The importance of microbiology reference laboratories and adequate funding for infectious disease surveillance

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Microbiology reference laboratories perform a crucial role within public health systems. This role was especially evident during the COVID-19 pandemic. In this Viewpoint, we emphasise the importance of microbiology reference laboratories and highlight the types of digital data and expertise they provide, which benefit national and international public health. We also highlight the value of surveillance initiatives among collaborative international partners, who work together to share, analyse, and interpret data, and then disseminate their findings in a timely manner. Microbiology reference laboratories have substantial impact at regional, national, and international levels, and sustained support for these laboratories is essential for public health in both pandemic and non-pandemic times.

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Introduction

In addition to its extraordinary death toll, the COVID-19 pandemic uncovered substantial fragilities in many systems and institutions around the world.[1,2] Although the full catalogue of lessons learnt from the pandemic continues to be explored, one central feature should not escape our focus: the importance of microbiology reference laboratories and the experts working within them. Microbiology laboratories were among the first to identify cases of COVID-19 (and so-called variants of concern), monitored case numbers in real time, deployed public health responses to the pandemic, advised on policies to protect the public, and informed COVID-19 vaccination programmes.[1]

Ordinarily, the functions of microbiology reference laboratories are to facilitate early detection and control of infectious diseases, including through outbreak detection, surveillance of endemic diseases, monitoring of antimicrobial resistance, and provisioning of data to monitor and assess vaccination programmes. They provide data and scientific expertise to public health authorities, support diagnostic stewardship and services in other regional laboratories, promote advocacy and linkages with patient support groups, and contribute to an overall reduction in disease burden.[3–5]

In addition, these laboratories facilitate reference diagnostics; produce reference materials, manuals, and tools; provide (and often lead) external quality assessments; perform pathogen genome sequencing; train personnel; and conduct research projects. Reference laboratories often maintain collections of specimens and microbes with corresponding metadata, allowing future access and characterisation as required. Reference laboratories also play crucial roles in disease risk forecasting, which improves epidemic and pandemic preparedness, and are often involved in investigating historical, neglected, or re-emerging diseases.[6,7] The demands on microbiology reference laboratories during the COVID-19 pandemic were therefore in addition to their routine laboratory work.

The importance of infectious disease surveillance

The COVID-19 pandemic showed the public the continuing importance of local, national, and international surveillance of infectious diseases in saving lives and informing vaccination programmes. The importance of surveillance was also highlighted more recently in WHO's *Global Research and Innovation for Health Emergencies* blueprint,[8] in which the recommendation for an improved, interconnected global laboratory capacity for pathogen surveillance was emphasised.

Many national surveillance programmes have been active for multiple decades and have made key contributions to microbiology and the control of infectious diseases both in their own countries and worldwide. Yet, despite their highly impactful work, many laboratories routinely struggle to secure ever diminishing funding for their surveillance programmes from governmental health and science budgets.[9] The dedicated work performed by microbiology reference laboratories is often not appreciated because the science is seldom innovative and the work seems repetitive and administrative.

