support for Ebola patients within a high-containment facility. The authors present an isolation laboratory designed collaboratively with the CDC several years prior to receiving 2 Ebola patients and list POC tests used inside. To avoid aerosol exposure, no centrifugation was performed. The experience highlighted the need for (1) FDA-cleared tests, (2) compact instruments, (3) direct whole-blood measurement, (4) consolidation of test clusters appropriate for the support of patients critically ill with highly infectious diseases, and (5) spatially discrete “safe houses” for POCT</td>
</tr>
<tr>
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<td>--------------------------------------------------------------------------</td>
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</tbody>
</table>
| Kost *Amer J Dis Med* 2015
*Clin Lab Intl* 2015
*Expert Rev Mol Diagnostics* 2015 | Southeast Asia (Bangkok, Thailand) and other settings at risk worldwide | **The Ebola Spatial Care Path: accelerating point-of-care diagnosis, decision making, and community resilience in outbreaks**
**The Ebola Spatial Care Path: point-of-care lessons learned for stopping outbreaks**
**Molecular detection and point-of-care testing in Ebola virus disease and other threats: a new global public health framework to stop outbreaks**
The authors designed and built several isolation laboratories for highly infectious diseases in hospitals in anticipation of Ebola outbreaks hitting Southeast Asia. POCT instruments are operated inside a biosafety cabinet within the controlled airflow isolation area by personnel wearing PPE, which is donned in a changing area within the isolation laboratory. POCT tests include critical care test clusters. After working, personnel doff PPE in a separate area under strict precautions that avoid contamination through autoclaving. Specimens are passed into the isolation laboratory through a double door isolator. The essence of the approach is discrete spatial isolation and simultaneous control of environmental conditions. |
Figures present clever isolator designs with POCT inside used in Sierra Leone and detail POC instruments. The authors conclude that limited access...contribute to the initial failure to contain the outbreak in West Africa and...outbreaks will be...terminated more efficiently...through greater access to portable, easy-to-use diagnostic assays. |
| Diers *Med Sante Trop* 2015 | Mali, West Africa | **Mobile laboratories for rapid deployment and their contribution to the containment of emerging diseases in Sub-Saharan Africa, illustrated by the example of Ebola virus disease**
The authors propose a framework in which these mobile laboratory units can strengthen epidemiological surveillance and contribute to containing outbreaks of emerging diseases in Sub-Saharan Africa. Rapidly deployable POC units can diagnose close to outbreak sites and significantly speed delivery of results, thus facilitating epidemic containment. |
| Mansuy *Lancet Infect Dis* 2015 De la Vega *ERAIT* 2016 | West Africa | **Mobile laboratories for Ebola and other pathogens**
**Diagnosis and management of Ebola samples in the laboratory**
The authors present outbreak response workflow from the point of view of mobile laboratories during the West African Ebola outbreak of 2014–2016. Mobile laboratories located in areas where Ebola was spreading in West Africa drastically reduced the time between collection of biological specimens and return of results. The shorter the delay in obtaining a test result, the better confirmed cases can be managed, and cases of potential but unconfirmed disease can be monitored, reducing virus transmission. A reactive network of mobile laboratories should offer differential diagnoses for Ebola, malaria, shigellosis, cholera, and typhoid in context of local epidemiologic data. |
| Racine *Hum Vaccin Immunother* 2019 | Canada | **Challenges and perspectives on the use of mobile laboratories during outbreaks and their use for vaccine evaluation**
Mobile laboratories provide diagnostic capabilities for routine surveillance and patient identification during an outbreak and should be used in the evaluation of novel vaccines and therapeutics in remote locations. Clinical mobile laboratories include similar diagnostic capabilities as outbreak response mobile labs, but also include additional POC instruments. |
Table 2. Continued

<table>
<thead>
<tr>
<th>Strategy 4</th>
<th>ACFs, Quarantine, and Integrated POCT</th>
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<tbody>
<tr>
<td>Kost</td>
<td>Enhancing standards of care using innovative point-of-care testing</td>
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<td>The Ebola Spatial Care Path: accelerating point-of-care diagnosis, decision making, and community resilience in outbreaks</td>
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<tr>
<td></td>
<td>Point-of-care testing for Ebola and other highly infectious diseases: principles, practice, and strategies for stopping outbreak</td>
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</tbody>
</table>

The authors designed an ACF to integrate SCP principles for urgent Ebola care. The floor plan embeds POCT to be used in support of patients being screened for EVD and for those seriously ill and in need of critical care while in isolation. The ACF is free-standing, modular, expandable, and independent of hospital facilities to avoid contagion as an integrated community resource that increases efficiency and decreases risk, while using POCT to accelerate diagnosis and decision making, PPE-trained staff oversee diagnostic instruments. Modular partitions can be moved to increase the number of individual isolation rooms for suspected, but not confirmed, patients. The overall gross dimensions can be enlarged to increase capacity. ACFs can be replicated to meet triage needs anywhere for quarantine of patients suspected of having highly infectious diseases during outbreaks and epidemics.

Abbreviations: ACF, alternate care facilities; AMR, antimicrobial resistance; CDC, Centers for Disease Control and Prevention; COVID-19, Coronavirus infectious disease-19; ER, emergency room; EVD, Ebola virus disease; FDA, Food and Drug Administration; GIS, geographic information system; HIV, human immunodeficiency syndrome; MTU, mobile testing unit; PPE, personal protective equipment; SCP, spatial care path; TB, tuberculosis; VL, viral load.
patient, and others had been in the same ward for times ranging from 5 minutes to several hours.

Middle East Respiratory Syndrome–Coronavirus was not suspected and healthcare workers did not treat the first patient in isolation. The 68-year-old patient wandered from emergency room to emergency room where staff did not, in view of the patient’s recent travel history, have artificial intelligence available to help identify symptoms and signs, and did not assess nor treat the sentinel case in isolation or even in relative isolation provided by personal protective equipment. He had traveled to the Middle East and was not diagnosed until 9 days after seeking medical help.

The Middle East Respiratory Syndrome–Coronavirus epidemic in South Korea had a significant detrimental impact on the gross domestic product of the country. According to the Korean health minister, not enough was done to detect the first wave, stop spread, and end the outbreak. Said Prime Minister Park Geun-hye, "there were (sic) some insufficiency in the initial response, including the judgment on its contagiousness." Worldwide, Middle East Respiratory Syndrome–Coronavirus infected 2494 and killed 858 in 27 countries.

When COVID-19 hit South Korea and with only 16 cases reported, mostly free diagnostic testing (private service ~$125 per test) became available February 4 from Kogene Biotech, and by March 2, ramped up to 13 000 tests per day, the most aggressive screening in the world, nearly leveling the epidemic at approximately 8000 cases, which 2 weeks later numbered only 413 more at 8413 with more than a quarter million people examined, or one per 200 citizens tested. Testing was central to reiniging in the epidemic, because it led to rapid detection and minimized spread.

A single payer healthcare system, fewer restrictions with fast-track test approval following 10-day review, five companies producing, and a sweeping infectious disease law sped the response. Fast creative action resulted in drive-through clinics and pop-up sites in front of newly infected buildings—20 000/day tested at 635 sites funneling to 118 labs with similar methods, and 1200 personnel analyzing results in 6 hours, plus 1-day reporting to hospitals and subjects using a shared national database.

Innovators were left to their own means to design from different disease models and craft tests from genetic codes released by China in January. Additionally, they were incentivized by the earlier failure during the Middle East Respiratory Syndrome–Coronavirus epidemic and facilitated by government to access to credit card transactions, smartphone data, and security camera footage of subjects and contacts, maneuvers less practical and possibly illegal in the United States. South Korea was the first to implement “walk-thru” testing (40 sites at Incheon International Airport), a concept invented by the author in 2016 (see Table 2 and Figure 5, A and B). Throughput at Incheon is 30 minutes, including 2 to 3 minutes for sampling and 10 to 15 minutes to disinfect the booth, a substantial improvement compared to clinic approaches.

