MOBILIZING MOLECULAR DIAGNOSTICS FOR THE NEXT PANDEMIC

A **360Dx/ZeptoMetrix** Virtual Roundtable Discussion

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WEBINAR AVAILABLE ON DEMAND

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PANELIST:
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PANELIST:
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PANELIST:
JENNIFER NUZZO, DRPH
Director of the Pandemic Center
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In the years since the height of the COVID-19 pandemic, infectious disease and public health experts have considered what went well and what could be improved before the next pandemic strikes. Molecular diagnostic tests are a key technology for not only clinical care but also surveillance, and streamlining the development and distribution of these tests will be an important part of any pandemic response.

This report summarizes a **360Dx** virtual roundtable discussion sponsored by **ZeptoMetrix**, an Antylia Scientific company, about the future of molecular diagnostics and strategies for deploying them effectively during the next pandemic. **Ben Butkus**, editorial director for **GenomeWeb** and **360Dx**, moderated the discussion.

The panelists were **Amesh Adalja,** senior scholar at the Johns Hopkins Center for Health Security; **Emmanuel Agogo**, director of the Pandemic Threats Program at the Foundation for Innovative New Diagnostics (FIND); **Claudia Denkinger**, director of the Department of Infectious Diseases and Tropical Medicine at University Hospital Heidelberg; and **Jennifer Nuzzo,** director of the Pandemic Center at the Brown University School of Public Health.

Butkus opened by pointing out that during the COVID-19 pandemic, molecular diagnostic tests were not developed and made available to laboratories with adequate speed. He asked the panelists to discuss their impressions of why this happened and what could be improved.

Adalja, who is also a practicing emergency medicine physician, said the rollout of diagnostic testing in the United States "couldn't have gone worse." Test manufacturers were pushed through the emergency use authorization pathway, creating a bottleneck and preventing universities from using laboratory-created tests. "I round with the University of Pittsburgh; they make their own tests. Quest LabCorp make their own tests. Those were not able to be used," he said. "We were relying on sending tests to the state health department."

Additionally, he said, guidelines limiting which patients could be tested caused problems. For example, testing was restricted to people who had recently been in China, even after the virus was known to be spreading elsewhere. "It took a major effort to get commercial scale testing available," he said. "And I think that really was a failure of policy, because it was not a technological problem. Once we removed those barriers, we saw tests flourish in every way possible, including home tests."

Denkinger said that Germany fared better in terms of the speed of developing and distributing tests. “Under the old IVD regulation in Europe, this was possible,” she said. However, she pointed out that the new IVDR, introduced in 2022, is much more stringent, and could limit how fast new tests could be approved. “I fear that with the next pandemic, Europe is actually even more poorly prepared in that respect,” she said.

Agogo shared the LMIC perspective. He said that many African countries were “at the back of the queue” for access to diagnostic testing. Although these countries had existing infrastructure for HIV and TB testing, they were not able to obtain COVID test kits and largely relied on materials provided by UNICEF. When a test from China did become more widely available, he said, “in many countries, that became a huge political hot potato.” Another important consideration for improving access, he added, was the use of proprietary platforms versus open PCR platforms, which can be more flexible and use common reagents.

Next, Butkus asked whether it’s possible to prepare for any threat that might emerge, or if it’s more effective to prepare for a short list of likely disease candidates.

Agogo pointed out that currently in the Democratic Republic of the Congo (DRC), there is an outbreak of an unknown respiratory virus with a 20% mortality rate, and various approaches have been considered. “At FIND, one of the key pieces of work we’ve been doing has been collaborating with the International Pandemic Awareness Secretariat and other partners to think about the 100-day mission,” he said. “Within 100 days of a qualifying declaration of a public health event of international concern, there should be various medical countermeasures in place, including diagnostics and RDT or near point-of-care tests, vaccines, as well as the right therapeutics.”

Adalja added that it’s also important to start by looking for known viruses. “We have so much technology to diagnose almost any [known] respiratory virus,” he said. Increasing routine testing for “normal” diseases helps identify novel diseases sooner, he said. “Not just in places like the DRC, but even in cities in the United States, where many patients have a nonspecific diagnosis of ‘pneumonia’ or ‘a viral infection,’ and we don’t know what it is until there’s enough of them.”