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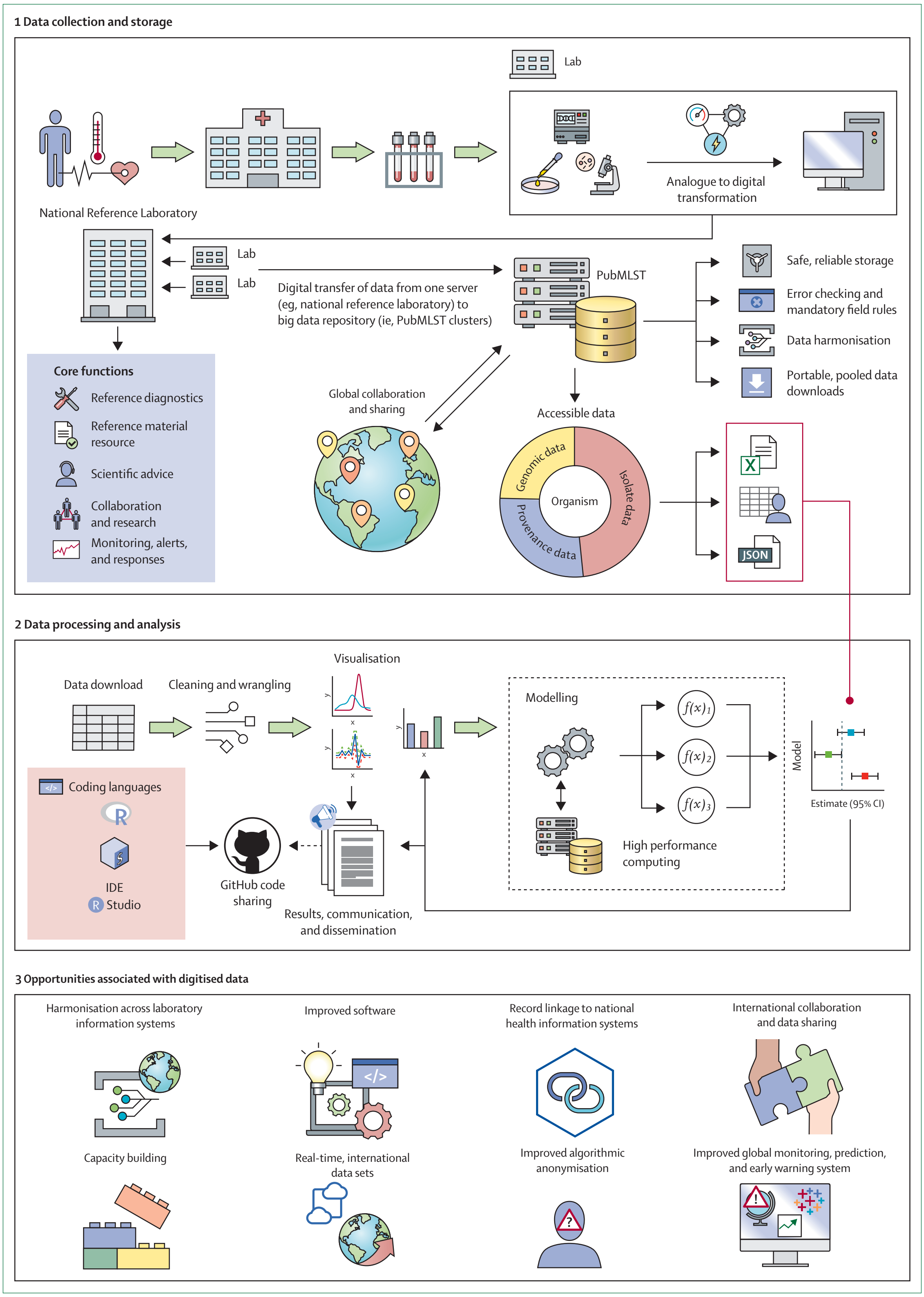

One coauthor of this Viewpoint described the work as "quiet but consistent", which is one of the key strengths of reference laboratories: consistency in data generation and analyses, and specialist knowledge over a long period of time, allowing for the recognition of trends and any deviations from long-term trends. Similarly to the success of the polio vaccination campaign, microbiology reference laboratories suffer from the public health paradox, meaning that after a successful intervention against a specific problem, surveillance no longer seems to be required and, consequently, public and governmental institutions lose interest.[10] Humans are creatures of agency—we need to see processes work to believe that they work. These laboratories are contributing tremendously to the public good and are providing crucial infrastructure, as evidenced by their impact on public health both in pandemic and non-pandemic times.

One of the most important functions of microbiology reference laboratories is the monitoring of vaccine performance through post-marketing surveillance of vaccine effectiveness and impact, disease rates, and changes in pathogen antigenic variants, in both target and non-target populations. These epidemiological data enable the assessment of national vaccination programmes and are routinely used to devise and amend vaccine policy decisions. For example, there was an invasive *Neisseria meningitidis* meningococcal disease outbreak in the Netherlands between 2015 and 2018. Through the national reference laboratory's surveillance, serogroup W meningococci were quickly identified as the cause of the outbreak, leading to the replacement of the MenC vaccine with the MenACWY vaccine in the Dutch National Immunisation Programme in 2018.[11] National reference laboratories, surveillance programmes, and vaccine monitoring will remain essential during the upcoming roll-out of the new *Streptococcus pneumoniae* (pneumococcal) vaccines and other vaccines in the pipeline.[12]