China.—China was caught off-guard and could not prevent the spread of COVID-19. At first, the Chinese central government denied it (Table 1). Figure 1 illustrates the rapid radial dissemination from the Wuhan epicenter to other cities and numerous other countries hastened by travel from the large international hub airport, high-speed train domestic connections, and national bus transit exchanges. A renowned POC expert who lives in Wuhan and publication colleague of the author noted there was no POC available at the time of the outbreak. Laboratory testing expanded from 200 daily late January to 7000/day mid-February. Infected and contacts were quarantined in hotels, schools, and 14 temporary and two new hospitals erected in 10 days. Overwhelmed, the virus spread among family members with mortality approximately 5%.

Misinformation, slow response to the sentinel case, and suppression of information by the Chinese central government misled health professionals. Draconian measures became necessary to limit geospatial dissemination with $R_0$ (reproduction number) estimated to be 3.68. Coronavirus is believed to live for hours in air particles and for days on surfaces. The key intervention is to separate the infected from healthy. Lockdown buys time, but testing identifies who has the disease. In Wuhan, doctors triaged and cared for up to 400 mild cases each shift. They knew who was infected, but some discharged tested positive again later, showing the virus had not been cleared. Next, those discharged went into quarantine for 2 weeks, rather than allowed home. By February 18, $R_0$ was 0.32.

The outbreak underscores the need to establish Point-of-Careology as a medical discipline in China and other countries and to enable public health with mobile diagnostics. More effective national strategies supported by national POC policy and guidelines would have helped allay panic among Wuhan citizens when they learned they were quarantined within the highest risk area in the world. They swamped local emergency rooms and hospitals. They could not leave the city to seek medical care, although 5 million did escape during the run-up to lockdown, just to spread COVID-19 to other cities like Beijing and Shanghai. Hence, efforts to control an epidemic without identifying and isolating cases and their contacts are at best partially effective.

United States.—With inadequate diagnostic testing and CDC guidelines initially limiting testing to only patients already seriously ill (see Figure 4), the United States was caught unprepared and extremely disadvantaged. Even 7 weeks from discovery of the first COVID-19 case, state testing was not consistent. By March, overall, only one in 800 to 1000 were being tested. Commercial laboratories could not provide timely results. With scant testing, states were unable to implement a strategic approach to containment. Hence, shutdowns ensued.

Of necessity, adaptive and innovative POC strategies appeared, shown by the path on the left in Figure 5A, to alleviate prolonged critical paths to diagnostic confirmation. Several regions still have to endure uncertainty, because testing is not widely available, even for those who are sick. Public health laboratories were never capacitated to be on the front lines of a pandemic. Not knowing who is infected generates fear and panic.

In California, Stanford Medicine led the paradigm shift to POC screening, and for good reason. Santa Clara County in which Stanford University resides had 459 cases and 17 deaths (at the time of writing), second highest in California behind much larger Los Angeles. The spread of COVID-19 regionally in Silicon Valley caught the attention of the wealthy elite living there. Other communities in California were stuck on the slowest (critical) path (see Figure 5B). The California epidemic is continuously being underestimated, because without adequate testing no one knows who has COVID-19.

In fear of saturation of hospital beds, especially intensive care already in short supply, and further human losses, a...
Table 3. Point-of-care (POC) Geospatial Concepts for Infectious Diseases

