別添1

海外における臨床情報、感染者検体及び病原体バンクを活用した感染症対策についての調査業務 一式

調査業務 報告書

特定非営利活動法人

日本医療政策機構

「本調査は、インタビューの結果をまとめたものであり、
インタビュー対象者の考えを含む可能性もあります」

Building a Domestic Research Infrastructure and Surveillance System with Biobank Integration for COVID-19 and Beyond

A Comprehensive Review of Seven Countries or Area

Report Compiled by the
Health and Global Policy Institute
31 March 2021

*This report is a summary of the interview.

May include the personal comments of the interviewees

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Denmark

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

In Denmark, the Statens Serum Institut (SSI) is responsible for the prevention and control of infectious diseases under the Danish Ministry of Health and Prevention. The national surveillance system tracks data on serious diseases, diseases that are particularly infectious, and most vaccine-preventable diseases.

If an outbreak is confirmed, the SSI is responsible for elaboration of case definitions, diagnosis verification, elucidation of the descriptive epidemiology of the outbreak, including spread and possible area or population at risk, development of a hypothesis as to the source of infection and risk factors, testing of this hypothesis by means of microbiological examinations and analytical epidemiology, development of a prognosis, and, finally, evaluation of the effect of countermeasures.

Mandatory Notification System. There are several Mandatory Notifiable Diseases that must be individually notified to health authorities. Physicians are required to submit "clinical notifications" on paper to the Ministry of Health and Prevention and SSI.

Electronic Reporting

SSI wishes to pave the way for the increasingly widespread and improved communication media to be used for easier, faster, and better coordinated reporting, analyses, and use of digital data across the Health Service System.

Financial and Human Resources

The SSI's annual budget for the 2019 fiscal year allocated DKK 79.4 million for infection preparedness including surveillance.[1]

2. Collection and Storage of Biological Samples

The Danish Biobank Register

The Danish Biobank Register is composed of 12 biobanks located throughout Denmark and provides researchers with an overview of biosamples held within participating biobanks. Large biobanks at hospitals, universities, and other institutions submit data to the register. Furthermore, all data can be linked to diseases codes and demographic information from national administrative registers on an individual level. Currently, there is data on 25.3 million biosamples from 5.7 million Danes which is accessible through a web-based search system.

[1] Statens Serum Institut, "Resultatkontrakt: Mellem Statens Serum Institut og Sundheds - og Ældreministeriet" (Denmark: Statens Serum Institut, 2019), https://www.ssi.dk/-/media/arkiv/dk/om-ssi/aarsrapporter/resultatkontrakt-ssi-2019.pdf?la=da.

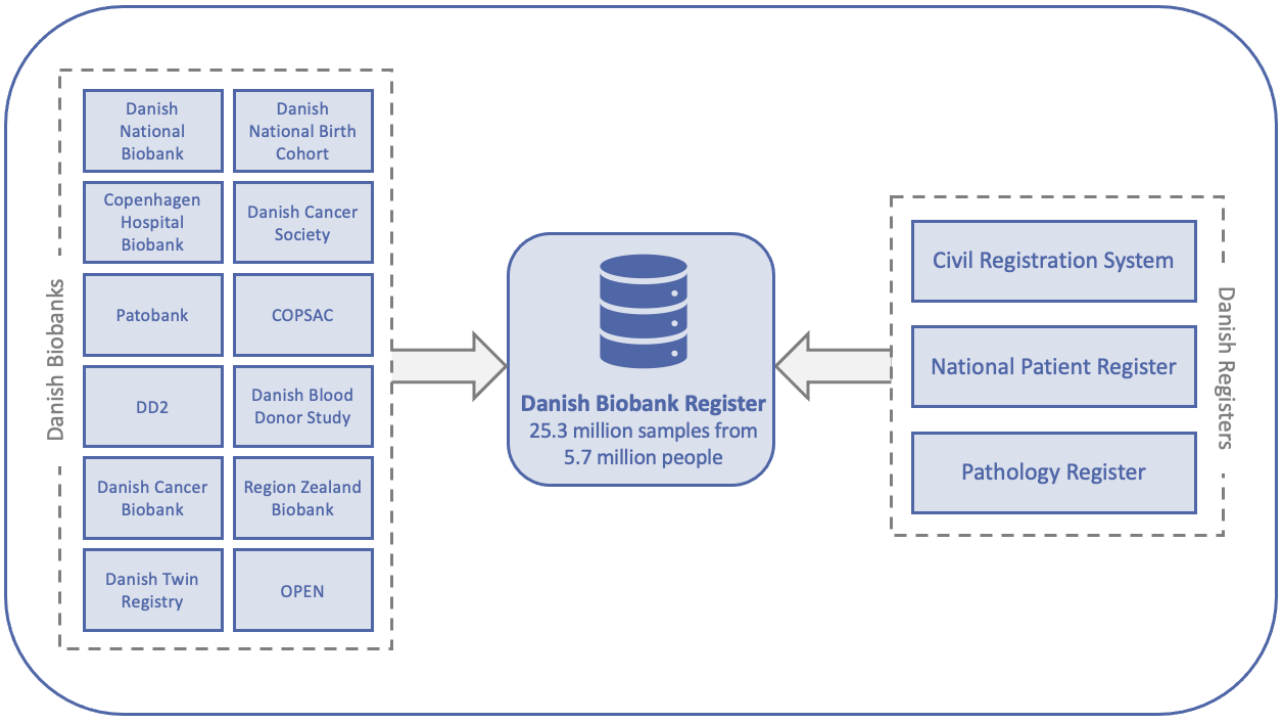

Figure 1. Danish Biobank Register[2]

The Danish National Biobank

Denmark has invested in building a range of national registers containing information on all residents in Denmark. The Danish National Biobank gives scientists in Denmark and abroad easy access to more than 25 million biosamples. The Danish health system has collected biosamples from a large number of individuals which can be linked to information collected from administrative registers. The Danish National Biobank is set to become the world's largest biobanks.

Sample Collection. Biosamples are regularly collected throughout the country and brought to the national biobank where they are redistributed into smaller aliquots and put in automated storage.

Access to Biosamples. The first step in accessing biosamples from the national biobank is getting approval from a Danish health research ethics committee. Projects are then reviewed by the DNB Evaluation Committee and if they are approved, the samples are retrieved and distributed to the researcher.

Approval by a research ethics committee is essential for gaining access to biosamples. Danish law requires that all projects involving human biological material obtain such approval. Researchers from abroad may collaborate with a Danish institution in order to gain access to biosamples and data.

Once a project has been approved by an ethics committee, the researchers must apply through the national access system for biosamples and health data. At this stage, researchers must submit a project description, samples retrieval list, and a statement that the funds necessary to retrieve the samples are available. Moreover, the Coordinating Center can arrange for the retrieval of samples that are located in other biobanks in Denmark so researchers are only required to apply once. The

[2] Statens Serum Institut, "The Danish Biobank Register," Statens Serum Institut, February 10, 2021, https://www.danishnationalbiobank.com/danish-biobank-register.

Coordinating Center is also available to provide support and advise about access to biosamples and data.

All applications are reviewed by the Scientific Board. The board consists of the following members: two people from SSI, among these the chairperson; one person from the Danish Council for Independent Research, Medical Sciences; one person from the Danish Regions, and one person from the organization Danish Patients. The board evaluates applications in the order they are received and responds within one month.

If a project is approved, the DNB laboratory will discuss the terms of retrieval with the researchers. The normal limit is set to 100 µl serum/plasma or 1 µg DNA.

Funding. The DNB was established with a major financial contribution from the Novo Nordisk Foundation and financial support from the Lundbeck Foundation and the Danish Ministry of Higher Education and Science. The total cost of the DNB was DKK 122 million with DKK 36 million contributed by the Ministry of High Education and Science and DKK 85 million from the Novo Nordisk Foundation.[3]

3. COVID-19 Response

Public Health Surveillance

Throughout the pandemic, Denmark has adopted three main strategies: containment, mitigation, and suppression. These strategies were complimented by a robust testing program as well.

