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EDITED BY Frontiers in Science Editorial Office, Frontiers Media SA, Switzerland

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RECEIVED 10 April 2024 ACCEPTED 11 April 2024 PUBLISHED 25 April 2024

#### CITATION

Koopmans MPG. Fast-forwarding collaborative surveillance. *Front Sci* (2024) 2:1415415. doi: 10.3389/fsci.2024.1415415

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# Fast-forwarding collaborative surveillance

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#### KEYWORDS

genomic surveillance, collaborative surveillance, One Health, pandemic, equity, open data

#### An Editorial on the Frontiers in Science Lead article

Real-time genomic surveillance for enhanced control of infectious diseases and antimicrobial resistance

# Key points

- Multistakeholder commitment and investment is needed to establish worldwide integrated, systematic, collaborative disease surveillance capacity, including in low- and middle-income countries, based on One Health principles.
- True One Health surveillance will require the engagement of actors across all relevant domains (public health, healthcare, animal health, and environmental health) to set common ecosystem-wide goals that consider the complex and often competing interests involved.
- Further progress is required toward real-time open sharing of genomic data to inform public health responses and research globally.

# Introduction

The detection, characterization, and tracking of pathogens is a hallmark of the work of clinical and public health laboratories focusing on human and animal health, food microbiology, and environmental microbiology. Examples of long-standing public health programs that use these tools are the global poliovirus and measles elimination program, the global influenza virus surveillance program developed by the World Health Organization (WHO), and programs focusing on unraveling outbreaks linked to pathogen dispersal through the food chain (Noronet, PathogenTrackr, HEVnet, and others). In parallel, pathogen detection, characterization, and typing are key components of programs focusing on (resistance to) treatment and the recognition of healthcare-associated infections. Over the past decade, the toolbox has been expanded through the addition of molecular detection and sequencing techniques, with dedicated reference centers focusing on specific pathogens or pathogen groups. This has led to a rather fragmented landscape of initiatives, with varying objectives often focusing on single pathogens or specific pathogen groups.

In their lead article, Struelens and colleagues have done a magnificent job reviewing the current state of the art in genomic sequencing of pathogens (1). Building from the experiences and lessons learned from the COVID-19 pandemic, this narrative review discusses key considerations and steps to be taken to implement pathogen genomic sequencing firmly into global public health surveillance, with consideration of a One Health approach. The authors argue for universal access and the integration of clinical microbiology and testing of randomly sampled individuals into epidemiological surveillance. They argue that maintaining and repurposing the genomic sequencing capacity that has become available during the pandemic could speed up the development of such core expertise and the matching databases.

Genomic sequencing for emerging disease outbreaks was mostly used in research studies prior to 2020 but became one of the pillars of the public health response with the emergence of SARS-CoV-2. Driven initially by (large) research efforts, early observations made the added value quite clear to a much wider group of stakeholders. Sequencing was used to study how the virus had been transmitted during outbreaks, to link cases, and to estimate the rate of evolution. Arguably the biggest impetus behind the acceptance of large-scale genomic sequencing came from its instrumental role in identifying and tracking variants (2). The COVID-19 pandemic was shaped by the emergence of such variants, i.e., viruses that had accumulated mutations that affected their ability to bind to receptors, their recognition by antibodies from vaccines or previous infections, or the process leading to invasion of a host cell. Countries across the globe started to add genomic sequencing to their public health toolboxes. The same would happen for wastewater testing, which provides an independent way of monitoring trends of pathogen circulation in a community. The review by Struelens et al. is very timely because the approaches developed for COVID-19 could potentially be redeployed. The authors describe developments in the field of pathogen genomic sequencing and its applications for a range of public health challenges, with examples of state-of-the-art employment for pathogens reaching beyond COVID-19. Their view is an optimistic one, listing the opportunities that lie ahead. For this to be successful, some key points will need to be addressed.

## Equity

Despite many calls for action, investment through capacitybuilding schemes, and political promises, access to critical infrastructure and capacity to allow for a global genomic pathogen platform is very biased (3). Some rebalancing will be important: the push for large-scale sequencing has lost its momentum with the transition to a post-pandemic reality. Most test and sequencing programs have been dismantled, and limited investments have been made into their future continuation. In addition, such investments are typically limited in scope rather than being the multistakeholder investment needed to build up our integrated disease-detection capacity. An in-depth analysis of the economic benefits of pathogen genomics would be needed to convince policymakers that this would be money well spent. While the large-scale use of genomics during COVID-19 yielded fascinating information well worth studying during an emerging disease epidemic of unprecedented scale, essential information for public health action could have been obtained with only a fraction of the effort, provided it was collected systematically and across the globe.

The newly launched International Pathogen Surveillance Network (IPSN) initiative aims to reduce the disbalance in (access to) pathogen genomic sequencing, with a recent call for proposals that need to be led by investigators from low- and middle-income countries (LMICs) to be eligible (https://www.who.int/initiatives/ international-pathogen-surveillance-network). According to its vision, the IPSN aims to change the culture of public health by opening up to a broader range of partners, launching a new term: "collaborative surveillance". This is a step in the right direction, particularly when aiming to move toward an integrated One Health system, as advocated by Struelens et al. (1).