<table>
<thead>
<tr>
<th>Concept 1</th>
<th>First Author, Journal/Y/Reference</th>
<th>Country, Setting, or Focus</th>
<th>Geospatial Science Tool, Title of Paper(s), Synopsis, and Impact Analysis</th>
</tr>
</thead>
</table>
| Concept 1 | Kost22 Am J Clin Path 2006        | Phang Nga, Phuket, Krabi, and Trang Provinces in coastal Thailand; and Louisiana | Geographic Risk Assessment and Infectious Disease Patterns  
Katrina, the Tsunami, and POC: optimizing rapid response diagnosis in disasters  
The authors assessed how POC can optimize diagnosis, triage, and patient monitoring during disasters. They recommended handheld POC, airborne critical care testing, and disaster-specific mobile medical units in SWNs worldwide in anticipation of future disasters, complex emergencies, and public health crises. In Thailand, tests for infectious diseases, microbiology laboratories, and blood culture capability are badly needed to deal with acute infections in small hospitals |
| Gundlapalli23 AMIA Symposium Proceedings 2009 | Salt Lake City, Utah, USA | Social network analyses of patient-healthcare worker interactions: Implications for disease transmission  
Patients and HCWs...represent a unique social network in which the risk of transmission of an infection is considered to be higher for both...In sum, the patient-HCW network exhibits strong small world property...that must be considered) to prevent the spread of infectious diseases in healthcare settings |
| Kamanga24 Malaria J 2010 | Rural health centers, Zambia | Rural health centers, communities and malaria case detection in Zambia using mobile telephones: a means to detect potential reservoirs of infection in unstable transmission conditions  
Adequate supplies of rapid diagnostic tests are essential in health centers. Mobile telephones facilitate case detections in multiple locations, thereby saving time. The system can be expanded throughout the country to support rapid strategic targeting of malaria interventions |
| Kleczkowski25 J R Soc Interface 2012 | United Kingdom (theoretical study) | Searching for the most cost-effective strategy for controlling epidemics spreading on regular and small-world networks  
The authors present a combined epidemiologic and economic model for control of diseases spreading on local and SWNs. Treatment is only desirable if the disease spreads on a SWN with sufficiently few long-range links; otherwise it is optimal to treat globally. The effectiveness of local (ring-vaccination or culling) and global control strategies is analyzed by comparing the net present values of the combined cost of preventive treatment and illness |
| Kost26 J Demography (Chulalongkorn University, Bangkok) 2012 | Chiang Rai Province, Northern Thailand and border regions of Laos PDR | HIV, population dynamics, and rapid strategies for medical diagnosis in the northern most province of Thailand—Chiang Rai  
Innovative, effective, and efficient HIV POC tests and viral load monitoring should be extensively implemented in province hospitals, primary care units, HIV clinics, and the home with self-testing, in order to meet the standard of care, improve case discovery, and facilitate evidence-based decision-making for therapy and its follow-up. Health facilities should be available in border areas and at entry points in order to perform HIV POC screening of migrants, tourists, traders, and traffickers |
| Kost27 Point of Care 2012 | Bangkok, Thailand | Diagnostic testing strategies for health care delivery during the Great Bangkok Flood and other weather disasters  
Feasibility of POC was demonstrated in previous flood episodes (e.g., Hurricane Katrina) and again during the Great Bangkok Flood, although on a limited basis. Leptospirosis was diagnosed by PCR, not yet amenable to testing directly at the site of need |
| Kost28 Point of Care 2012 | Phang Nga Province, South Thailand | Strategic point-of-care requirements of hospitals and public health for preparedness in regions at risk  
The authors studied health resources and POC requirements for urgent, emergency, and disaster care in Phang Nga Province, Thailand, after the tragic 2004 Andaman Sea Tsunami; determined instrument design specifications through a direct needs assessment survey; described POC test menus useful in the SWN; and assessed strategies for preparedness. Staphylococcus aureus, SARS, Streptococcus pneumoniae, and hepatitis B virus were top infectious disease problems. Temperature, vibration, humidity, and impact shock were 4 important environmental conditions during extreme conditions. The results tell us how to integrate POC infectious disease testing |
| Kost29 Point of Care 2013 | Phang Nga Province, South Thailand | POC value proposition for disaster preparedness in small-world networks: post-Tsunami Phang Nga Province, Coastal Thailand  
This study identified geographic sites at high risk in the event of a new tsunami. Value proposition strategies built on post-tsunami advances enhance SWN POC preparedness, as well as daily emergency care. Daily use of POC improves chances of high-quality response during epidemics, if POC is positioned shrewdly in vulnerable geographic sites |
<table>
<thead>
<tr>
<th>First Author, Journal/Y/Reference</th>
<th>Country, Setting, or Focus</th>
<th>Geospatial Science Tool, Title of Paper(s), Synopsis, and Impact Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piggott30,31 eLIFE 2016</td>
<td>Sub-Saharan Africa and Oxford University</td>
<td>Mapping the zoonotic niche of Ebola virus disease in Africa30 and Updates31 Investigators mapped the risk of Ebola infection in Sub-Saharan Africa from the west coast (Guinea, Liberia, Sierra Leon) across the Democratic Republic of the Congo to the east coast (Somalia, Kenya, Tanzania). A risk map helped design spatial grids comprising SWNs, GISs, and topomaps with POCT embedded at essential nodal points to help contain Ebola outbreaks</td>
</tr>
<tr>
<td>WHO32 Global TB Report Chapter 3 (2019)</td>
<td>Global</td>
<td>TB disease burden—patterns of resistance In 2018, there were ~500 000 new cases of rifampicin-resistant TB of which 78% had MDR TB with the largest global share in India (27%), China (14%), and Russia (9%). The challenge for POCT is to detect cases of multiply resistant TB worldwide</td>
</tr>
<tr>
<td>WHO32 Global TB Report Chapter 4 (2019)</td>
<td>Worldwide</td>
<td>TB diagnosis and treatment—use of rapid diagnostic testing Increasing access to early and accurate diagnosis using a WRD is one of the main components of TB laboratory-strengthening efforts under the End TB Strategy. Countries should adopt policies that include diagnostic algorithms in which a WRD is the initial diagnostic test for all people with signs or symptoms of TB. Globally, 2.2 million new and relapse TB cases were identified by a WRD in 2018</td>
</tr>
<tr>
<td>Kost1,34 InCon Symposium and AMR Grand Challenge Panel (2020)</td>
<td>COVID-19 panepidemic and antimicrobial resistance worldwide</td>
<td>Geospatial “Hot Spots” Need Rapid Point-of-Care Diagnostics to Stop Highly Infectious Threats and Antimicrobial Resistance33 and Addressing Antimicrobial Resistance Through Public-Private Partnerships and the NIH-BARDARA Grand Challenge34 Increasingly, we observe the adverse personal, societal, economic, and cultural impact of outbreaks, antimicrobial resistance, and disasters. POC strategies can mitigate risk, reduce harm, and improve crisis standards of care. Global solutions integrate national POC policy and guidelines, distributed financial burden, and reasonable business models. The NIH-BARDARA Grand Challenge offers a $20 million prize for the best antimicrobial resistance POC diagnostic technology</td>
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<tr>
<td>Concept 2</td>
<td></td>
<td>Space-Time Cluster Analysis and Geosentinel Surveillance</td>
</tr>
<tr>
<td>Glatman-Freedman16 / Infect. 2016</td>
<td>Israel</td>
<td>Near real-time space-time cluster analysis for detection of enteric disease outbreaks in a community setting Stool isolation data for Salmonella, Shigella, and Campylobacter from patients of a large Health Maintenance Organization were analyzed weekly by ArcGIS and SaTScan. Cluster analysis demonstrated capability to complement enteric disease surveillance. Scaling up the system can further enhance timely detection and control of outbreaks</td>
</tr>
<tr>
<td>CDC37 Antibiotic Resistance Threats in the United States 2019</td>
<td>East Asia, South Asia, Africa, &amp; South America</td>
<td>Drug-Resistant Candida auris (Pathogen Summary) A vector map illustrates geospatial spread of resistant C. auris, which was first identified in Asia in 2009 and quickly caused severe infections around the world, including antimicrobial resistance clusters in several states in the United States. C. auris can be carried on skin without causing infection, allowing spread to others. Deemed a global urgent threat, C. auris often is MDR, with some strains (types) resistant to all 3 available classes of antifungals</td>
</tr>
<tr>
<td>Concept 3</td>
<td></td>
<td>Newdemics, Public Health, and Point-of-Careology</td>
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<tr>
<td>Kost19 Point of Care 2006</td>
<td>Public health vision</td>
<td>Newdemics, Public Health, Small-World Networks, and POCT Newdemics are defined as unexpected and disruptive problems that affect the health of large numbers of individuals in a crowded world. Newdemics demand dynamic value strategies in complex adaptive systems. POCT allows demographic care units to continue serving critically ill clusters of people by relocating diagnostic, monitoring, and therapeutic resources through fast, patient-focused, and disease-specific evidence for decision making during outbreaks, complex emergencies, and disasters. The COVID-19 pandemic is an example of a newdemic uniquely devastating in a world of more than 7 billion people highly connected by air transportation, unsafe and unprepared for infectious crisis, not cooperating peacefully to survive, and crowded together, yet severely interdependent socially, economically, and culturally</td>
</tr>
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</table>
national emergency was declared, local communities were ordered into lockdown, enterprises were closed, safe spacing was mandated (by law, ordinances), and strong guidelines enforced (e.g., 2-m separation). The military was called in to increase both testing and hospital capacity. In effect, alternate care facilities (Figure 6) cropped up to deal with the surge. One company (Ativa, St. Paul, Minnesota) claimed the ability to detect telltale immune response within a couple of days, which would improve civil management.

**STEALTH TRANSMISSION**

We define delta \( t_{Dx} \) as the time the diagnosis is confirmed minus the time the patient is infected, or, \( \Delta t_{Dx} = t_{confirmed} - t_{infected} \). The goal of POC strategies is to minimize \( \Delta t_{Dx} \). Next, the time delay from infection to symptoms, \( \Delta t_{Sx} = t_{symptoms} - t_{infected} \), tells us how quickly the patient responds pathophysiologically. Note that both \( \Delta t_{Dx} \) and \( \Delta t_{Sx} \) are > 0.

We do not know when a patient is infected, so subtracting the two deltas, \( \Delta t_{Dx} - \Delta t_{Sx} = \left[ t_{confirmed} - t_{symptoms} \right] - \left[ t_{infected} \right] \), an interval of maximum risk during which safe spacing and sheltering are crucial. This interval should be minimized, so providers can counsel patients wisely, whether in person or via telehealth. Hence, let people self-test and have public health practitioners screen freely with accurate testing in the community.

Stealth (silent) carriers may never notice or have symptoms. Among those mingling socially, uncountable SARS-CoV-2 stealth transmissions have fueled regional epidemics at exponential rates. Infectious individuals pass SARS-CoV-2 to others, both unaware (\( \Delta t_{Dx} - \Delta t_{Sx} \) can be < 0). Additionally, repeat testing may be needed to rule out stealth recurrence and potential transmission to others when supposedly recovered patients return to social interaction and gainful employment.

Ideally, proactive POC diagnosis results in \( \Delta t_{Dx} < \Delta t_{Sx} \). That is, the patient is diagnosed before becoming symptomatic, for example, when there is a history of exposure and viral load enables detection by the test method. Therefore, testing must transition away from the delays and mistakes of distant reference laboratories to accurate POC and rapid tests that are highly accessible.