Nuzzo pointed out that environmental testing is key to early detection for several reasons. “The regulatory hurdles for testing an environmental specimen are not the same as the regulatory hurdles for testing a human being,” she said. She shared an example of a patient who recently tested positive for H5N1influenza. The patient was only tested at all because they came in during the influenza off-season, and the state wastewater surveillance program was only testing for SARS-CoV-2. “We’re not using the infrastructure we have in the sentinel watch system,” she said. “And I think that’s really problematic.”

Butkus next asked the panelists their thoughts on the differences in lab testing capacity and flexibility between low-and high-income countries, and how that disparity can be addressed to maximize pandemic preparedness.

Agogo opened by pointing out that diagnostic testing is often not a priority in LMICs, and most diagnoses are made based on symptoms. “Governments are not driven to invest in diagnostic systems, and a lot of the diagnosis is driven by the vertical disease programs, so TB, HIV, malaria,” he said. “In many countries, what really helped them was that the infrastructure that had been built around HIV diagnosis was leveraged in terms of the molecular tests.” He added that improving the testing infrastructure will also depend on empowering patients to advocate for molecular diagnostics and appropriate treatments rather than simply a course of antibiotics.

Adalja contrasted the infectious diseases approach with that of modern oncology. “We would never say, ‘You’ve got some cancer, here’s some chemotherapy. It might work, it might not,’” he said. “That’s what we do in infectious disease, because we’re spoiled by broad spectrum antibiotics that usually will work.” He agreed that patient empowerment is key to creating demand for more diagnostic testing.

Nuzzo provided a public health perspective, adding that current surveillance methods rely on an aggregation of clinical diagnoses, which isn’t fast enough in an emergency situation. “It’s not just a question of, ‘do we have the tools?’ but ‘do we have the systems that enable the use of those tools?’” she said. “There are other ways that we can use tests

that are not just purely for diagnostic purposes." Population-level studies will be critical, she said, to get real-time information about the spread of the disease.

Denkinger cautioned that "diagnostic stewardship" is important to help people correctly understand the results of the testing. Having patients demand molecular diagnostic testing can lead to misunderstandings, she said. "What I do every day here is say, 'No, what you found is not a cause of the disease,'" she said. "We need to have diagnostic stewardship so that people are empowered to know how to interpret the test results. We have to strike a balance there, and I think focusing on surveillance is going to be a critical aspect of that."

In addition, she said, although the COVID response helped increase access to PCR platforms across LMICs, most technicians still use them solely for COVID testing. "Workflows to integrate multiple different tests have not been established," she said. "So, it's also an implementation challenge, but at the same time, a great opportunity to have a more nimble system to adopt new tests."

For the final question, Butkus asked the panelists to share what new and emerging technologies they were hopeful about for improving molecular diagnostics.

Adalja mentioned rapid molecular diagnostic tests that are point-of-care and CLIA-waived, which can diagnose many different respiratory infections. "Those types of technologies can operate in resource-poor settings," he said, such as urgent care clinics. He also mentioned nanopore DNA sequencers, such as the MinION, comparing them to the Star Trek "tricorder" device. "These can be operated in very rugged environments in a way that couldn't be done in the past," he said. "It's going to get even simpler and easier with home tests and laypeople being able to do these tests."

Denkinger added that it will be critical to address the quality control aspect of testing in the context of less-trained operators, including patients. She also mentioned that advances in sampling methods could improve point-of-care tests, for instance, breath testing.

Nuzzo pointed out that it's important to think through potential use cases and design a test to meet the needs of those use cases. For instance, she said, for a mother of school-age kids, a home test would be a big improvement over pediatrician visits – but only if the home test were affordable. "A test in the store that costs $50 to tell me if I have COVID, flu, or neither is probably not a realistically useful tool to have," she said.

Agogo mentioned improvements in ease of sampling. Nasopharyngeal swabs were complicated and required a trained clinician, he said, whereas saliva tests were much simpler to administer. "Noninvasive sampling as a way of improving testing is one key area that needs a lot of innovation," he said. He also mentioned that self-testing is important for improving equity of access on a large scale, but that sensitivity remains a challenge for many of these tests. Finally, he reiterated that open platforms are key, allowing people to innovate new tests for unknown pathogens. That ability, he said, will help strengthen diagnostic systems in LMICs and everywhere.