# **One Health**

According to the definition recently adopted by the quadripartite-comprising the WHO, the Food and Agriculture Organization of the United Nations (FAO), the United Nations Environment Programme (UNEP), and the World Organization for Animal Health (WOAH)-One Health takes an integrated or holistic look at the health of humans, animals, and ecosystems, embracing the complexity and interconnectedness of health (4). This has far-reaching consequences if taken seriously: currently, most initiatives labeled as "One Health" do not actually fit this definition and are anthropocentric. For instance, One Health surveillance typically addresses the collection of data from different domains (humans, animals, food, etc.) with a focus on human health protection. True One Health thinking acknowledges the complex and often competing interests involved in (eco)systems thinking. This also applies to what has been labeled as One Health surveillance (5). Important questions to consider include the following: What is the problem? Who sees it as a problem? How important is it and to whom? Who is affected? Who needs to act? Who bears the costs of intervention? Who benefits? Who needs to collect data? What is in it for them? How sustainable are the proposed solutions? What are the costs? How are benefits defined? What risks are associated with false positive or false negative signals?

Answering these questions is challenging even when dealing only with public health actors; the challenges increase with the necessary engagement of all One Health actors. Therefore, the way forward toward an open, globally connected surveillance system will not be a simple straight line. The article by Struelens et al. (1) is focused on public health, and one interesting step forward could be to invite perspectives from the different stakeholders involved in a One Health approach.

# Co-developing genomic and phenotyping capacity

Genomic data has its own merits, as clearly advocated in the review, but it is crucial to understand that it builds on years of investments in laboratory science. The importance of this foundation became clear during the pandemic, during which the massive investments in sequencing outpaced the capacity of laboratory validation studies-which were done in a fragmented manner depending on the local capacity of public health institutes or by competitively funded research initiatives. Despite all efforts, changes in the pathogenicity or transmissibility of a SARS-CoV-2 variant cannot be determined from genomics alone. Moreover, while key epitopes now are known, it is difficult to measure whether their mutation leads to increased population-level disease-this requires integrated analysis considering population immunity levels. Therefore, building a robust genomic surveillance system for the future requires a vision that includes phenotype validation and, ultimately, prediction (6).

#### How open is open?

Struelens et al. (1) mention the open sharing of information. This indeed became the default during the pandemic, although dedicated platforms for open data sharing such as the International Nucleotide Sequence Database Collaboration (INSDC) were used less than the Global Initiative on Sharing All Influenza Data (GISAID) platform launched to protect data providers. The GISAID has without a doubt served its purpose: it provided an easily accessible, intuitive platform for sharing sequence data and metadata, with analyses and overviews generated by a small core team. As the GISAID was initially developed in response to debates over influenza virus genomic data and their downstream uses, there are rules for access and technically the data are not open. Public health experts and institutes must walk a tightrope here: information generated by pathogen genomic sequencing may provide insights that lead to actions that may not be universally agreed upon. For example, the rapid sharing of genomic data by the South African scientists who identified the novel Omicron SARS-2-CoV variant led to response actions banning direct flights from South Africa, which directly impacted the national economy. This happened despite repeated public reminders by the WHO Director-General that travel restrictions have very little effect on the spread of SARS-CoV-2. Also, the sentiment at the root of hesitance to share information was reinforced when-despite promises to the contrary-LMICs drew the short straw when COVID-19 vaccines became available.

Struelens et al. point out that only a few global genomic surveillance initiatives allow real-time support of public health action as there are insufficient publicly available sequence repositories like those that exist for SARS-CoV-2 and influenza. This is a case in point. For instance, global polio genomic surveillance data and measles genomic data are not publicly available. Moving forward, one would hope to see some evolution there: will the demand from public health actors lead to a forest of dedicated platforms, accessible under specific conditions? Or will the sequence data and metadata eventually be released into the public domain, possibly with data digital object identifiers (DOIs) to allow the tracking of information and the crediting of data producers? Here, the public health actors maintaining these databases could set an example by working toward opening these repositories for reuse by the global research community.

# Conclusion

The review by Struelens et al. is a must-read for anyone interested in genomic surveillance as part of epidemic preparedness. The tools are there, the ambition is there-the next step is to build collaborative infrastructures for future global health. This will require bringing in the human factor: rethinking how we have structured the separate siloes of public health, healthcare, animal health, and environmental health, each coming with their own stakeholder communities (7). The COVID-19 pandemic has shown what can be accomplished when the stakes are high and there is a common goal on the horizon. Redefining the common goals will be our joint challenge in the years ahead. An important step is to take a much broader approach: goal setting in a true One Health manner is not straightforward and no doubt will lead to regional or even local differences in priority setting. Yet, building an ecosystem in which such local initiatives and the people involved feel that they are co-owners of a greater joint movement is critical to reach the ambitious goals set out in this review. Here, regions with less-established health systems might lead the way since there are fewer positions to defend. An important step will be how countries will negotiate the proposed pandemic treaty, which will lay down some of the rules of engagement for better preparedness. Interesting times ahead!

#### Statements

#### Author contributions

MK: Conceptualization, Writing – original draft, Writing – review & editing.

#### Funding

The author(s) declare financial support was received for the research, authorship, and/or publication of this article. The author receives funding from research related to pathogen genomics, data sharing and platform development from the European Union Horizon 2020 research and innovation programme under grant agreement No. 874735 (VEO-Versatile emerging infectious disease observatory: Forecasting, nowcasting and tracking in a changing world) and from the European Commission Health Emergency Preparedness and Response Authority (HERA) for project DURABLE. The funders were not involved in the study design,

collection, analysis, interpretation of data, the writing of this article or the decision to submit it for publication.

#### Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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