OraSure has received a Biomedical Advanced Research and Development Authority contract for in-home testing. The test will use oral fluid to detect antigens in 20 minutes. An Emergency Use Authorization (EUA) is expected in 4 to 6 months. Home testing would improve access and avoid provider exposure, but a false-negative result could lead to a false sense of security and social risk.

SARS-CoV-2 pulmonary infection compromises gas exchange swiftly, leading to respiratory collapse, but the virus also causes multi-organ failure. According to news interviews of Italian intensivists, pneumonia is highly tissue destructive. Patients complain of “chest hurting,” “lungs smaller,” and “trouble breathing.” Nasal and oral specimens may not capture adequate quantities of Coronavirus, which may be present in low dose initially.

Therefore, the false negative rate (FN) will vary as a function of both time, FN = FN(0), in the patient’s course of disease and also the site of sampling. With some tests, informal news reports have claimed FNs as high as 40%. Shared human specimen banks and global resources can help test developers quickly decrease FN to increase sensitivity \( \left[ \frac{TP}{TP + FN} \right] \), given appropriate assay genome targeting optimizes specificity \( \left[ \frac{TN}{TN + FP} \right] \).
While still handicapped by inadequate diagnostic testing and yet to be clarified through US epidemiology studies, it appears 25% to 50% of infected patients carry the virus silently.72,73 In Wuhan prior to travel restrictions, infection went undetected in approximately 86% and stealth (silent) transmission to confirmed cases was 79%.74 Some patients discharged had not cleared the virus. In some cases, it takes up to 2 months for a diagnostic test to become negative, a long period for possibly mandatory shelter and time away from family, friends, and work.73

**COVID-19 AND EBOLA DIAGNOSTICS**

Diagnostic testing is needed to reveal stealth transmission, guide treatment decisions, accurately track the spread of outbreaks, and stop them. A diagnostic outcomes review by Pang et al52 documented one study that showed respiratory specimens were positive for the virus while serum was negative in the early period. The same authors found 7 potential commercial diagnostic kits, mostly reverse transcriptase-polymerase chain reaction, for SARS-CoV-2 from various countries, while Sheridan53 published a list of 13 as early as mid-February. Table 3 summarizes the FDA EUA status of Ebola diagnostics and EUAs for Coronavirus up to mid-March when regional epidemics morphed into a global COVID-19 pandemic and the United States had to declare a national emergency.

Early classified reports by the United States intelligence community about the spread of COVID-19 increased in volume and intensity in January and February and might have slowed the outbreak, had they not been ignored by the White House and Congress, some members of which profited from inside information by quietly selling stock.75 At that time China was engaged in a cover-up (see Table 1). CDC advice about the seriousness of the outbreak was sidelined by misdirected officials in the White House, which left states unprepared. But then, early flaws in the CDC diagnostic test disabled the nation’s ability to trace and track COVID-19.

Colorado had access to only 250 tests per day by March 20.76 Police blocked the entrance to a mobile clinic set up by the Colorado Health Department, and people in hundreds of cars waited for hours to be tested in the Denver Coliseum, only to be turned away without being tested and find out testing would shift to hard hit privileged ski areas near Telluride with no further services available in Denver.76 Elsewhere, some NBA players and politicians received privileged testing. The United States was forced to shift to safe spacing/social distancing, shelter-at-home, and lockdown, foregoing the opportunity of building sound strategies for individual communities based on accessible widespread POCT.

In early March, more than 70 companies were reported by the Wall Street Journal to be vying for commercial production and introduction of COVID-19 tests based on a variety of detection principles, such as virus antigen, antibody-based serology, and molecular detection, including real-time polymerase chain reaction on a POC platform.77 Soon, numerous antibody tests entered the commercial race, but because of inaccuracy, few received an EUA. On February 29, the FDA implemented new policy that allowed individual states to approve Coronavirus tests and enabled companies to release them without approval pending retrospective review, which drew criticism from experts.78 False negatives would lead to heightened exposure, that is, more harm than good, while false positives (possible from use of ordinary water or cotton swabs for sampling) would lead to waste of time, misused resources, and drug depletion. March 20, the FDA cleared a 45-minute molecular diagnostics test, which adds to testing capacity, but is not fast enough for high-throughput patient screening.79

**Figure 5.** Safe spacing diagnostic testing. FAST/POC (facilitated-access, self-testing at the point of care) means the patient performs self-testing (A) with the help of a safely spaced facilitator. POCT/Pod (POCT personal outbreak [outcome] detection [device]) means the patient in an isolation pod (B) follows e-instructions for testing, say using telehealth. After the patient exits, the pod begins a self-cleaning hygiene cycle. Implementations include walk-in/through, drive-up/in/through, triage near emergency rooms, pop-ups near factories, airports, and any safely spaced testing sites at points of care.
This author repeatedly has observed reverse-engineered POC tests pirated and manufactured in China, then rolled out in surrounding countries in Asia. Physicians forced to see 100 to 150 patients per day in stressful limited-resource rural settings quickly learn, usually within 1 week, inaccurate tests are worthless and abandon them, a kind of failure under fire that separates the good from the bad by brute force. Being inside one of the Chinese manufacturing plants and talking to the scientists typically reveals little or no clinical validation, just small-sample cross-over studies performed with lax sensitivity and specificity thresholds. However, standards will improve, motivated by the initial failure of Coronavirus testing in China.

Trial and error, or learning the hard way, does not substitute for sound laboratory science, and under no circumstances should POC ever be an excuse for inaccuracy. Retailers in the United States are planning drive-through testing sites in order to improve access to diagnostics. Subjects being tested will be required to remain in vehicles and cannot enter stores. Front-line operatives don personal protective equipment to avoid the kind of disaster that occurred during the 2014 to 2016 Ebola epidemic in West Africa where untold numbers of healthcare providers perished from the disease.

Until multiplex testing is available, affordable, timely, and deliverable at points of need, one should use the POC or rapid COVID-19 testing method with the best proof of high sensitivity and high specificity, both at least 97.5%. Sensitivity of 100% would help slow contagion. We do not want infected people (false negatives) unknowingly walking around spreading the disease. Amid severe shortages of test kits, reagents, nasal/oral swabs, and other supplies, the United States has had to prioritize testing to those older than 65 years, frontline healthcare workers, and patients hospitalized with symptoms.

Rationing in the United States is in great contrast to the highly rational approach established weeks prior in South Korea. Propelled by volumes in the tens of thousands per day, testing in that country generally is allocated to those with symptomatology based on written questionnaire, abnormal vital signs (especially body temperature) determined by measuring on site, and direct evidence garnered by brief interview in the drive-through. With orders of magnitude more testing available, South Korea checked the outbreak by the end of March when test volume hit 300,000 (10 times US volume) and daily reporting was facilitated by an internet accessible national cloud database repository updated each morning.