Investing in surveillance to promote public health

Surveillance activities help prevent disease in a population at a price, which includes personnel, equipment, consumables, information technology infrastructure, facilities, and administrative costs. Despite their indisputable value to public health, competing demands on existing funds can mean that less money is made available to some reference laboratories, sometimes requiring them to seek additional sources of financial support. Some governments deter industry funding partnerships (fearing a real or perceived conflict of interest) whereas some do not have a framework to accommodate funding from industry or other third parties. In other countries, industry funding is an appreciated source of additional financial support to their budget portfolio. These challenges exist even though cutting expenditure on public health services, including microbiology reference laboratories, is widely understood to increase health-care costs and widen health inequalities.[13,14]

In 2016, the European Centre for Disease Control and Prevention (ECDC) commissioned a cost–benefit analysis of national reference laboratories for human pathogens.[3] The ECDC's chief concern was the possible integration of disparate national reference laboratories into a centralised European Reference Laboratory, and the report detailed monetary and non-monetary costs and benefits associated with European reference laboratories. The Commission concluded that the benefits of national reference laboratories (especially of an integrated network of laboratories) exceeded the costs, both monetary and non-monetary. The Commission also acknowledged the difficulties in quantifying the work

	Location	Type	Citations (N)
National Institute for Public Health and the Environment	Netherlands	Government; research centre	4
Belgian Federal Public Services	Belgium	Government	2
Sciensano	Belgium	Government; health-care agency	2
Finnish Institute for Health and Welfare	Finland	Government; health-care agency	2
European Centre for Disease Prevention and Control	EU	Government; agency	1
Parliamentary Office for Scientific and Technological Assessment	France	Government	1
Health Protection Surveillance Centre	Ireland	Government	1
Office of the Prime Minister's Chief Science Advisor	New Zealand	Government	1
The UK Government	UK	Government	1
National Health Service Trusts	UK	Government; health-care agency	1
Centers for Disease Control and Prevention	USA	Government; health-care agency	1

Data obtained from Overton on July 9, 2024.

Table: **Policy impact of the Invasive Respiratory Infection Surveillance Consortium evidenced by its citation by government, national, and international documents**

Figure 1: **Illustration of the various stages and types of digital laboratory data processing in microbiology reference laboratories and the opportunities that arise with digitised data**
This figure illustrates the various stages and types of digital laboratory data processing in microbiology reference laboratories (panels 1 and 2), and the opportunities that arise with digitised data (panel 3). IDE=interactive developer environment.

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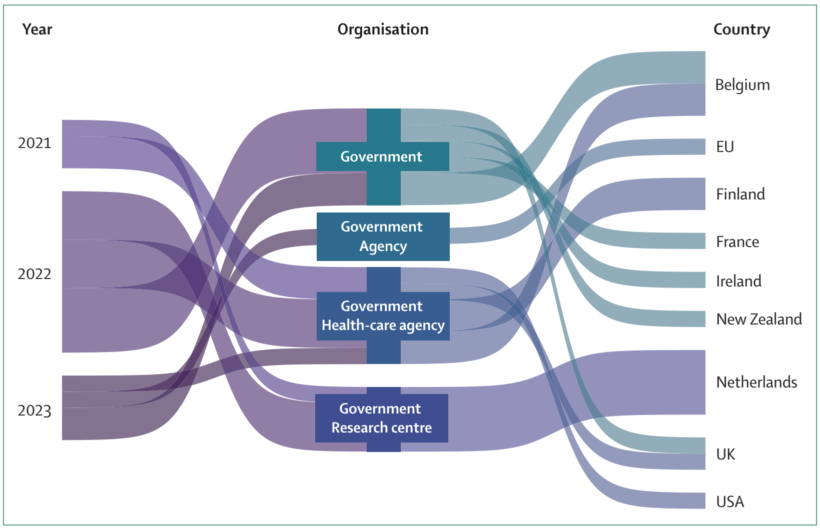

Figure 2: **Sankey diagram illustrating the policy impact of the IRIS Consortium**
The data visualisation depicts policy documents that have referenced IRIS papers as connections between the year of publication of the policy document, the type of organisation that published it, and the country in which the policy document originated. Data were obtained with Overton on July 9, 2024. Details of the documents can be obtained from the corresponding author. IRIS=Invasive Respiratory Infection Surveillance.