The containment strategy was adopted at the beginning of the pandemic and aimed at impeding or delaying the introduction of the novel virus into the country. Denmark began a border surveillance program under which people returning from affected areas were tested for the virus. Containment strategies are contingent on the ability to establish and case definition to delimit possible cases. A clear case definition determines who should be tested. Positive cases can then be isolated and exposed persons, quarantined. While the containment strategy was successfully deployed for SARS and MERS-CoV-2, it was not successful against SARS-CoV-2. There are two reasons for the failure of the containment strategy. The first is that it became difficult to determine where the disease was coming from because community transmission was starting to occur in several locations throughout Europe and other parts of the world. The second reason was that the virus was being transmitted by pre-symptomatic and asymptomatic patients. These two reasons made it increasingly difficult to establish a sufficient case definition.

As a result, Denmark made the decision to divert to a mitigation strategy. The mitigation strategy focused on protecting vulnerable populations against serious infections, but not necessarily those who fell outside of that group. Testing was offered to at-risk individuals and those with serious symptoms.

The suppression strategy aims to suppress the epidemic as much as possible while allowing social and economic activities to continue to some degree. While this strategy had not been a part of European pandemic plans, it had been deployed in many Asian countries. The suppression strategy

[3] Danish Ministry of Higher Education and Science, "Denmark To Set Up World-Class National Biobank — Uddannelses- Og Forskningsministeriet," Press release, Danish Ministry of Higher Education and Science, February 24, 2009, https://ufm.dk/en/newsroom/press-releases/archive/2009/denmark-to-set-up-world-class-national-biobank.

is accompanied by a toolbox of preventive measures such as hand hygiene, coughing etiquette, self-isolation when symptomatic, use of surgical masks, restricting some community activities, and travel restrictions among others. Mass testing is also an essential part of the suppression strategy to break the chain of infection as much as possible. Denmark faced challenges when it came to testing. Clinical microbiology laboratories were facing severe supply shortages, and for several weeks they were unable to meet desired testing levels. However, the SSI responded by expanding the countries testing capacity, and by late March 2020 Denmark was able to test 100,000 samples daily. Denmark's successful deployment of a suppression strategy allowed for a slow, controlled reopening in the spring and summer of 2020.

Collection and Storage of Biological Samples

Denmark quickly established a COVID-19 biobank in the Bio- and Genome Bank, Denmark (RBGB) to oversee the collection and storage of COVID-19-related biosamples. The goal is to increase access to COVID-19-related biosamples and data to strengthen the possibility for improved treatment and understanding of the disease. Some questions researchers hope to answer include how mediation for the chronically ill affects the treatment course and why some patients get seriously ill while others only suffer from minor symptoms.[4] Answering these questions would have a profound effect on prevention and primary triage.

All biosamples are collected and stored in accordance with the biobank's existing principles and guidelines and in collaboration with the DNB. Blood and throat swab specimens are handled and stored at hospitals and the data is registered with the biobank. The RBGB is working with the DNB to collect as many samples as possible in an organized manner. All biosamples and data are available to clinicians and researchers across the country who can apply for access via the regular channels.

[4] Danish Ministry of Foreign Affairs, "The Danish Regions Have Established a National Danish Covid-19 Biobank in Hope of Improved Treatment," Danish Ministry of Foreign Affairs, April 3, 2020, https://investindk.com/insights/the-danish-regions-have-established-a-national-danish-covid-19biobank-in-hope-of-improved-treatment.

France

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

In France, Santé publique France (SPF) (former French Institute for Public Health Surveillance, InVS) is responsible for infectious disease surveillance. SPF works closely with local and regional public health authorities to collect surveillance data.

Mandatory Reporting Diseases. France has a list of 30 Mandatory Reporting Diseases in order to collect data to precisely analysis developments throughout the country. Mandatory reporting is based on the transmission of individual case data to health authorities and enables preventive activities and programs. It is complimented by other surveillance programs such as syndromic surveillance.

Syndromic Surveillance

The syndromic surveillance system in France, SURSAUD, is composed of four information sources: the OSCOUR network (coordinated emergency department surveillance organization), the SOS Médecins network, mortality data from the National Institute of Statistics and Economic Studies (INSEE), and INSERM data on causes of death.

The OSCOUR Network. The OSCOUR Network was established in 2004 to collect data on patients from volunteer hospital emergency departments. Data on the patient's age, sex, severity, medical diagnosis (based on ICD-10 standards), and short-term outcome is de-identified and subsequently transferred to regional health authorities or directly to SPF. As of 2007, the OSCOUR network included 98 hospitals with 8,000 to 9,000 cases reported each day. That being said, there is still room to improve the quality of the reports. Nevertheless, the French government has found the OSCOUR network to be a successful tool for the surveillance of several diseases.

The SOS Médecins Network. The SOS Médecins Network was established in 2006 and is a counterpart to the OSCOUR Network for private medical entities. Various SOS Médecin groups submit data via a computerized telephone switchboard. Data reported includes sex, age, postal code, reason for call, source, diagnosis, and short-term outcome. As of 2007, 37 out of 59 French associations of SOS Médecins were transmitting about 4,000 cases each day.

Mortality Data. The third and fourth components of SURSAUD are based on mortality data. The use of mortality data was introduced in two phases. The first phase took place in 2004 when 1,042 municipalities began reporting data on recorded deaths daily. The second phase began in 2006 with the establishment of electronic death certificates that are automatically transmitted to SPF (InVS at the time). This data can be accessed by regional epidemiologists in real time via a secure website.

Financial and Human Resources

In 2007, InVS's total expenses equaled EUR 51.5 million with EUR 19 million designated to infectious diseases and EUR 6.5 million to surveillance systems. Furthermore, the organization was supported

by 381 staff (190.7 epidemiologists, 34.6 scientists, 45 managers, and 110.7 administrative and support personnel).[5]

2. Collection and Storage of Biological Samples

French Biobanks

France has a nationwide infrastructure to support biomedical research called BIOBANQUES. This system is composed of 94 individual biobanks and covers over 700 research projects that currently use biological collections.[6] Moreover, BIOBANQUES is responsible for coordinating with the European BBMRI-ERIC to represent French interests.

In France, most biobanks are based in hospitals and operate within a flexible framework with regard to biosample access. While in most countries, biobanks have established protocols determining how researchers can acquire biosamples and data, France leaves that determination to the clinicians who established the biobank. This structure conflicts with the idea that biobanks are one method of promoting public health and acts as a barrier to innovative research.

Financing

Since 2005, with the "tarification à l'activité" (T2A), the financing of biobanks has been partly ensured by a budgetary envelope called "MERRI" (for "Mission d'enseignement, de recherche, de référence et d'innovation"), which amounted to EUR 25 million in 2018 and is intended for university hospital centers and distributed among the centers. However, this allocation only partially covers the costs of the biobanks and, as a result, due to the lack of other perennial funding, most biobanks' budgets are not balanced and the deficits must be compensated for from hospital budgets. This creates a challenge for hospitals which are constantly trying to reduce costs. Recently, hospital management has been reluctant to compensate biobanks and encourages them to estimate costs and seek revenue from other sources. However, this practice raises concerns about the regulation of the uses of biosamples and data, as well as the collective benefit of biobanking in France.

3. COVID-19 Response

Public Health Surveillance

France has struggled to successfully establish surveillance for COVID-19. This is due in part to the characteristics of the disease that hinders the identification of cases, but was exasperated by a limited testing capacity at the onset of the epidemic. Testing in France was limited to severely ill patients and studies have suggested that up to 90,000 symptomatic infections, or 90% of all cases, went undetected by the surveillance system from 11 May to 28 June 2020.[7] Only 31% of symptomatic individuals sought medical attention, leaving the rest to go undetected. This situation may have been negatively influenced by barriers to testing such as prior consultation, prescription, and a laboratory appointment. France has since eliminated these requirements in an effort to expand testing and surveillance.

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[5] French Institute for Public Health Surveillance, "Annual Report 2007" (Paris: French Institute for Public Health Surveillance, 2007).

[6] Ministère de l'Enseignement supérieur, de la Recherche et de l'Innovation, "Infrastructure nationale-BIOBANQUES," Ministère de l'Enseignement supérieur, de la Recherche et de l'Innovation, April 5, 2016, //www.enseignementsup-recherche.gouv.fr/cid99477/infrastructure-nationale-biobanques.html.