Figure 6. Spatial care path with molecular diagnostics and hybrid solution. The spatial care path is the fastest route to diagnosis, care, and treatment. Quarantine and isolation (left) prevent infected patients from spreading contagion. Diagnostics can alter the course of an outbreak. To rule out COVID-19, highly sensitive tests are needed. However, false negatives may vary with changes in prevalence over time, so caution is advised.
<table>
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<tr>
<th>Medical Indication</th>
<th>Action Graphic</th>
<th>Status/Description</th>
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<tbody>
<tr>
<td><strong>I. COVID-19</strong></td>
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<tr>
<td>I.A. First FDA EUA</td>
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<tr>
<td>&quot;CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel (CDC)&quot;</td>
<td>FDA EUA</td>
<td>February 4, 2020</td>
</tr>
<tr>
<td>Oligonucleotide primers/probes target regions of the virus nucleocapsid (N) gene, 1 set for universal detection of SARS-like coronaviruses, and 2 sets for specific detection of COVID-19. An additional set detects human RNase P gene (RP) in control samples and clinical specimens. Assay subject to modifications.</td>
<td>March 15 (reissuance)</td>
<td>Presumptive qualitative detection of nucleic acid from the COVID-19 in upper and lower respiratory specimens (e.g., nasopharyngeal/oropharyngeal swabs, sputum, lower respiratory tract aspirates, bronchoalveolar lavage, and nasopharyngeal wash/aspirate or nasal aspirate) collected from individuals who meet CDC criteria for COVID-19 testing. Testing is limited to CDC-qualified laboratories certified under CLIA '88 to perform high-complexity tests. Positive results indicate active infection, but do not rule out bacterial infection or co-infection with other viruses. Negative results do not preclude infection and should not be used as the sole basis for treatment or other patient management decisions. Negative results must be combined with clinical observations, patient history, and epidemiologic information. Runs on Applied Biosystems 7500 Fast Dx RT-PCR instrument with SDS 1.4 software.</td>
</tr>
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<p>| I.B. Next Set—Summaries | | |
| New York SARS-CoV-2 | EUA Feb 29, reissuance | Real-time RT-PCR Diagnostic Panel performed at the Wadsworth Center, NYSDOH. Amended as resulting positives, rather than presumed positives. |
| Cobas SARS-CoV-2, Roche Molecular Systems | EUA March 12 | Cobas 6800/8800 technology. |
| TagPath COVID-19 Combo Kit, Thermo Fisher Scientific, Inc. | EUA March 13 (CE Mark) | Uses Applied Biosystems 7500 Fast Dx Real-Time PCR instrument or other authorized instruments and results in 4 h. |
| Panther Fusion SARS-CoV-2, Hologic, Inc. | EUA March 16 | Performed on the Panther Fusion System for integrated nucleic acid testing. Automates sample processing, amplification, detection, and data reduction. Time to first result 2.4 h. Throughput 1150 tests in 24 h. |
| COVID-19 RT-PCR Test, Laboratory Corporation of America | EUA March 16 | Purified nucleic acid reverse transcribed into cDNA followed by PCR amplification and detection with the 1-Step RT-PCR Master Mix on the Applied Biosystems QuantStudio7 Flex. |
| Lyra SARS-CoV-2 Assay, Quidel Corp. | EUA March 17 and 23 amended | Purified nucleic acid is reverse transcribed into cDNA followed by PCR amplification and detection with the Lyra SARS-CoV-2 Assay on the Applied Biosystems7500 FastDx Real-Time PCR instrument. Amended EUA allows additional instruments to be used. |
| Quest SARS-CoV-2 rRT-PCR, Quest Diagnostics Infectious Disease Systems | EUA March 17 | Uses Applied Biosystems 7500 Real Time PCR System or ABI 7500 fast system run as a standard ABI 7500. |
| Abbott RealTime SARS-CoV-2 assay, Abbott Molecular | EUA March 18 | Performed on the Abbott m2000 System consisting of a sample preparation unit, the Abbott m2000sp, and an amplification and detection unit, the Abbott m2000rt. Batch testing. |
| Simplexa COVID-19 Direct, DiaSorin Molecular LLC | EUA March 19 | Uses the LIAISON MDX with LIAISON MDX Studio Software, the Direct Amplification Disc, and associated accessories. |
| ePlex SARS-CoV-2 Test, GemMark Diagnostics, Inc. (BARDA $749 000 grant for incorporating test into respiratory panel) | EUA March 19 | The ePlex instrument automates nucleic acid testing including extraction, amplification, and detection, combining electrowetting and GemMark's eSensor technology in a single-use cartridge for detection of SARS-CoV-2 RNA from nasopharyngeal swabs. |
| Genesig Real-Time PCR COVID-19 Primerdesign Ltd., Novacyt Group, UK | EUA March 20 | Detects using an authorized RT-PCR Master Mix on authorized real-time PCR instruments. Results within 2 h. Accurate controls to confirm extraction and assay validity. Lyophilized components for ambient conditions. No cold chain shipping. CE-IVD marked for in vitro diagnostic use in Europe. |
| Xpert Xpress SARS-CoV-2 test Cepheid | EUA March 20 | Qualitative detection in 45 min of nucleic acid from SARS-CoV-2 in nasopharyngeal swab and/or nasal wash/aspire specimens collected by healthcare provider. Uses the GeneXpert Dx and GeneXpert Infinity systems. |
| BioFire COVID-19 Test, BioFire Defense, LLC, BioMerieux | EUA March 23, Others pending | Uses the FilmArray2.0 and FilmArrayTorch instrument systems. Detects virus in nasopharyngeal swabs in 45 min. Also offer control kit, SARS-CoV-2 R-Gene on PCR platform, and RP2.1 respiratory panel that detects 21 other pathogens. |</p>
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<tbody>
<tr>
<td>Accula SARS-CoV-2 Test, Mesa Biotech Inc. (BARDA $561,000 grant for development of the test)</td>
<td>EUA March 23</td>
<td>POC qualitative test using visual detection in 30 min for detection of nucleic acid from the SARS-CoV-2 in throat swab and nasal swab specimens combined, run on the AcculaDock and SilarisDock. Designed for screening facilities, physician office labs, urgent care centers, and long-term nursing settings. Purified nucleic acid is reverse transcribed into cDNA followed by PCR amplification and detection using an authorized real-time PCR instrument. Detects ORF 1a and N genes down to 20 copies/mL using a 400-μL sample. Does not meet certain requirements otherwise required by applicable federal law.</td>
</tr>
<tr>
<td>PerkinElmer New Coronavirus Nucleic Acid Detection Kit, PerkinElmer, Inc.</td>
<td>EUA March 24 (CE Mark)</td>
<td>Cartridge-based test that reports positives in 5 min, negatives in 13 min on 6.6-lb portable ID NOW molecular platform. Bench-top instrument suitable for physician offices and urgent care clinics. Other tests available are influenza, strep, and RSV.</td>
</tr>
<tr>
<td>Fluzergy partnered with Infectious Disease and Global Health at the University of California, San Diego</td>
<td>EUA Pending</td>
<td>Cardiograph and test card-based portable system. Preanalytical processing method is collect patient sample following standard practice, transfer flocked swab into 1 mL FluxergyBuffer and vortex, use 14 μL of sample and add 130 μL of Master Mix, and load onto sample port and start the 45- to 60-min run.</td>
</tr>
<tr>
<td>Diazyme Laboratories, Life sciences affiliate of General Atomics</td>
<td>Pre-EUA release, March</td>
<td></td>
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<tr>
<td>I.C. Foreign</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ViroKey SA201 COVID-19 RT-PCR Test, Vela Diagnostics, Singapore</td>
<td>February, 2020, Report submitted for EUA</td>
<td>The ViroKey SA201 COVID-19 RT-PCR test will be able to detect and differentiate the Wuhan Coronavirus from other closely related Coronavirus, such as SARS and MERS. To enable high-throughput processing of 96 samples in 4 hr, the test is configured for an automated workflow consisting of the Sentosa SX101 instrument, in conjunction with the Applied Biosystems 7500 Fast Dx Real-Time PCR instrument (ABI 7500 FAST DX) or the Sentosa SA201.</td>
</tr>
<tr>
<td>A*Star (Agency for Science, Technology, and Research) RT-PCR test kit, Singapore</td>
<td>February</td>
<td>Approved by the Health Sciences Authority, Singapore. The Diagnostics Development (DxD) Hub—a national initiative led by A<em>celerate, the commercial arm of A</em>Star—supported the verification, validation, and production of the test. The test kit comprises a prepacked mix of reagents to test patient samples. The procedure allows hospitals and laboratories to conduct their own tests, widening the network of Singapore facilities that can screen patients for Coronavirus and reducing wait time for results allowing those infected to be treated quickly. Also shipped to China.</td>
</tr>
<tr>
<td>Wuhan Coronavirus Assay, Roche Diagnostics, Singapore</td>
<td>February</td>
<td>LightCycler 480 (MagNA Pure 24) Coronavirus (TIB MOLBIOL LightMix) modular assays for screening and confirmation: Wuhan E-gene assay to detect SARS and Wuhan 2019 Coronavirus pneumonia virus, Wuhan RNA-dependent RNA polymerase assay specific for the detection of Wuhan Coronavirus, and Wuhan N-gene assay to detect presence of Wuhan Coronavirus and other SARS-related viruses. Research use only.</td>
</tr>
<tr>
<td>Credo Diagnostics Biomedical, Singapore (EUA, EUAL pending)</td>
<td>CE Mark, March</td>
<td>Assays results in 20 min on POC platform called VitaPCR.</td>
</tr>
<tr>
<td>QIAstat-Dx Respiratory 2019-nCoV Panel, Qiagen, Hilden, Germany</td>
<td>February</td>
<td>Integrated sample prep and RT-PCR detection of 21 respiratory pathogens. Samples and reagents delivered in assay cartridges and analyzed in desktop QIAstat-Dx Analyzer. Results in 1 h. Prototype panel including COVID-19 test shipped for clinical performance assessment in 4 hospitals in China after clinical evaluation in a Paris hospital.</td>
</tr>
<tr>
<td>BioChip Technology and Focused Respiratory Panel, Randox Laboratories, UK</td>
<td>March</td>
<td>Identifies the lethal strain of SARS-CoV-2 and differentiates other nonlethal variants with the same symptoms. Evidence Investigator semi-automated instrument reports 54 patient multiple results in 5 h. Vivalytic Viral Respiratory Tract Infection Array identifies SARS-CoV-2 and differentiates it from 9 others, including all known Coronavirus—Influenza A/B, Influenza A/B, RSV.</td>
</tr>
<tr>
<td>Mologic and partners in UK, Wuhan, Malaysia, Latin America, and Senegal, Africa</td>
<td>March</td>
<td>Producing 10-min sensitive (1 pg/mL) lateral flow visually read immunoassays, one for antigens in saliva to be used for triage, track, and trace, and another for IgG and IgM antibodies in blood to be used for patients in isolation and recovering or recovered. Funded by the Joint Initiative on Research for Epidemic Preparedness, Wellcome Trust, and Department for International Development.</td>
</tr>
<tr>
<td>SARS-COV-2 RNA Testing Kit, Sansure Biotech, Changsha, Hunan Province, China</td>
<td>February</td>
<td>Developed as a portable molecular workstation based on a 1-tube platform with no extraction lysis buffer that releases target at room temperature. Sample prep 10 min. Deployed for high specificity in Wuhan City Hospital.</td>
</tr>
<tr>
<td>Medical Indication</td>
<td>Action Graphic</td>
<td>Status/Description</td>
</tr>
<tr>
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<tr>
<td>DNBSEQ-T7 Gene Sequencer, MGI Tech Co., Ltd., China</td>
<td>February</td>
<td>Used in Wuhan, Hubei Province. MGI DNA sequencing instruments utilize the state-of-the-art core technology called DNBSEQ. DNBs (DNA nanoballs) are pumped with the fluidics system and loaded onto a patterned array chip. Sequencing primer is then added and hybridized to the adaptor region of the DNB. The sequencing reaction starts by pumping sequencing reagents containing fluorescently labeled dNTP probes and DNA polymerase. Images are taken after the fluorescently labeled probes on the DNB are excited with lasers. The images are converted into a digital signal using MGI propriety software, then used to determine the DNA sequence of the sample.</td>
</tr>
<tr>
<td>Coronavirus nucleic acid assay, Chinese National Institute for Viral Disease Control and Prevention</td>
<td>February</td>
<td>Primers and probes for detecting the novel Coronavirus with RT-PCR. In widespread distribution in China.</td>
</tr>
<tr>
<td>Real-time fluorescent RT-PCR kit for detecting 2019-nCoV, BGI Group, Beijing, China</td>
<td>February</td>
<td>RT-PCR results in several hours. Also producing 2019-nCoV nucleic acid detection kit using combinatorial probe-anchor synthesis method. Emergency approval granted for both by China’s National Medical Products Administration.</td>
</tr>
<tr>
<td>Coronavirus Gene Detection Kit, Amoy Diagnostics, Xiamen, China</td>
<td>February</td>
<td>PCR-based rapid detection kit. Seeking emergency approval from China’s National Medical Products Administration.</td>
</tr>
<tr>
<td>Canon Medical Isothermal Fluorescent Detector and Nagasaki University, Japan</td>
<td>March</td>
<td>Based on LAMP method developed by Eiken Chemical Co.</td>
</tr>
<tr>
<td>I.D. Industry and Other Sources</td>
<td>Companies with SARS-CoV-2 tests</td>
<td>March</td>
</tr>
</tbody>
</table>