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performed by these laboratories in reducing disease burden since this is influenced by many factors. The ECDC report stated that European society benefits directly along four axes: first, laboratory preparedness and the capacity for a coordinated response to outbreaks; second, more timely and accurate detection of pathogens; third, improved public health surveillance; and fourth, a reduction in disease burden and the related costs.

Although the public health microbiology network across Europe was deemed strong, the report also highlighted challenges and limitations for reference laboratories in Europe. Many of these difficulties are common among reference laboratories worldwide. For example, the need to harmonise surveillance, reporting, and operating standards; uneven country capacities and variation in the types of reference laboratory activities that are performed; political and bureaucratic limitations for sharing data, at least partly due to privacy issues; whether or not to adopt new diagnostic tools and more broadly, how to implement technological advances in the field; the implementation of standardised genomic methods for genotyping, including the prediction of phenotypes (eg, antimicrobial resistance); and how to ensure that sustainable funding is available both for routine work and when emergencies occur.

Recently, the ECDC facilitated a programme to assess where improvements to public health infrastructures might be required, and in 2019, Bajoriniene and colleagues[4] performed a needs assessment for microbiology laboratories in western Balkan countries. They identified key areas for public health investment and concluded that these efforts enhanced health security in these countries and in Europe in general.[4] This work illustrated the indirect and nonlinear effects of adequate laboratory funding: not only does the country benefit by enhanced health security and disease control, but neighbouring countries and the global community benefit as well. When considered from this perspective, the price at an individual level is rather small relative to the large effect of the outcomes—similar to other public health interventions such as smoking cessation.[15] A 2017 systematic review of public health expenditure in a number of high-income countries also supports the benefits and cost savings associated with population-level efforts to prevent disease.[16]

Similarly, a qualitative study commissioned by the Center for Global Development in 2022 examined the costs and benefits of investing in laboratory systems in Africa.[17] The authors found that the wide-ranging benefits exceeded the necessary costs, and these benefits have potentially transformative impacts at the individual, population, and health-system levels.[17] Discussions at the Third International Conference on Public Health in Zambia in November, 2023, resulted in pledges of support and political endorsement for national public health institutions and reference laboratories.[18]

The Invasive Respiratory Infection Surveillance Consortium

The Invasive Respiratory Infection Surveillance (IRIS) Consortium, with a network of microbiology reference laboratories at its centre, was established early (April–May, 2020) in the COVID-19 pandemic to track changes in the incidence of invasive bacterial disease caused by four organisms: *S pneumoniae*, *Haemophilus influenzae*, *N meningitidis*, and *S agalactiae* (group B streptococcus).[19] The IRIS Consortium comprises more than 100 collaborators working in over 50 laboratories in 30 countries. The central components of the IRIS Consortium surveillance are wide population capture plus accurate, timely, and precise data—an important illustrator of why setting up robust surveillance systems in every country is so pertinent.

The IRIS Consortium includes high-income and middle-income countries across the northern and southern hemispheres to rapidly monitor changes in invasive bacterial disease at a global level. The strength of the IRIS Consortium lies in the collaborative nature of this project: national and regional microbiology reference laboratories have come together to share robust and reliable data via private databases in PubMLST as a consortium of collaborating laboratories. These digital data have been (and continue to be) analysed collectively and disseminated in a timely and mutually agreed manner (figure 1).[20] The multidisciplinary nature of expertise within the IRIS Consortium is an additional asset, bringing together complementary fields of expertise not only in microbiology, but also in epidemiology, pathophysiology, medicine, immunology, and bioinformatics. The IRIS Consortium has produced two papers on describing changes in the distribution of invasive bacterial disease by location, age, and serotype or serogroup before, during, and after the COVID-19 pandemic, and these papers are contributing to public health policy (table; figure 2).[19,21]

The effects of such a collaboration are multiplicative rather than additive: in addition to performing surveillance on a global scale for four leading bacterial pathogens, we can pool data across all countries and by defined regions to generate robust estimates due to large sample sizes and increased statistical power. We can measure the impact of different prevention and control interventions among countries or regions and evaluate antimicrobial susceptibility patterns.