[7] Giulia Pullano et al., "Underdetection of Cases of COVID-19 in France Threatens Epidemic Control," *Nature* 590, no. 7844 (February 2021): 134–39, https://doi.org/10.1038/s41586-020-03095-6.

Collection and Storage of Biological Samples

The Louis Pasteur Hospital University Biobank in Nice, France established a collection of blood samples from positive COVID-19 patients. The collection began after receiving approval from the Ethics Committee at the Nice Hospital Center and written consent from all patients. The first biosamples from COVID-19 patients were registered on 15 March 2020.

Blood samples were taken from each patient on the first day of admission and after weeks one and two of hospitalization. The hospital followed biosample collection guidelines established by the French Society for Microbiology and all blood samples were placed in plastic bags. The time between venipuncture and centrifugation was no more than one hour in order to maintain the quality of the samples.

Biosamples were accompanied by electronic biological data records that include data on treatments administered and patient follow-up. Clinical data was recorded by clinical research associates and secured with established health and safety protocols.[8]

[8] Virginie Tanga et al., "Establishment of a Collection of Blood-Derived Products from COVID-19 Patients for Translational Research: Experience of the LPCE Biobank (Nice, France)," *Biopreservation and Biobanking* 18, no. 6 (November 10, 2020): 517–24, https://doi.org/10.1089/bio.2020.0055.

Germany

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

In Germany, the Robert Koch Institute (RKI) has been responsible for managing infectious diseases since 1981. RKI is the central organization responsible for the collection, analysis, and interpretation of epidemiological data of infectious diseases under the German Infection Protection Act. Germany has a robust countrywide system called SurvNet to aggregate data on infectious diseases.

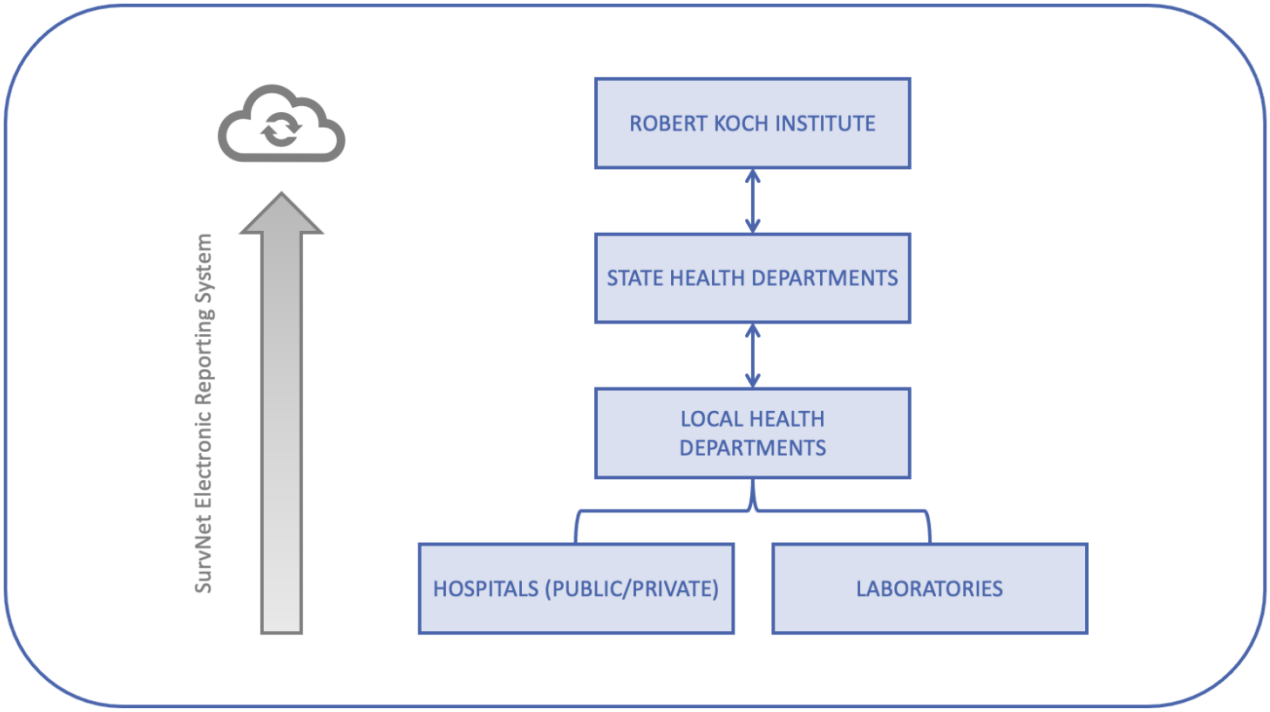

Figure 2. German Surveillance Information Flow

Demographic, treatment, vaccination, diagnostic, and risk factors are electronically recorded at local healthcare entities and forwarded to local and state health departments. Data is then transferred to the RKI for further action and analysis. In 2013, an amendment to the Infection Protection Act mandated that local and state health departments must report surveillance data within one day instead of one week. The amendment was successfully implemented and did not have a negative effect on data quality or workload.[9]

Sentinel Surveillance

In 2015, Germany established an ICD-10 code-based sentinel surveillance system for severe acute respiratory diseases. Each week de-identified data on discharged patients and in patients with respiratory illnesses are transferred from local healthcare entities to RKI. A study conducted in 2017

[9] Jakob Schumacher et al., "Timeliness in the German Surveillance System for Infectious Diseases: Amendment of the Infection Protection Act in 2013 Decreased Local Reporting Time to 1 Day," *PLOS ONE* 12, no. 10 (October 31, 2017): e0187037, https://doi.org/10.1371/journal.pone.0187037.

found that the available data and implemented reporting system are sufficient to provide timely and reliable information on the status of severe acute respiratory diseases in Germany.[10]

Electronic Reporting

In 2001, RKI introduced an electronic surveillance system, SurvNet, for infectious diseases across all levels of the German health system. This centralized system helped to ensure that epidemiological data was exchanged among healthcare institutions at the local, state, and federal levels. It was adopted by local and state health departments and the RKI in 2006. The RKI has data surveillance and data management units which are responsible for supporting SurvNet.

Financial and Human Resources

The Robert Koch Institute is owned and funded by the Federal Ministry of Health and had a budget of EUR 105 million in 2017. There were 1250 professional staff and 230 support staff employed at the institute.[11]

2. Collection and Storage of Biological Samples

German Biobank Node

The German Biobank Node (GBN) is the central organization responsible for coordinating cooperation among the German biobank community and representing German interests in the European biobank network.

German Biobank Alliance. The German Biobank Alliance (GBA) was formed in 2017 under the GBN and was composed of eleven German university hospitals and two IT development centers. Since 2017, the alliance has grown to include 20 biobanks across Germany.[12] Members of the GBA have worked to create consistent quality management protocols and IT infrastructure in order to make their biosample accessible for biomedical research throughout Europe. The GBN is funded by the German Federal Ministry of Education and Research (BMBF).

Steering Committee. The GBN Steering Committee supports members of the alliance to ensure that they are cooperating effectively. The committee is responsible for setting the alliance's agenda and strategic vision. Originally, the committee was composed of a representative from each biobank, but as the alliance expanded, a decision was made to reduce the size of the committee.

Scientific and Ethical Advisory Board. The Scientific and Ethical Advisory Board (SEAB) advises the activities of GBN and GBA and supports the Steering Committee in solving issues related to its mission. The SEAB is an independent committee and is composed of international scientists and experts who act independently of their organizational affiliation.

Quality Management. In the past, scientific journals have reported on studies with poor-quality biosamples which led to irreproducible research results. These studies were found to have led to

[10] Silke Buda et al., "Establishing an ICD-10 Code Based SARI-Surveillance in Germany – Description of the System and First Results from Five Recent Influenza Seasons" 17, no. 612 (2017), https://doi.org/10.1186/s12889-017-4515-1.
[11] International Labour Organization, "Germany - RKI - 2017," Database on OSH Agencies, Institutions and Organizations, 2017, https://www.ilo.org/dyn/interosh/en/f?p=14100:1100:0::NO::P1100_ISO_CODE3,P1100_SUBCODE_CODE,P1100_YEAR:DEU,RKI,2017.
[12] German Biobank Node, "German Biobank Alliance," German Biobank Node, accessed March 29, 2021, https://www.bbmri.de/about-gbn/german-biobank-alliance/?L=1.

significant time and financial losses. Germany recognizes the importance of high-quality biosamples and their associated data in achieving reliable and reproducible scientific results. For that reason, the GBN developed a Quality Management Manual in 2018 that is regularly updated and covers the acquisition, processing, storage, and dispensing of biosamples. The manual helps maintain consistency and quality across all of the biobanks in the GBA.

