A proposal to develop an equitable global pathogen surveillance network in 2021 that can prevent and respond to emerging and endemic infectious diseases at speed and at scale

This report has been written by Sir Jeremy Farrar, Director of Wellcome, at the request of the UK Presidency of the G7. It draws on contributions from a large number of practitioners and global health experts. A full list is set out at the end of the document.

EXECUTIVE SUMMARY

1. The development and utilisation of pathogen surveillance at scale and its integration in real time with classical public health, epidemiology, genomics, research, clinical medicine and allied data has been one of the success stories of the COVID-19 response in some parts of the world.

2. The COVID-19 experience and those of previous epidemics, (Nipah, SARS-CoV1, H5N1, MERS, Ebola, Zika, H1N1, cholera, C. difficile, other multi-drug resistant infections etc), demonstrate the imperative of integrating and funding classical public health, clinical medicine and the research and academic communities with these new technologies, through an equitable global partnership.

3. Once established, this global partnership would help identify new variants of SARS-CoV2 and pre-emergent zoonotic coronaviruses and provide invaluable resources for the rapid development of diagnostics and countermeasures (public health measures as well as drugs and vaccines). The creation of this global partnership would enable the detection and full characterisation (genotype, phenotype, clinical and epidemiological features) of current and future epidemics involving known and emerging infections before they become pandemics.

4. The partnership would have continuous and cost-effective utility by providing surveillance of endemic infections. Excellent surveillance systems already exist for HIV, TB, malaria, influenza and these could be augmented by including other pneumonia, meningitis, typhoid, cholera, STIs, drug resistant pathogens and clusters of defined clinical syndromes, as well as tracking the interplay between animal and human pathogens.

5. In this way, the partnership would equip public health systems to respond with greater speed and precision to all local infectious health risks by keeping people, skills, technical infrastructure, and connections in place where needed in order to respond to new threats as they emerge.

6. Urgent work is needed to make this vital global capacity a reality – including; i) defining and coordinating partnership ‘hubs’ and ‘spokes’; ii) putting key infrastructure and training in place, and defining the necessary policies, principles, and an underlying ethical framework essential for global cooperation within the network. With the right political

   impetus, financial investment and technical focus, building on existing centres would see a global capacity operational in 2021. An implementation timetable, standing up a temporary Implementation Group working with global health actors, is proposed.

Introduction

7. This report advises the G7 Presidency of the key ingredients required to establish a high level international architecture (a super-network) that would strengthen our collective defences against health epidemics and endemic health risks. To ensure such a system is useful and sustainable through non-pandemic periods, it needs to include and complement current efforts to tackle threats to both human health - polio, HIV, malaria, TB, (antibiotic drug resistance and include animal health such as swine and avian flu

8. Learning from existing successful disease surveillance networks in other disease areas, we propose five 'key ingredients' that together could enable an integrated global pathogen surveillance network to mitigate or even prevent epidemics, pandemics, and the on-going systemic harm of endemic infections.

Ingredient 1: A 'mesh network' of pre-existing expert centres

9. Much like a WiFi mesh network, successful global pathogen surveillance super-network requires bandwidth to be put aside for 'hotspots' where particular risks and demands are likely to arise, while ensuring 'notspots' are avoided (and potentially vital signals therein) by networking active nodes together to create better overall coverage. Recent epidemics have not necessarily begun where we thought they "should" have (e.g. H1N1 in Mexico, rather than SE Asia; Ebola in West Africa, rather than Central Africa).

10. These active nodes of the super-network could consist of existing national public health centres or collaborative regional organizations/infrastructure[1](e.g. Africa CDC, China CDC, ECDC, PAHO, US CDC and the planned WHO-Berlin Hub etc.) with strong links to clinical medicine, animal health, biomedical research and population cohorts connected to regional and international reference centres. Within these centres, classical public health epidemiology and clinical medicine would be integrated with enhanced genome sequencing and data infrastructure; providing the population basis and linkage with clinical impact, burden of disease and cause-specific mortality information that allow for assessment of disease rates and mortality burden and thus determine which of very many signals are of significant concern. These platforms would be enhanced by the integration of privately available data describing health systems functioning and demand, commercial activity, and human-centred signals. The connection between these hubs would be essential and outlined in the design phase.

11. These super-network nodes would be linked with clinical trial and research networks, increasing the chance that rare events or variant pathogen signals are detected very early, and attracting a cadre of world-class academic scientists interested in translational research to strengthen and sustain the global infrastructure.