Surveillance in an age of digitalisation and big data

For the IRIS Consortium and other rapid surveillance systems to function efficiently and effectively, various types of digital data (often in non-standardised formats) must be shared, harmonised, stored, and analysed (figure 1). This requires laboratory information systems to manage large datasets, appropriate tools for analyses, and sufficient computing power. Data sharing is currently a major challenge for many laboratories. Human curation and expertise are also essential to place results in the correct context and check for errors. If a robust digital infrastructure is missing, gathering laboratory data and linking those data to patient information becomes more challenging, and showing the public health impact of reference laboratories becomes harder.

Although data management infrastructure is established in many laboratories, opportunities exist for further improvements. For example, digital record linkage to other national health information systems can provide richer datasets that allow risk factors, health outcomes, and interventions to be jointly investigated. Data privacy and protection are crucial when working with patient data but might restrict data linkage between different systems; however, improved algorithmic patient anonymisation could facilitate data linkage while still retaining privacy. Furthermore, digital data formats from different laboratories could be harmonised to accelerate data processing and analyses. Reference laboratories are also well positioned to show leadership in the areas of genomic surveillance and data science (including artificial intelligence), given their vital role in public health surveillance and data analytics.[22] Finally, building robust data management infrastructure should be a priority when building laboratory and surveillance capabilities in countries that currently have reduced capacity.

Conclusions

Prevention is better than cure. Microbiology reference laboratories are fundamental to informing measures that reduce mortality and minimise human suffering. Therefore, continued support for national reference laboratories is crucial to avoid the risk of hampering hard-earned scientific progress. Calls to increase investment in public health have amplified since the COVID-19 pandemic: we are specifically advocating for increased and sustained funding for microbiology reference laboratories, since sustained funding is crucial for their core work and for these networks and collaborations to develop.[15,23] Notably, components of the core public health infrastructure such as reference laboratories deliver continuously and provide a base framework for expansion, in contrast to investment that does not build on existing core resources and established networks. As a network of international collaborators, we hope to add weight to these calls to increase investment in microbiology reference laboratories. At best, we hope this Viewpoint can be used as evidence of the need for sustained funding, but at a minimum this Viewpoint should be used to start the conversation.

Microbiology reference laboratories, along with other public health interventions, provide the protection that keeps societies safe as we navigate the health risks of our daily lives. This safety has a price and without it, the price will not just be monetary but paid for with the lives of the citizens we are supposed to protect. Public health policies and interventions have made great progress in reducing the burden of disease and increasing health and hygiene standards. Increasing the funding for microbiology reference laboratories in all countries is necessary to ensure a safe future for everyone.

Contributors

DS and ABB directly accessed and verified the underlying data reported in this Viewpoint and wrote the first draft of the manuscript. All authors made edits to and reviewed the manuscript, and approved the final version of the manuscript for submission.

Declaration of interests

EV has received research grants from the French Public Health Agency, Pfizer, and MSD (paid to Centre Hospitalier Intercommunal de Créteil). SD has received a research grant from Pfizer; and advisory board and speaker fees from Merck-MSD (paid to University Hospitals Leuven). MH and CC have received funding from the Federal Office of Public Health (paid to The Swiss National Reference Center for Invasive Pneumococci). MH has participated on a data safety monitoring board or advisory board for both Pfizer and MSD. MH also holds investigator-initiated grants from Pfizer and MSD paid to his institution. However, the sponsors had no role in the data analysis and content of this manuscript. AS and AKu have received funding from the National Science Centre, MSD, and Pfizer; and equipment from The Great Orchestra of Christmas Charity Foundation and the Clinical Microbiology Center Foundation (paid and sent to The National Medicines Institute, Warsaw). AKu has received payments from Sandoz, and Pfizer for lectures. AS has received payments from MSD and Pfizer for lectures; and from MSD, Pfizer, and Sanofi Pasteur for participation on advisory boards. LL and MT have received research funding from Pfizer (paid to The Finnish Institute for Health and Welfare). ABB has received funding from MSD for IRIS pneumococcal genome sequencing. ABB is an unpaid advisor to WHO, providing expertise related to vaccines and antimicrobial resistance. ABB is also an unpaid General Assembly member (from 2022 onwards); and was a board member from 2016 to 2022, and Secretary from 2018 to 2022 for the

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