Accessing Biosamples. Researchers are able to search for biosamples and associated data in academic biobanks online via the Sample Locator. The online tool was developed by a team from the GBA and uses open-source coding to allow for collaboration.

The first step entails a feasibility query which shows researchers how many samples meet the requested search criteria. An institutional email address and account password are required to access information on where and how many samples are available. To request samples, researchers must register and then select the desired biobanks.

The next step is to access Negotiation, a communication platform that allows researchers to communicate with multiple biobanks at the same time. Through this platform, biobanks are able to share information on the availability of biosamples and data.

IT Infrastructure. The GBN has an extensive IT infrastructure that consists of a network of bridgeheads—data integration servers established by each biobank that are filled with relevant information on biosamples and clinical data. Each biobank is responsible for its own local operation and retains full control over its data. The system is governed by a Data Protection Concept that fully complies with the EU General Data Protection Regulation.

3. COVID-19 Response

Public Health Surveillance

In accordance with the Infection Protect Act, German health authorities transmit data on COVID-19 cases to the RKI. Germany has established a series of surveillance systems to support this effort. The German government expanded its Antimicrobial Resistance Surveillance program to support laboratory surveillance of SARS-CoV-2 and publishes weekly reports. There are also sentinel surveillance programs in 73 hospitals around the country that use ICD-10 standards to report on acute respiratory diseases, including COVID-19. Moreover, Germany established a new syndromic surveillance system called SUMO that collects real-time data from 20 emergency departments in Germany. All data collected through the SUMO system is de-identified before being transmitted to the RKI for evaluation.

Collection and Storage of Biological Samples

The German Biobank Node was quick to establish a collection of SARS-CoV-2 and COVID-19 biosamples. As for July 2020, 13 biobanks in Germany storing SARS-CoV-2 samples (serum, plasma, PBMC, whole blood, swabs, and urine).[13] The RKI established protocols for biobanks and researchers working with SARS-CoV-2 samples that cover processing, storage, and disposal. Pursuant to Section 52 of the Infection Prevention Act, material containing pathogens may only be supplied to persons authorized to handle these or working under the supervision of an authorized person.

[13] German Biobank Node, "German Biobank Node: Sample Availability," German Biobank Node, July 3, 2020, https://www.bbmri.de/covid-19/sample-availability/?L=1.

South Korea

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

South Korea's democratic unitary political system means that local governments have limited autonomy which allows for a centralized public health governance system. While local governments have authority over local health units, the national government has authority over city and provincial departments of health, as well as the Korea Disease Control and Prevention Agency (KDCA).[14] South Korea has a robust countrywide system called the National Notifiable Infectious Disease Surveillance System (NNIDSS) which is composed of hospitals and healthcare providers; local health centers; city and provincial departments of health; and the KDCA.

Notification. During the first stage of the surveillance process, hospitals and healthcare providers are responsible for notifying local health centers of conditions that are on the list of National Notifiable Infectious Diseases (NNID). Local health centers are responsible for reviewing notifications of infectious diseases and for reporting their findings to city and provincial departments of health.

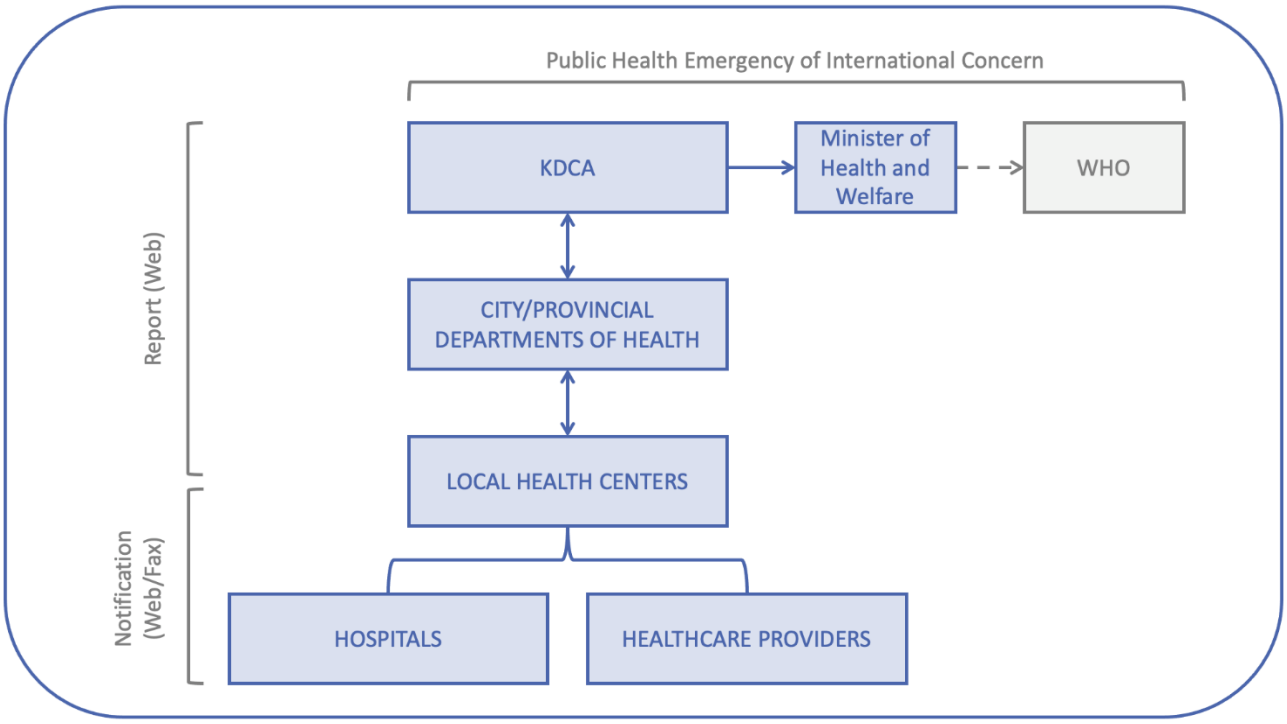

Figure 3. South Korean Surveillance Information Flow

Report. City and provincial departments of health examine the outbreak report of infectious diseases at local health centers and report the findings to the KDCA. Data regarding infectious disease outbreaks and epidemics is released each week or month and reported to the governor of each city and province.

[14] Formerly known as the Korea Centers for Disease Prevention and Control (KCDC).

At the national level, the KDCA is the main operational agency for infectious disease prevent and control, and it is responsible for ensuring monitoring of infectious disease outbreaks and facilitating cooperation throughout all networks in the country.

National Notifiable Infectious Diseases. The South Korean government monitors all infectious diseases in the country and established a list of NNID. The NNID list is divided into five groups (plus an additional category for designated diseases) with each group having different notification timeframes. Groups one to four require immediate electronic notification, whereas group five and the list of designated diseases require notification within seven days. In the event a national notifiable infectious disease has been reported, an epidemiological investigation is performed to track the source of the infection. Epidemiological investigations include actors from all levels of the surveillance system. The KDCA oversees the planning, implementation, and evaluation of the investigation across all networks and reporting jurisdictions. City and provincial Epidemiological Investigation Units are responsible for the planning, implementation, and evaluation of the investigation within their jurisdiction. In the event that a subset of reports falls within the scope of a Public Health Event of International Concern (PHEIC) under the International Health Regulations (IHR) (2005), the KDCA informs the Minister of Health and Welfare who subsequently notifies the World Health Organization (WHO).

Laboratory Surveillance

Laboratory surveillance contributes to the identification and trend analysis of infectious diseases. It also plays a major role in determining the case for a suspected disease that may otherwise be difficult to diagnose clinically. When it comes to disease outbreaks and epidemics, it is important that data is highly accurate. Laboratory surveillance is not only highly accurate, but supplies detailed information about region, date, sex, age, and clinical characteristics which contribute to a smooth epidemiological investigation.