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[1] Many such networks and centres currently exist – for example, Africa CDC's Pathogen Genomics Initiative, Aga Khan Network, BMGF, China CDC, EU-CDC, EMBL-EBI, EU Initiatives (COMBACTE, VEO etc), FETP Enterprise, FIND, Fogarty & NIH, Global Fund, IANPHI, India Public Health, Institut Pasteur, PAHO/Central/South America network, UKHSA, Nigeria CDC, Robert Koch Institute, Rockefeller, UNITAID, USA CDC, UKHSA, Wellcome, and other national and regional public health, academic, philanthropic and industry networks.

Ingredient 2: Core infrastructure to sequence, analyse data and share information

12. The long-term national and regional participation needed to put this infrastructure and human capital in place and sustain it can only be guaranteed by the network delivering continuous benefit to all health systems. Increased precision and pace of local disease control requires an operating model and supporting policies enabling continuous feedback loops with local (e.g., primary care through to critical care facilities), national and regional health systems. Ease and equity of accessibility by local public health and clinicians, along with appropriate terms for academic use ensures its sustainability.

13. There are already excellent examples of networked local, national and international surveillance – e.g. for global cholera and typhoid, polio, SARS-CoV2 and Ebola surveillance as well as the WHO influenza network. These utilise and support regional hubs involving public health reference laboratories (building on work such as Pulsenet using pre-genomic approaches). The super-network must draw on these and expand capacity at all levels – linking to existing veterinary (One Health) and environmental (water, zoonosis, ecological) microbial/metagenomic efforts, and integrating closely with new initiatives (for example the proposed One Health Intelligence Hub) as they emerge.

14. Genomic sequencing and bioinformatics infrastructure (people, training, equipment, and sustained access to consumables and maintenance) are essential for effective sequencing, computational data analysis and data storage. Sequencing, computing and data infrastructures will need significant sustained and distributed investment in order that they are available at a national and regional level to minimise the need for large-scale movement of samples which would add risk and cause delay.

15. Metagenomics, artificial intelligence (AI) and associated technologies will support super network nodes in identifying trends and trigger more in depth analyses. As the super network develops, there will be considerable value in building and sharing databases to enable it to identify and track spatio-temporal changes in infectious disease features and where reservoirs of threat (e.g., antimicrobial resistance (AMR)) exist or develop and thereby identifying threats before they emerge. Over time this 'archive of microbial life' would also be an invaluable scientific resource useful for surveillance, epidemic control, AMR monitoring and even climate change analysis.

16. Expanded expert workforces in the nodes of the super-network must be considered. Strong training, career development and skills exchange programmes for clinicians, scientists, technologists and technicians (involving academia and industry) will need to be developed from existing and additional resources. These should cover epidemiology, virology, clinical, One Health, sequencing and other technologies, informatics, social science, data science, ethics, policy and product development. The super-network could therefore coordinate an ideal national and international training environment with exchange programmes, PhDs, fellowships and career progression.

17. Public sector and multilateral efforts will achieve greater success by engaging leading private sector entities over the long-term, including but not limited to leading companies in informatics, technology, biotech, telecom, digital/social platform, and banking.

Corporate partners will enhance the work of major research universities/institutes and local and global NGOs. In addition to being critical to data collection, curation, analysis and the dissemination of actionable knowledge, this participation will augment systems strengthening efforts and help minimize funding gaps required to rapidly scale up the global infrastructure network that is required.

Ingredient 3: Modernised sampling, governance and ethics framework

18. A coherent underpinning ethics and governance framework will be key to making a functional global super-network – as a minimum covering (i) Harmonised sample collection and sharing and (ii) Minimum standards of meta data sharing and access, data use and reporting. The recent report by the Science Academies of G7 countries proposed a range of measures to enable better 'data readiness' for future health emergencies[2], some of which are described here. They should now work with the WHO, G20 and other partners to develop a roadmap for implementation of their recommendations.

19. Sample collection would need be fully embedded in local health systems, and might include: systematic targeted sampling as follow
    a. Systematic sampling of acute febrile illness in people from the community in hospitals and critical care facilities (all epidemics since Nipah 1999 were first identified among very sick individuals and as clusters of cases as the initial warning signal);
    b. Occupational high-risk individuals who are exposed to zoonotic pathogens through connections to wildlife, and industrial farming, allied with sampling of animals and environmental materials (e.g. air, wastewater) and the collection of the associated clinical and epidemiological data.
    c. Environmental routes of infections. Routine sampling in geographical areas where ecological niche mapping or animal surveillance suggest risk of emergence of high threat pathogens on both sides of the species barrier, including using locally defined thresholds for clusters meriting investigation e.g. highly pathogenic avian and swine influenza, henipaviruses and filoviruses.
    d. Critical febrile illness in hospitals. Clinical settings where there is enrichment for severe cases and consideration of sentinel surveillance of specified syndromes i.e. systematic sampling across core clinical syndromes (respiratory, enteric, nervous system, haemorrhagic, unknown clusters) in the community and clinical facilities including critical care.
    e. Opportunistic population sampling. Longitudinal cohorts, mass gatherings and wastewater are a few examples.