II. Ebola Virus Disease

The OraQuick Ebola Rapid Antigen in vitro diagnostic single-use immunoassay for the qualitative detection of antigens from viruses within the Ebola virus genus does not differentiate between these viruses. Negative results do not preclude infection. Testing must only be performed when public health authorities have determined need and in accordance with current public health guidelines for specimens from (1) individuals with epidemiologic risk factors with signs and symptoms of Ebola or (2) recently deceased individuals with epidemiologic risk factors who are suspected to have died of Ebola.

<table>
<thead>
<tr>
<th>Medical Indication</th>
<th>Action Graphic</th>
<th>Status/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDC Ebola Virus NP and VP40 Real-time RT-PCR Assay (CDC)</td>
<td>October 8, FDA EUA (amended)</td>
<td>FDA allowed marketing of a rapid diagnostic test, first in the United States, to detect Ebola virus antigens (proteins) in human blood from living individuals and samples from recently deceased suspected to have died from Ebola (cardiaveric oral fluid). The test provides a rapid, presumptive diagnosis that must be confirmed. Reviewed under the de novo premarket review pathway, a regulatory pathway for low-to-moderate risk devices of a new type. Along with this marketing authorization, the FDA established criteria called special controls that determine the requirements for demonstrating accuracy, reliability, and effectiveness of tests intended to identify Ebola virus antigens. These special controls, when met along with general controls, provide a reasonable assurance of safety and effectiveness for tests of this type. This action also created a new regulatory classification, so subsequent devices with the same intended use may go through the 510(k) pathway and obtain clearance by demonstrating substantial equivalence to a predicate device.</td>
</tr>
<tr>
<td>FilmArray Biothreat-E test (Biofire Defense, LLC)</td>
<td>November 12, FDA EUA (amended)</td>
<td>Modified the authorized instructions for use to include additional data on analytical exclusivity wet testing and inclusion of associated limitations. If Ebola is suspected based on current clinical and/or epidemiologic screening criteria and testing is recommended by CDC and state and local public health, presumptively diagnose Ebola in ~1 h. Detects Ebola Zaire virus in whole blood specimens and also can be used with urine specimens when tested in conjunction with a patient-matched whole-blood specimen. If outside the United States, testing can be deployed in the field and also used for post-outbreak surveillance.</td>
</tr>
<tr>
<td>DPP Ebola Antigen System (Chembio Diagnostic Systems, Inc.)</td>
<td>April 2, FDA EUA (amended)</td>
<td>Modified the instructions for use labeling to update the cross-reactivity performance for Plasmodium malariae and Streptococcus pneumoniae in whole blood; and the endogenous interference data for rheumatoid factor, glucose, unconjugated bilirubin, cholesterol, and HAMA.</td>
</tr>
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</table>
TRANSFORMING PUBLIC HEALTH

Public health in the United States must adapt to the new normal of emergency preparedness and management.\(^{81,82}\) Practitioners must master social epidemiology, part of the basic science of public health; outbreak investigation; surveillance; laboratory science comprising POC detection, characterization, and confirmatory testing; and data networking for connectivity in order to tackle exposure to hazards.\(^{82}\) Education, hands on training, and experience with POCT is missing from public health schools, colleges, and programs, and these deficits should be corrected.\(^{39,58}\)

The Coronavirus pandemic is making this deficiency all too obvious and painful, as nations stagger through wave after wave of contagion under the increasing force of regional outbreaks without the ability to detect SARS-CoV-2 by objective diagnostic testing. Better strategy calls for revision of public health curricula to include POCT and for fundamental change in accreditation requirements, so all public health schools, colleges, and programs must teach the principles and practice of POCT. This will generate a newly capable workforce with adequate numbers of personnel responding to outbreaks at points in need. Recently introduced legislation would establish a national testing workforce.