In particular, acute respiratory infections such as the common cold place a major burden on South Korea's healthcare system. The lack of data on these infections makes it difficult to evaluate the situation. However, the implementation of laboratory surveillance has allowed for the collection of data to analyze such diseases.

Sentinel Surveillance

South Korea also operates a sentinel surveillance system for national notifiable infectious diseases. As of 2007, there were about 3,400 sentinel surveillance health facilities that include primary and secondary care institutions, general hospitals, and public health centers among others. These facilities are responsible for reporting to local health centers which then relay the information to the city and provincial departments of health and the KDCA. In some cases, sentinel surveillance institutions will report directly to the KDCA. Some infectious diseases included in the sentinel surveillance system include influenza; parasitic diseases; hand, foot, and mouth diseases; healthcare-associated infections; gastrointestinal infections; acute respiratory infections; and enterovirus infections. Notifications must be made within seven days and the KDCA publishes a monthly report with the findings from all sentinel surveillance institutions.

Electronic Reporting

In 2000, South Korea implemented an Electronic Data Interchange (EDI) based on a client-server generated system to facilitate surveillance activities. In 2007, the system was reorganized to operate as a more accessible web-based reporting system. As a result, South Korea was able to solve the problem of missing or delayed reports and now has higher report and notification rates. The electronic reporting system is also useful for practitioners because they can use the system to search for treatments for diseases based on variables including disease-specific factors, region, gender, and age among other identifiers. The government sees this as a significant achievement for computerized report systems for all infectious disease surveillance in the public health sector.

Financial and Human Resources

In 2013, the KDCA's (KCDC at the time) total budget was USD 311,966,102 with USD 6,967,043 allocated to controlling infectious diseases and USD 4,356,874 allocated to fortifying the response system for novel infectious diseases.[15]

There are about 1,400 staff[16] for prevention, investigation, quarantine, testing, and research of infectious diseases at the KDCA. Furthermore, there are 10 Rapid Response Teams (RRT) at the KDCA that can be deployed for epidemic investigations. In the event that there is a large-scale epidemic, these teams are supported by Emergency Investigation Officers who are trained through the Field Epidemiology Training Program. Moreover, private sector healthcare professionals can be mobilized if necessary. South Korea also places great importance on workforce development in order to strengthen its public health emergency preparedness. Recently, infectious disease specialists are being hired and trained to contribute to the KDCA, departments of health, and local health centers.

2. Collection and Storage of Biological Samples

Korea Biobank Network

The Korea Biobank Network (KBN) is composed of the National Biobank of Korea (NBK), 17 regional biobanks established in collaboration with university hospitals, and two KBN-collaborative biobanks.

National Biobank of Korea. The NBK was established by the Korea National Institute of Health (KNIH) in 2008 and is the national control center for the collection, management, and utilization of human biosamples in Korea. The NBK is responsible for managing the KBN and as such contributes to the development of policies related to human biosamples, standardization of human biosample management, and advancement of domestic biobanks. The Biobank Coordinating Center (BCC) provides researchers with assistance when accessing biosamples housed at any of the 17 biobanks throughout the country.

Regional Biobanks. Regional biobanks are located throughout South Korea in various public and private university hospitals. They are granted permission to store human biosamples under Article 41 of the Bioethics and Safety Act and operate with financial support from the Ministry of Health and Welfare. Regional biobanks are responsible for collecting and storing biosamples from patients visiting the hospital for several conditions.

[15] Ministry of Health and Welfare and Korea Foundation for International Healthcare, "2013 Modularization of Korea's Development Experience: Establishment of Korea's Infectious Disease Surveillance System," 2014, 92.
[16] As of 2020.

While most regional biobanks focus on diseases such as cancer and tuberculosis, two regional biobanks, Soon Chun Hyang University Hospital Bucheon and Wonkwang University School of Medicine and Hospital, have biosamples relating to respiratory diseases. It is notable that South Korea has a separate collection for pathogens that falls outside of the KBN (see *National Culture Collection for Pathogens* below).

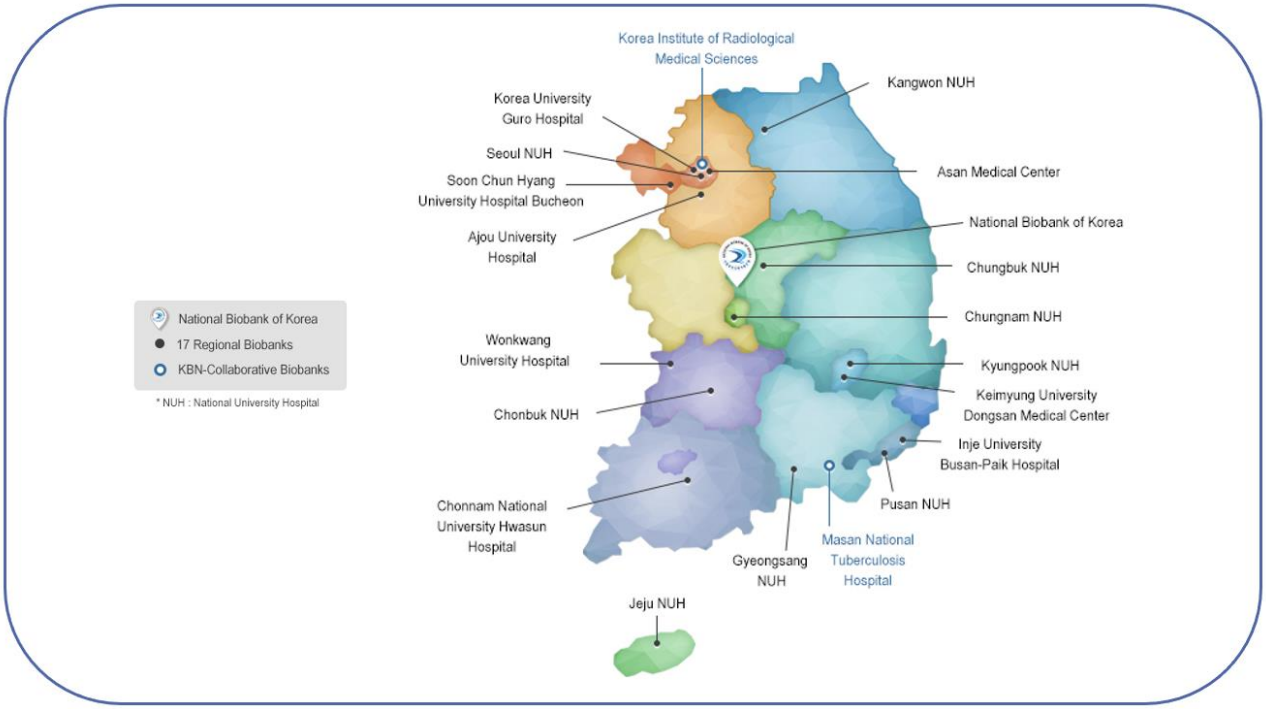

Figure 4. Map of the Korea Biobank Network[17]

KBN-Collaborative Biobanks. KBN-Collaborative Biobanks are located in hospitals that have a cooperative agreement with the KNIH to share the KBN operating system. They are responsible for collecting, storing, and distributing biosamples to individual hospitals for research purposes.

Accessing Biosamples from the Network. Research projects that are conducted for public interest, funded as a national development initiative and conducted by national organizations, government-funded institutions, or private research centers may gain access to biosamples. Researchers are required to file a distribution application, written pledge, research plan, assessment by the Institutional Review Board, and other related documents online. Upon receiving an online application, the biobank conducts a distribution review and decides whether the application will be approved or rejected. The review is conducted by a Distribution Review Board composed of experts such as epidemiologists, genomicists, and bioethicists. Researchers who are approved for the distribution of biosamples are required to register their research results with the KBN.

National Culture Collection for Pathogens

The National Culture Collection for Pathogens (NCCP) is South Korea's national pathogen resource bank that was established for the promotion of research and development relating to the

[17] National Institute of Health, "Korea National Biobank," National Institute of Health, November 4, 2019, http://www.nih.go.kr/contents.es?mid=a50402030100.

preparedness, diagnosis, and treatment of infectious diseases. The NCCP has four main objects that include networking, resource management, standardization initiatives, and distribution.