20. To better understand underlying immunity, past exposure and susceptibility at a population level, the super-network will need to complement DNA sample collection with a programme of sero-sampling through multiplex (i.e. protein arrays, phage display, spectroscopy etc) immunological assays – including routine seasonal sampling, sampling of cohorts and global networks, and serological monitoring of people working at the human-animal interface and, random age-stratified sampling of excess routine blood

[2] https://royalsociety.org/-/media/about-us/international/g-science-statements/G7-data-for-international health-emergencies-31-03-2021.pdf

samples through national surveillance networks.

21. This sampling should be integrated with other sources of data, including WHO's EIOS, PROMED, and non-traditional sources, e.g. informal reports, social media, research and industry-led surveillance, should also be used, where of an appropriate standard and in keeping with the principles of sharing and access to data.

22. Once collected, data should be FAIR (findable, accessible, interoperable, and reusable) to the greatest extent possible, as recommended in the S7 report. Long experience of data sharing of DNA sequence data from INSDC (GenBank/ENA/DDBJ) and other databases such as GISAID shows that daily data sharing and exchange at scale is feasible.

23. Potential concerns about data sharing can be removed or mitigated by a governance framework iterated by super-network participants that carefully structures when and how data is shared, and informs a global agreement on future product access. Different arrangements will be needed for rapid, public health-focussed data, and longer time frame data which can be more sensitive to scientific recognition of participants and longer-term scientific progress – ensuring benefits are shared at the institutional and national level (such as immediate guidance on national responses) and at the individual level (such as publication credit & career advancement). A close, trusted partnership between the public health and research communities is critical for the success of this, both need sustained, reliable core funding support.

Ingredient 4: Using data to drive development of new tools to fight disease

24. The rich real-time information and data generated within the network could offer a critical source of insight to increase the precision and utility of diagnostics, vaccines and drug development. Rapid availability of sequence and sero-surveillance data from the first detection of SARS-CoV2 and the subsequent variants has enabled researchers to more quickly develop lines of enquiry resulting in the new tools that have started to reduce the long-term threat of COVID-19. This integration of ongoing surveillance and research data into product development has been a successful feature of the WHO Influenza Network over the last 70 years.

Ingredient 5: Global normative leadership to bring this all together

25. The leadership of global health authorities – specifically WHO, coordinating with 'One Health' partners in OIE, FAO and UNEP – will be vital to enable the technical and other conditions for national participation to support coordination across the network and to ensure that its findings can be quickly incorporated into a coordinated global emergency response and supporting normative guidance.

Getting Started

26. Some of the key elements above are in place in some countries, although often fragmented, and a significant investment and coordination effort is required to link these elements together and ensure they are in place on a sustainable basis in the geographies where and when they are most needed. While there is no pre-existing group or network

that can provide all the elements outlined here, a new pathogen surveillance network could follow a similar model to the WHO-coordinated Global Influenza Surveillance and Response Network (GISRS), which successfully brings together 144 National Influenza Centres to detect and respond to emerging flu threats and makes recommendations on updates to seasonal flu vaccines. The ACT-Accelerator model developed for COVID-19 may be one model to explore, keeping WHO at the core, but working closely and integrating with external partners.

27. By drawing together existing infrastructure and capabilities and building off successful models – and with the committed participation of key partners – it should be possible to build the backbone of a global infections surveillance network in 2021 which could then be grown organically as funding and national participation allows. National public health institutes, their infrastructure and associated research groups have key roles, both need sustained, predictable core funding.

28. Over time, it should be possible to integrate existing 'vertical' sequencing structures focussed on individual disease, and potentially coordinate more closely with the GISRS – but the focus in the first instance must be to get an initial network up and running with the underpinning governance, practice and policies that will enable equitable and strategic national participation and sustained global integration.

29. The integration of data from this network and amplification of findings to promote rapid action will be another element of the start-up phase. The nodes in the super-network need to be able to coordinate requests, information, and calls to activation must be able to move quickly and to incorporate data, perspectives, and skills from the public, private, and civil sectors.

30. Such a super-network needs to build off the initial announcement of a new WHO global hub for pandemic and epidemic intelligence, data, surveillance and analytics based in Berlin. The Hub is expected to lead innovations in data analytics across the largest network of global data to predict, prevent, detect and prepare for and respond to pandemic and epidemic risks worldwide.

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