Transforming public health will allow more professionals in the public health field to work closer to points of actual need and do so by adopting POC strategies and concepts. POC strategies also are needed to support critically ill patients placed in isolation, to quickly detect sentinel cases upstream on geospatial care paths before they visit emergency rooms, and to improve the efficiency and effectiveness of quarantine and treatment centers. Faster nucleic acid tests have become suitable to field use and cover a range of pathogens.

Therefore, moving public health directly to points of need must occur through understanding of diagnostic principles (e.g., evidence-based medicine), extension of the WHO primary care test list, and professionally integrated teamwork. Despite advances in knowledge with each outbreak, progress in public health preparedness is inadequate. CDC funding, even in the relief legislation, still is not adequate to assure the sustainability and capability of rapid diagnostic response in the United States and abroad.

POINT-OF-CARE CULTURE

Characteristic of emerging POC culture,\(^{83-85}\) people now urgently expect rapid diagnosis\(^{83}\) of high-risk viruses, namely SARS-CoV-2, implemented in conjunction with or at safe drive-up/in/through sampling stations. By mid-March, the FDA started allowing testing through commercial prereleases and direct sales of test kits to the public.\(^{78}\) However, the FDA disallowed use of EUAs for home testing, further log-jamming public access.\(^{86}\)

Nonetheless, numerous test formats and approaches are emerging, including disposable test strips, self-contained automated technologies, and other mobile or near-patient cartridge-, cassette-, or cuvette-based approaches, as well as assays in academic laboratories (see Table 4). Immunoassays are well suited to triage, track, and trace contagion in time,

### Table 4. Continued

<table>
<thead>
<tr>
<th>Medical Indication</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Xpert Ebola Assay rRT-PCR (GeneXpert, Cepheid Innovation, Inc.)</td>
<td>March 23, 2015, FDA EUA The Xpert Ebola Assay is a dual NP/GP target real-time RT-PCR test with a self-contained cartridge system that was detected during the 2014–2016 West Africa outbreak. It is listed here as an example of an Ebola diagnostic used in conjunction with the contemporary outbreak in the Democratic Republic of the Congo. Testing is performed in makeshift isolation laboratories near sites of migratory outbreaks, and when specimen transport is feasible, in reference laboratories.</td>
</tr>
</tbody>
</table>

Abbreviations: BARDA, Biomedical Advanced Research and Development Authority; CDC, Centers for Disease Control and Prevention; CE-IVD, European Conformity in vitro diagnostics; CLIA, Clinical Laboratory Improvement Act; COVID-19, coronavirus disease-2019; CPA, clinical practice advisory; CEPH, Cepheid; D-dimer, fibrinogen split product; FDA, Food and Drug Administration; HAMA, human anti-mouse antibody; LAMP, loop-mediated isothermal amplification; POC, point-of-care; RT-PCR, reverse transcriptase PCR; RSV, respiratory syncytial virus; SARS, severe acute respiratory syndrome; SARS-CoV-2, severe acute respiratory syndrome-coronavirus-2. Please see Kost et al\(^{15}\) for description, review, and chronologic development of the FDA EUAs for Ebola generated in conjunction with the 2014–2016 West Africa epidemic and its spread to the United States and other countries.
place, and space. They are also inexpensive, an advantage for limited-resource settings.

The COVID-19 pandemic demonstrates the need to think globally and act locally, but test locally where the people are in the context of their own culture. That properly fulfills expectations, the key to motivation, while delivering high sensitivity, specificity, and predictive values, to help stifle outbreaks like COVID-19. Public health failed to recognize the importance of POCT and the government could not provide diagnostic testing of any sort in a timely fashion.

POCT supports fundamental public health principles. Traceability of infected individuals by knowing test results, locations, and movement over time and across borders can help diminish the force of an epidemic and contain the spread of contagion within a given cultural dimension. Some countries (e.g., Thailand) now demand COVID-19 testing and physician certification of wellness within 72 hours before immigration of a foreigner.

Huge world financial losses warrant investment, which should be directed not just to vaccines, but also to the development of POC molecular diagnostics, for which there is both precedent and urgent need as the pandemic mushrooms. In the United States, public-private partnerships were called to task about the time the WHO declared a pandemic. Next, a declaration of a national emergency opened doors for funding and entrepreneurial enterprise supplying needed test volume. POC diagnostics should be available upstream for immigration screening, on cruise ships, in industrial sites, and at other points of first encounter worldwide.

Adaptations in south-eastern Asia and in individual US hospitals are notable, but have not yet generated isolation bed capacity or adequate experience quickly enough to deal with potentially large numbers of critically ill with COVID-19. People need access to testing. Ultimately, individual communities across America should be prepared to develop their own broad bases of response to threats. Alternate care facilities and diagnostic centers for community small-world networks will allow the new POC culture to respond efficiently and effectively.

**GOVERNMENT ROLE**

On February 26, 2019, the CDC, FDA, and Center for Medicare and Medicaid Services announced a new “Tri-Agency Task Force for Emergency Diagnostics” to help facilitate rapid availability of diagnostic tests during public health emergencies. The charter can be found at a link in Reference 87. The consortium states, “through the Tri-Agency Task Force for Emergency Diagnostics, CDC, FDA, and Center for Medicare and Medicaid Services, where appropriate, intend to coordinate the implementation of EUA in vitro diagnostics assays in laboratories within the US healthcare system, with the ultimate goal of improving responses to public health emergencies.” However, there was no task force plan to train public health students or POCT specialists in the use of EUA devices and associated quality control.

Except for one medical technologist, laboratory medicine professionals, public health educational institutions, and industries developing new EUA technologies appeared not to be represented. The Tri-Agency Task Force for Emergency Diagnostics’ focus on EUA in vitro diagnostics assays falls short of the need for strategically selected POC technologies that integrate and consolidate a broad range of tests. The CDC lost crucial time detecting initial COVID-19 by bungling information handling, test kits, reagent supplies, communications, and distribution. However, FDA EUA and WHO Emergency Use and Assessment Listings clearance/approval processes recently have facilitated several clever technologies, some now being implemented rapidly for COVID-19.

The FDA-issued guidance for COVID-19 on February 28, expanded it on March 16 to let states (“B,” 4 pursuing) authorize molecular, antigen, or antibody tests (without EUA), and then on March 26, clarified 3 more pathways. High-complexity Clinical Laboratory Improvement Act (“A”) and commercial (“C”) laboratories can validate internally, notify (98 notifications received), and then file an EUA within 15 days. C includes POCT, but not home testing. “D” applies only to antibody-based serology tests (38 tests in pathway) not requiring an EUA. Later, the FDA required 90% sensitivity and 95% specificity for antibody tests. Roche Diagnostics introduced an antibody test for venipuncture specimens, claimed the test has 100% sensitivity and 99.8% specificity, and recommended testing 14 days after infection. The current acceleration of EUA clearance using retrospective test review and open market concept must be refined and protocols codified for future sustainability. For details, please see FAQs.