Networking, Resource Management, and Standardization. Networking entails the operation and management of field-specific pathogen resource banks, as well as exchanging pathogen resources and information with domestic and overseas resources banks. The NCCP is responsible for overseeing and implementing the collection and management of a variety of resource strains. It also characterizes and authenticates all resources with a systematic management system. The NCCP has collected pathogen resources through active collaborations with various entities. As Specialized Pathogen Resource Banks, two organizations, Catholic Kwandong University International St. Mary's Hospital and Korea University, focus on medical fungi and viruses. The NCCP also undertook projects to collect rarely isolated pathogens and obligate intracellular bacteria. Moreover, the NCCP focuses on establishing protocols to standardize pathogen resources and information, as well as management systems and materials.

Distribution. The NCCP operates the Pathogen-resource Information Management System (PIMS) and pathogen resource banks so that researchers can in various fields can access them. The NCCP distributes a variety of resources including pathogens isolated from clinical patients, statutory infectious diseases and high-risk pathogens, characteristic information on pathogens (i.e., serotype, genotype, antibiotic resistance, clinical and epidemiological information, etc.), materials derived from pathogens (i.e., nucleic acid, antigen, antibody, cellular materials, etc.). For reference, the NCCP distributed 128 species and 1,460 strains to researchers and institutes in 2017.[18] Institutions must be required with sufficient research facilities and educated researchers meeting strict biosafety standards in order to be supplied with pathogen samples.

3. COVID-19 Response

Public Health Surveillance

South Korea initiated an extensive COVID-19 surveillance program with testing and aggressive contact tracing at its core. South Korea's more complex prevention efforts began in April when it mandated a 14-day self-quarantine or isolation in facilities and expanded surveillance efforts at points of entry.

In addition to testing everyone entering the country, South Korea launched an extensive testing campaign around the country that including walk-in and drive-through testing centers. As a result, South Korea had the highest proportion of tests per capita in the world.

South Korea has employed aggressive contact tracing procedures to isolate cases and reduce community transmission by conducting interviews, reviewing credit card transactions, CCTV footage, and GPS data from mobile phones. Local governments are responsible for contact tracing and are supported by the KDCA (former KCDC).

The majority of South Korea's cases at the early onset of the epidemic were traced back to Shincheonji Church in Daegu City. Korean health authorities were able to trace, test, and, if

[18] National Institute of Health, "Pathogen Resource Management: NCCP," National Institute of Health, May 14, 2019, http://www.cdc.go.kr/contents.es?mid=a50401070000.

necessary, isolate or quarantine every member of the church throughout the country (nearly 250,000 people).

Taiwan

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

In 2001, Taiwan established a National Notifiable Diseases Surveillance System (NNDSS) overseen by the Taiwan Centers for Disease Control (Taiwan CDC) that uses web-based reporting for infectious disease surveillance. The centralized system can be accessed by medical professionals with their medical personnel ID card to report suspected or confirmed cases and submit clinical specimens if necessary. In 2014, the Taiwan Health Cloud Program was implemented to automatically report information collected in hospital electronic medical records. This has improved the timeliness of reporting to the NNDSS. As of 2016, 47 hospitals had implemented the new system representing half of all reports to the NNDSS. As a result, the average time for a healthcare worker to complete the report process to the Taiwan CDC is 6.3 minutes.[19]

Laboratory Surveillance

The National Laboratory Surveillance Network monitors the spread of viruses in the community and is the foundation of influenza and enterovirus surveillance. Taiwan uses a Laboratory Automated Reporting System (LARS) that was developed to improve efficiency and the scope of community-based laboratory reporting for 20 microorganisms of public health concern. The system adopts the Logical Observation Identifiers Names and Codes (LOINC), a universal standard for identifying medical laboratory observations, and automatically submits information from laboratories on a daily basis. By using a standardized system for reporting, 51 medical centers and metropolitan hospitals are able to submit information to the LARS. That data is sent via a cloud data exchange to the Taiwan CDC's data warehouse and converted to an open data format for dissemination through the national open data platform.

Syndromic Surveillance

Taiwan learned from the SARS outbreak and shortly thereafter established a hospital emergency room-based real-time outbreak and disease surveillance system in 2004. The aim of the system is to collect individual ICD-10 codes from patient ER visits from designated emergency rooms and send the data to the Taiwan CDC. Ninety percent of patient records are uploaded to the Taiwan CDC's servers within one hour and the remaining 10% within one day. From 2012 to 2015, the system covered more than 96% of all ER visits recorded by the National Health Insurance (NHI) system in Taiwan.

2. Collection and Storage of Biological Samples

As of 2020, there are 32 biobanks in Taiwan, in addition to the Taiwan Biobank (TWB).

Taiwan Biobank

The Taiwan Biobank (TWB) was established in 2012 and plans to conduct both a large-scale community-based cohort and several patient cohorts on local chronic diseases from medical centers. The community-based cohort study will recruit 200,000 volunteers between 30 and 70 years of age with no history of cancer, and the hospital-based cohort study will recruit 100,000 patients affected

[19] Shu-Wan Jian et al., "Real-Time Surveillance of Infectious Diseases: Taiwan's Experience," *Health Security* 15, no. 2 (April 1, 2017): 144–53, https://doi.org/10.1089/hs.2016.0107.

by the most common chronic diseases. The program is divided into eight steps: recruitment, reservation, informed consent, physical examination, biosample collection, questionnaire, feedback survey, and biosample and data storage.[20]

Access to Biosamples and Data. On 1 September 2014, information on community volunteers was made available. Data can be divided into five categories including questionnaire, physical examination, blood and urine tests, biological samples (i.e., DNA, blood plasma, etc.), and experimental data (i.e., whole-genome genotyping, whole-genome sequencing, DNA methylation, HLA typing, and blood metabolome).

The TWB conducts extensive experiments to collect biomedical data on biosamples in its repository in order to avoid sample depletion and to establish a reference information database. Data collected is then made available to researchers for further study. These experiments help to reduce the burden on the Taiwanese research infrastructure and eliminate repetitive data collection.

Taiwan Centers for Disease Control Biobank

The Taiwan CDC operates a biobank to preserve samples of infectious diseases. The Taiwan CDC Biobank was established in 1992 and stores, manages, and distributes samples with other research institutions. Moreover, it cooperates with biotechnology companies to develop diagnostic reagents. Taiwan plans on expanding its biobanking capacity by establishing a more sophisticated biobank information system, improving the capacity of infectious biomaterials, getting international certification for the biobank, and training staff.

3. COVID-19 Response

Public Health Surveillance

As of 30 June 2020, Taiwan successfully eliminated the COVID-19 outbreak through a variety of public health and surveillance measures including border controls, enhanced surveillance, case detection with contact tracing, isolation and quarantine, and population-based interventions like face mask use. Taiwan also successfully decreased the time between disease onset to notification from five days before 1 March 2020 to one day after 1 March 2020.[21] Travel restrictions with mandatory quarantine protocols helped minimize disease spread and resulted in fewer clusters than other countries.

Collection and Storage of Biological Samples

Taiwan was the first to establish a biobank for COVID-19 biosamples. The Minster of Health and Welfare requested that the NHRI Biobank establish a COVID-19 biobank in February 2020 to collect blood samples for Taiwanese researchers and industries. The biobank was set up within three weeks and has collected blood samples from patients in more than 10 hospitals throughout Taiwan.[22] Researchers can apply for biosamples including serum, DNA and RNA, as well as clinical and genomic data. The goal is to enhance treatment and prevention research in Taiwan.

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[20] For a detailed overview of each step, see: Taiwan Biobank, "Participation Program," Taiwan Biobank, n.d., https://www.twbiobank.org.tw/new_web_en/join-flow-before.php.

[21] Hao-Yuan Cheng et al., "Taiwan's COVID-19 Response: Timely Case Detection and Quarantine, January to June 2020," *Journal of the Formosan Medical Association*, November 2, 2020, https://doi.org/10.1016/j.jfma.2020.10.023.

[22] Shiu-Feng Huang et al., "Rapid Establishment of a COVID-19 Biobank in NHRI by National Biobank Consortium of Taiwan," *Biomedical Journal* 43, no. 4 (August 1, 2020): 314–17, https://doi.org/10.1016/j.bj.2020.05.018.

