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Global Influenza Surveillance and Response System: 70 years of responding to the expected and preparing for the unexpected

When a cluster of respiratory viral infections occurs, early recognition by clinicians linked to a global network is essential for rapid identification of the causal pathogen and subsequent risk assessment and public health response. Crucial to this process are sentinel physician and hospital networks where samples are collected from patients with febrile respiratory infections; trained laboratory staff identify the causative pathogen; and epidemiologists and public health staff to collect data to evaluate pathogen spread and disease severity in susceptible populations.

In 1947, members of the Interim Commission tasked with developing plans for WHO to be established in 1948, recognised the need for coordinated laboratory surveillance of influenza, and in 1952 the Global Influenza Surveillance and Response System (GISRS) was launched.^{1,2} Since its establishment 70 years ago as one of the WHO's first operational programmes, GISRS has had a central role during expected seasonal influenza epidemics, unexpected influenza pandemics, pandemic threats caused by avian and other animal influenza viruses, and outbreaks of novel coronaviruses. GISRS participants are country nominated and WHO designated entities, including 148 National Influenza Centres (NICs), seven Collaborating Centres for Influenza, four Essential Regulatory Laboratories, and 13 H5 Reference Laboratories.² GISRS has grown from having representation in 25 countries at its inception to include 158 institutions in 127 countries, areas, and territories at present.²

During the past seven decades, clinicians, scientists, and other personnel have used cutting-edge laboratory techniques and epidemiological tools to deliver GISRS's three key outputs: recommendations for the composition of seasonal and pandemic influenza vaccines; scientific support for public health decision makers; and contributions to global pandemic preparedness for influenza and other respiratory pathogens. Data obtained from antigenic and genetic characterisation of viruses are used for antigenic cartography and a variety of bioinformatics analytic approaches to estimate the extent of antigenic and genetic change, geographical spread, and fitness of viruses. These data, along with estimates of vaccine effectiveness, support biannual vaccine recommendations.³

Integrated, year-round surveillance is the foundation of seasonal influenza preparedness with monitoring to identify new antigenic and genetic variants and increases in antiviral resistance. Every year, sentinel physician and hospital networks contribute about 3–4 million clinical specimens with related information to NICs for virus detection and preliminary analyses. Of these viruses, about 40 000 are sent to WHO Collaborating Centers, where a subset of about 10 000 viruses is characterised for antigenic and genetic properties. Twice a year, data produced by GISRS are formally reviewed to determine if vaccine strains should be updated. GISRS surveillance is also the cornerstone for early

detection and routine monitoring of arising pandemic threats, such as influenza viruses crossing the animal–human barrier. This work is done in coordination the Food and Agriculture Organization of the UN (FAO) and World Organization for Animal Health (WOAH). Specialised laboratories prepare viruses and related reagents that can be used for seasonal and pandemic vaccines. Importantly, GISRS was instrumental in informing vaccine decisions for the 1957, 1968, and 2009 influenza pandemics.

Although GISRS was established to monitor influenza, it helped identify other emerging respiratory viruses, such as SARS-CoV in 2003 and MERS-CoV in certain countries since 2012.⁵ GISRS also contributed to the COVID-19 response in 2020 by adapting existing influenza systems to support SARS-CoV-2 testing and reporting. The GISAID database was rapidly adapted for uploading and analysing SARS-CoV-2 sequence data.^{6,7} Under WHO leadership, simultaneous monitoring of influenza viruses and SARS-CoV-2 with integrated epidemiological and laboratory surveillance⁷ became a crucial component for WHO's COVID-19 pandemic response and post-pandemic monitoring.⁸ More than 100 countries are now conducting cost-effective surveillance for influenza viruses and SARS-CoV-2 built on existing country and global assets of GISRS.

As we move beyond the acute COVID-19 pandemic response, advocacy to support routine surveillance, address insufficient resources (eg, trained workforce, laboratory space, equipment, reagents, and funding), and provide needed political support is needed to maintain gains made during the pandemic and strengthen global respiratory virus monitoring system. The integration of additional viral respiratory threats into the GISRS platform would maximise the value of the existing network and support sustainable global public health decision making and operations, especially in resource-limited countries. Expanding GISRS to integrate influenza, SARS-CoV-2, respiratory syncytial virus, and possibly other respiratory viruses is under consideration by WHO and its member states.^{9–12} Now is an opportune time to think through the optimal way to broaden GISRS's scope to other respiratory viruses and simultaneously strengthen GISRS.

In the meantime, improvements in GISRS surveillance platforms are underway, including further integration of laboratory and epidemiological surveillance, sentinel and non-sentinel surveillance, routine and outbreak surveillance, use of data generated from point-of-care tests, and participatory surveillance using digital tools. A system to more rapidly assess disease severity for public health decision making is also being developed. These improvements, together with capitalising on expanded genomics capacity and other new laboratory technologies, will support rapid characterisation of influenza and other viruses. As we mark its 70th anniversary, GISRS, with an expanded scope, is uniquely prepared to respond to future viral respiratory disease threats and serve as a foundation for future respiratory disease prevention and control.^{11,12}

TZ worked as director of the National Influenza Center in Finland and after retirement served as temporary consultant of the WHO Global Influenza Programme. AM was US Centers for Disease Control and Prevention (CDC) programme and technical support for GISRS from 2004 to 2017 as CDC Associate Director for Extramural Program and support and was WHO Chief of Influenza Preparedness and Response from 2017 to 2021. WZ is the Head of the WHO Global Influenza Programme at WHO headquarters in Geneva; the WHO Programme coordinates influenza surveillance, preparedness, and response, and the functioning of GISRS. NJC served as Director of the WHO Collaborating Centre for Surveillance, Epidemiology and Control of Influenza from 1992 to 2014 while also Chief of the Influenza Branch and subsequently Director of the Influenza Division at the CDC; after retirement she served as a temporary consultant for the WHO Global Influenza Program from 2015 to 2017 and for the Task Force for Global Health from 2019 to 2021 and is a consultant and retired affiliate of the CDC. We declare no other competing interests.

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