Other nations (e.g., Malaysia and Thailand) required only 2 to 3 years to develop consensus guidelines, albeit omitting POCT for disasters, epidemics, and other public health crises. Notably, under extreme pressure, South Korea published guidelines for diagnosis of COVID-19 quickly, while calling for faster testing with “a system for developing, accrediting, and distributing rapid diagnostic testing, such as POC–nucleic acid tests,” similar to the mission of the “Grand Point-of-Care Challenge” published by the POCT•CTR in 2008.

**CONCLUSIONS AND RECOMMENDATIONS**

The United States must reinvent public health to survive and prosper. Notions like “flattening the curve” have merit as mitigation. However, POC geospatial strategies can supersede these public health measures by stopping and containing outbreaks as soon as they appear in time, place, and space.

POCT enables effective and efficient rapid response at points of need where specimens can be procured safely and testing performed quickly by providers and patients. Twenty-one recommendations follow (please also refer to Figure 7).

**Prepared Public Health Practitioners**

1. Public health professionals must adapt to the new normal of emergency preparedness for highly infectious diseases. They must be able to deliver diagnostic tests quickly and to points of need and to use molecular assays, serological surveillance tests (i.e., antibody tests), and case tracing to document immunity, certify wellness, and classify risk.

2. Public health academics, students, and practitioners must train in the principles and practice of POCT.

3. This can be achieved by embedding POCT education in public health schools, programs, and continuing education and accrediting the new learning objectives and practicum experiences.
4. Teaching, workshops, and continuing education can be drawn from POCT curricula tailored to meet the institutional goals and inspected under public health accreditation standards for inclusion of POCT. Apropos the pandemic, POCT courses are available online for distance learning via the Public Health Institute in San Diego.92

5. In China, the visionary concept of Point of Careologists has already been put forward,40 but did not have time to mature before the outbreak hit Wuhan. This valuable and timely clinical specialty will integrate medicine, public health, and POCT for immediate decision making.

**Expedited Innovation**

1. The FDA must codify the faster emergency use authorization pathways it introduced in order to ramp up production of POC technologies to meet crisis needs, but still assure accuracy through scientifically rigorous retrospective reviews of results.

2. Reviews should be conducted periodically and cumulatively with knowledge of the patient’s course and ultimate outcome.

3. Test performance should be available to the public in a national database on the FDA website.

**Point-of-Care Diagnostics**

1. Rapid response diagnostic tests must be both highly sensitive (to rule out) and highly specific (to rule in) in order to effectively manage surges of highly infectious diseases. Specimen banks would facilitate the development of accurate tests with high predictive values. Diagnostics also have a role in badly needed early warning systems and support of critically ill COVID-19 patients being transported by trains and other means to intensive care sites.

2. Providers may need to rule out influenza A/B and other respiratory infections, and if these tests are positive, then rule out SARS-CoV-2 co-infection. Testing of the febrile patient at fever clinics must differentiate viral from bacterial infections, but both could be present. Ruling in COVID-19 downstream when a febrile patient has obvious symptoms and signs is useful for confirmation and should be available to the public.
3. Fundamental investment should support research that reveals early diagnostic indicators of infection, such as daily trends in immune response, and that produces ultra-high sensitivity (100%) and ultra-high specificity (≥99%) multiplex diagnostics. Claims exceeding 97.5% should be validated by independent investigators with new subject and control groups because of the possibility of selection bias in the original COVID-19 patient population. Selection bias tends to overestimate predictive values.

4. POC assays may not rule out COVID-19 because the virus is not at the sampling site or viral load is too low. One company claims (unpublished personal communication) to have an immune response assay that can signal infection in 2 to 3 days. If so, it will add an important dimension to what should be in a multiplex respiratory panel used when the patient presents.

5. POCT will help facilitate rapid identification of COVID-19 carriers and their contacts; rational safe spacing and sheltering; protection of vulnerable groups; smart deployment of resources, healthcare workers, and isolation facilities; certification within 72 hours of noncarrier state before clearing immigration in other countries; workforce testing before returning to work; and importantly, alleviation of fear, panic, layoffs, and economic fallout.

**Stealth Transmission**

1. People have a right to know. They should be able to self-test at will or have free access to provider testing and follow-up to assure the virus has been cleared, to lessen stealth transmission in the community. Importantly, test results must be available promptly, not delayed up to 2 weeks, as observed in April.95

2. The recent pattern of COVID-19 stealth transmission demonstrates people must be tested irrespective of symptoms and isolated if confirmed. If not, seriously ill patients with pneumonia quickly saturate scarce critical care beds, as has happened in New York, and healthcare small-world networks may fail.

**Policy and Guidelines**

1. The White House must respond honestly. Safe spacing, sheltering, and lockdown are not enough. Infected persons must be prioritized into asymptomatic, mild, severe, and critical cases. That requires diagnostic testing, and so do attempts to categorize counties and regions as high-, medium-, and low-risk, in order that people can resume work.

2. Academic, commercial, and military partnerships can make the nation capable of vastly increased diagnostic testing capacity on short notice. The United States can use widespread, but targeted diagnostic testing mitigation policies in order to shift away from measures that are disruptive to work, business, and the economy.94 A permanent action plan is needed.

3. Inventors, innovators, POC experts, professionally certified POC coordinators, and geospatial scientists designing geospatial care paths can contribute to collaborative development of national POCT policy and guidelines. The guidelines should help prevent medical errors in POCT.95

**Environmental Robustness**

1. Environmental stresses, such as high or low temperature or humidity, can cause both false-negative and false-positive POCT test results.96–100 POC diagnostics for COVID-19 must be environmentally robust, certified for the conditions encountered, and monitored. Environmental stress research96–100 is pivotal to national security and to successfully defeating the COVID-19 pandemic.

**Global Superfund**

1. Global sharing of the financial burden for POC strategies and the associated development of sustainable business models with adequate and reliable supply chains to supply diagnostics in short order will enhance crisis standards of care.

2. Now is the time to create a Global Superfund for POC Strategies to assure freedom from outbreaks and new pandemics. Geospatial strategies, including development of suitable POC platforms for testing and reliable supply chains for manufacturing in the United States, will help alleviate smoldering epidemics, cultural deterioration, and economic recessions.

**DISCLAIMER**

Devices must comply with jurisdictional regulations in specific countries, operator use limitations based on patient conditions, federal and state legal statutes, hospital accreditation requirements, and emergency decrees. Not all POC devices presented are FDA cleared for use in the United States. FDA EUA is limited in scope and term. FDA polices are in flux. Please check with manufacturers for the current status of diagnostics and POC tests within the relevant domain of use. FDA EUA status and updates for SARS-CoV-2 diagnostics can be found here: https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#2019-ncov.

This work was supported in part by the Point-of-Care Testing Center for Teaching and Research (POCT•CTR) and by Dr Kost, its director. Professor Xiguang Liu provided insights directly from Wuhan, the epicenter of the initial COVID-2 outbreak. The author thanks the creative students who participate in the POCT•CTR and contribute substantially to knowledge in point of care and is grateful to have received a Fulbright Scholar Award (2020–2021) that supports POC geospatial strategies research in ASEAN Member States and lectures throughout Asia. Figures and tables are provided courtesy and permission of Knowledge Optimization, Davis, California.

**References**