United Kingdom

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

Public Health England (PHE) is the organization responsible for overseeing surveillance efforts throughout the country. PHE collects, analyzes, and interprets data from National Health Service healthcare entities. All data collected by PHE is de-identified with the exception of certain data collected during outbreaks. In the event identified data is required, there are strict security protocols to ensure its protection.

Syndromic Surveillance

In preparation for the 2012 London Olympics, the United Kingdom established a substantial syndromic surveillance program known as the Public Health England Emergency Department Syndromic Surveillance System (EDSSS), throughout many emergency departments in the country. Data collected from the network of hospitals is updated in real time and monitored by PHE.

Financial and Human Resources

The 2020-2021 PHE budget allocates GBP 89.9 million to "protection from infectious diseases" which supports national centers, regional network, and the country's capability to identify infectious disease, establish surveillance, and manage of outbreaks. 2082 staff have been allocated to help implement these efforts.[23]

2. Collection and Storage of Biological Samples

UK Biobank

UK Biobank is an extensive biomedical database that contains genetic and health information from about 500,000 UK participants aged between 40 and 69 years old. The database is regularly updated with additional data and is accessible to researchers from the UK and abroad. By consistently collecting blood, urine, and saliva samples, as well as detailed information on the participants' lifestyles, researchers are able to gain a deeper understanding of how individuals experience diseases.

Governance. UK Biobank is governed by a board of directors that brings experience from academia, philanthropy, and industry and is responsible for the direction, management, and control of the biobank.

The board and funders are advised, supported, and guided by the UK Biobank International Scientific Advisory Board (ISAB). Members of the board volunteer their time and expertise to discuss projects that strengthen the biobank.

The UK Biobank Steering Committee advises the project's Principal Investigator and Chief Executive Officer and is composed of scientists from a wide range of backgrounds.

[23] Public Health England, "Annual Report and Accounts 2019-2020" (London: Public Health England, 2020), https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/964244/Annual_Report___Accounts_2019_20_book.pdf.

The UK Biobank Ethics Advisory Committee (EAC) is a committee within the UK Biobank Board that provides advice on ethical issues relating to the maintenance, development, and use of the biobank.

Linkage to Healthcare Records. UK Biobank has complete coverage in respect to hospital admission data, death, and cancer records on all of its participants. Data is de-identified and made available to researchers as part of the biobank's data resource. This collection of data was made possible by establishing partnerships with NHS Digital and the Royal College of General Practitioners.

Access to Data and Biosamples. UK Biobank has a series of protocols that determine how researchers gain access to data and biosamples. More specifically, the protocols ensure that data are released to researchers for health-related research that is in the public interest. Furthermore, the biobank has an established material transfer agreement that prohibits researchers from trying to re-identify participants.

The procedures to access information from the biobank do not discriminate between academic, charitable, or commercial applicants, nor between national and international applicants. All applicants, with the exception of students and those from low/middle income countries, pay the same fees. A majority of applications are for data held at the UK Biobank's data resource center. The UK Biobank now has over 19,000 registered researchers from over 80 countries.

Access to physical samples is more restrictive due to their depletable nature. The biobank has an established release policy that sets guidelines for approving the release of biosamples. Since 2012, there have been 15 projects approved for use of physical samples. All data created by these projects must be returned to the UK Biobank to be made available to the research community.

Funding. UK Biobank was established by the Wellcome Trust medical charity, Medical Research Council, Department of Health, Scottish Government, and the Northwest Regional Development Agency. It also received funding from the Welsh Government, British Heart Foundation, Cancer Research UK, and Diabetes UK and is supported by the National Health Service (NHS). The medical research project is a non-profit charity which has received core funding of around £133 Million. Core funding continues to be received from the Wellcome Trust, the MRC, and more recently, from Cancer Research UK, and NIHR.

3. COVID-19 Response

Public Health Surveillance

The United Kingdom has implemented six main sources of data that is used to conduct surveillance for COVID-19 and monitor the pandemic: confirmed cases in England, community surveillance, primary care surveillance, secondary care surveillance, mortality surveillance and sero-prevalence surveillance.[24]

Confirmed Cases in England. Confirmed cases in England is the cumulative number of positive COVID-19 cases reported by NHS and PHE labs across England. There are two systems used for collecting data from laboratories: Second Generation Surveillance System (SGSS) and Respiratory DataMart. SGSS was designed to capture data on infectious diseases and antimicrobial resistance,

[24] For detailed information on each category, see Public Health England, "Sources of COVID-19 Surveillance Systems," GOV.UK, October 2, 2020, https://www.gov.uk/government/publications/national-covid-19-surveillance-reports/sources-of-covid-19-systems.

while Respiratory DataMart has been used to monitor major respiratory viruses since 2009. Both systems have now been adapted and combined to collect data on SARS-CoV-2. SARS-CoV-2 testing in England began on 24 January 2020.

Community Surveillance. Community surveillance consists of acute respiratory infection outbreak reporting, syndromic surveillance, and internet-based surveillance. The Respiratory Surveillance Section at PHE is responsible for collating data on acute respiratory infection outbreaks in institutional settings through the HPZone public health management system. Moreover, the Real-time Syndromic Surveillance Team (ReSST) at PHE is responsible for collecting and analyzing de-identified health data from several sources to identify increases in the prevalence of illness. Finally, internet-based surveillance including Google search queries and FluSurvey for COVID-19 have been employed to monitor trends in the community.

Primary Care Surveillance. Primary care surveillance is conducted by the Royal College of General Practitioners (RCGP) Research and Surveillance Centre (RSC). The RCGP RSC provides surveillance data from 500 general practitioner practices around England. Specifically, GP consultation rates for ILI, pneumonia, lower and upper respiratory tract infections (LRTI/URTI) are used to monitor COVID-19 activity. The RCGP also conducts sentinel swabbing of patients presenting with ILI and LRTI to monitor positivity rates over time.

Secondary Care Surveillance. Secondary care surveillance in the United Kingdom can be divided into two pillars. The COVID-19 Hospitalisation in England Surveillance System (CHESS) was adapted from the UK Severe Influenza Surveillance System (USISS) to collect epidemiological data on COVID-19 patients requiring hospitalization. The program "monitor the impact of severe COVID-19 infection on the population, inform understanding of natural history of disease, clinical severity of cases and provide data to inform models of transmission dynamics to forecast and estimate disease burden and health services utilization."[25] CHESS was expanded across all NHS Trusts on 15 March 2020. The second pillar of secondary care surveillance is the USISS Severe Respiratory Failure Centres (SRFs) which collects data on every patient accepted by a SRF Centre. There are 6 SRFs in the UK (5 in England and 1 in Scotland).

Mortality Surveillance. Weekly mortality surveillance helps detect and report excess mortality above historic levels. Mortality Monitoring in Europe (EuroMOMO) is a project that calculates age-specific and region-specific excess mortality rates in England and Wales.

Sero-prevalence Surveillance. The United Kingdom introduced sero-prevalence surveillance to detect asymptomatic and mild infections that would not otherwise be detected through existing surveillance system. The government saw this as an important step in understanding the real number of infections in the community and informing control measures. PHE established a number of serological collections with age-stratified geographically representative blood donor samples across England supplied by NHS Blood and Transplant (NHS BT). The samples are currently undergoing Euroimmun IgG assay testing to determine the presence of detectable antibodies.

[25] Public Health England.

Collection and Storage of Biological Samples

UK Biobank has taken swift strides to help tackle the global pandemic by undertaking four major initiatives including a serology study, COVID-19 repeat imaging study, coronavirus self-test antibody study, and health data linkage.

The serology study focused on measuring antibodies for the coronavirus which causes COVID-19 over six months and revealed the proportion of the population that had been infected. 20,000 UK Biobank participants were recruited for the study and had their blood samples collected and tested. One of the most significant findings of the study is that 99% of participants who had tested positive for previous infection retained antibodies to SARS-CoV-2 for 3 months after being infected, and 88% did so for the full 6 months of the study. This discovery provides an early indication that the antibodies produced following natural infection may protect most people against subsequent infection for at least 6 months.[26]

The coronavirus self-test antibody study aims to collect information that can be used to understand the long-term effects of COVID-19 and facilitate other health related research. The COVID-19 repeat imaging study was established to understand how COVID-19 affects internal organs and aims to conduct scans on over 3,000 people. These images can be compared to a collection of 50,000 images taken before the pandemic to further understand the disease. Lastly, the health data linkage initiative provides national and international researchers with data on 500,000 UK Biobank participants to gain insight into the genetic and lifestyle determinants of COVID-19 and its long-term health consequences. Data from health records includes COVID-19 diagnostic test data, hospital inpatient data, death data, and GP primary care data.

[26] UK Biobank, "COVID-19 Hub," UK Biobank, March 18, 2021, https://www.ukbiobank.ac.uk/learn-more-about-uk-biobank/covid-19-hub.

United States

1. Public Health Surveillance

Organizational Structure and Passive Surveillance

In the United States, infection disease reporting is mandated by law or regulation at the local, state or territorial levels, not at the federal level. The list of reportable diseases, who is required to report the conditions, reporting methods, and the timeline for reporting also differs between states and territories. However, there is a general infectious disease surveillance infrastructure that applies to the entire country and includes healthcare entities; local, regional, and state public health authorities; and the Centers for Disease Control and Prevention (CDC).

Case Reporting. The first phase of the public health surveillance information flow in the United States is case reporting. This phase begins in healthcare entities such as hospitals, healthcare providers, and laboratories which are all mandated by state law to identify and report certain conditions to their local, regional, or state public health authorities. Individual cases are reported with identified data and include personal details such as the patient's name, address, and phone number. This information is reported via morbidity forms, and depending on the jurisdiction, can be submitted by mail, fax, phone, or electronically. Data is first collected by local public health authorities and is passed in a hierarchical fashion to regional, state, or territorial authorities. Once a morbidity form has been submitted, public health staff may launch a follow-up investigation to verify the case based on the case definition and establish whether measures need to be taken for prevention and control. Local public health authorities maintain quality by auditing data collected from healthcare entities. Most jurisdictions audit 10% of all data reported (ex. if 100 cases of syphilis are reported in a given area, 10 of those charts will be audited to verify accuracy and quality). Labs are required to follow strict guidelines for quality control that are consistent across the country.

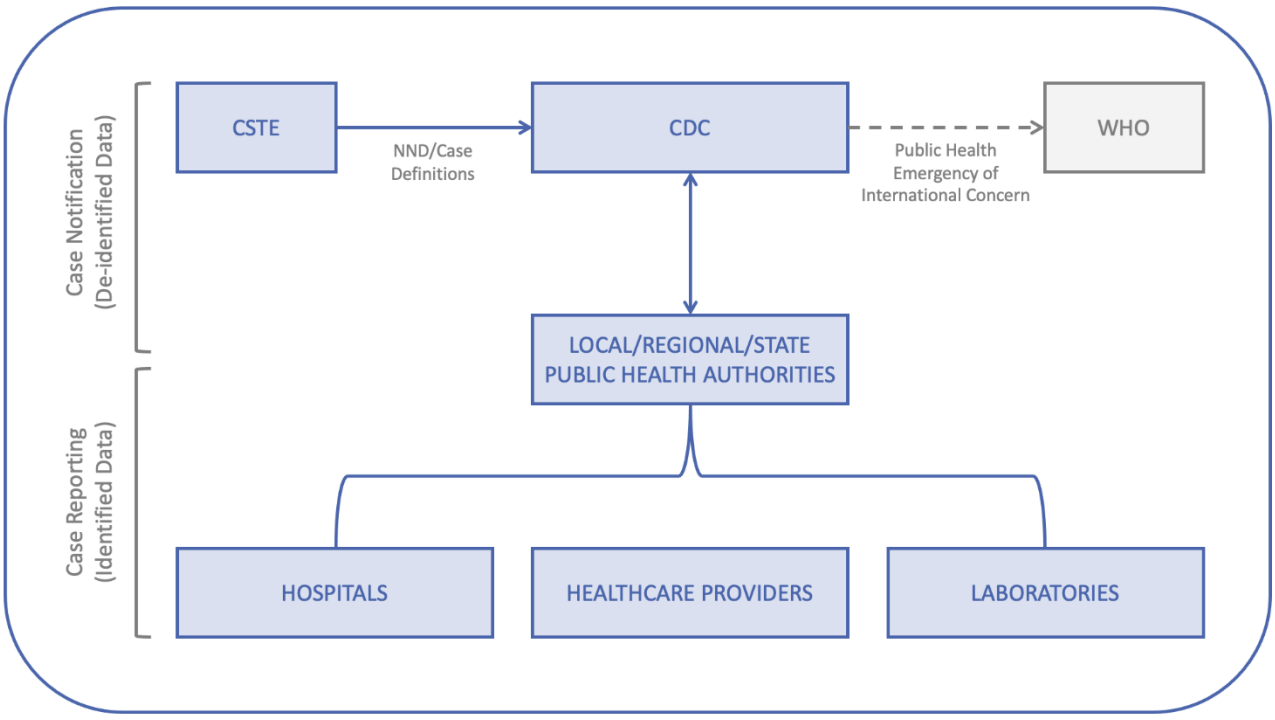

Figure 5. American Surveillance Information Flow

Case Notification. The second phase of the public health surveillance information flow in the United States consists of case notification. The CDC aggregates and analyses de-identified data on Nationally Notifiable Conditions (NNC) from 57 reporting jurisdictions including all 50 US states; New York City; Washington, DC; and five US territories under its National Notifiable Disease Surveillance System (NNDSS). It is notable that states are not legally mandated to report conditions on the NNC list and that all data submissions are voluntary. Preliminary data collected through the NNDSS is published in the CDC's Morbidity and Mortality Weekly Report (MMWR), and finalized data is published annually in the MMWR: Summary of Notifiable Diseases, United States.

National Notifiable Diseases. To maintain consistency and allow for comparability across jurisdictions, the Council of State and Territorial Epidemiologists (CSTE) establishes a list of NNC and national surveillance case definitions which are used by the CDC to conduct public health surveillance. The CSTE NND list categorizes notifiable conditions based on the timeframe within which they should be reported to the CDC. The three categories of conditions are immediate extremely urgent, immediate urgent, and standard notification. All conditions, regardless of their categorization, are reported via an electronic submission protocol. Additionally, electronic submissions for the two urgent categories of conditions are complimented with an initial voice notification to the CDC's Emergency Operations Center. In the event that a subset of case notifications falls within the scope of a Public Health Event of International Concern (PHEIC) under the International Health Regulations (IHR) (2005), the CDC will subsequently notify the World Health Organization (WHO).

Syndromic Surveillance

Health authorities in the United States operate a series of syndromic surveillance programs that collect data from emergency rooms, volume of sales data on over-the-counter medicines, workplace or school absenteeism, and drop-in surveillance programs. According to a 2008 survey of US health departments, 88% of respondents said that they routinely use syndromic surveillance. However, the scope and structure of syndromic surveillance programs varies across reporting jurisdictions which complicates the aggregation of data across jurisdictions.

Sentinel Surveillance

Sentinel surveillance in the United States is more structured than syndromic surveillance, especially for diseases like influenza. For example, the Sentinel Provider Network for Influenza is a network of representative healthcare providers that provide weekly counts of influenza-like illness and submit laboratory data for subtyping during influenza season. Outreach, recruitment of providers, and specimen transportation is the responsibility of local health entities. Data is entered into a web-based system managed by the CDC.

Electronic Reporting

In 1999, the CDC launched the National Electronic Disease Surveillance System (NEDSS) to help public health agencies accept electronic data exchanges from healthcare entities and enable health departments to create and send standardized case notifications to the CDC. To be considered NEDSS-compatible, a system must allow for data entry on an Internet browser-based program and integrate multiple health information databases into a single repository. As of 2021, all 50 US states

and Washington, DC have NEDSS compatible surveillance information systems to send case notifications to the CDC. Moreover, the NNDSS Modernization Initiative (NMI) was established to enhance the NNDSS's ability to collect more comprehensive, high-quality data in a timely manner for public health decision making. Nevertheless, there are still challenges with inconsistencies in Electronic Health Records that need to be addressed. Some experts have suggested working with private companies that develop EHRs to mandate a common framework to improve the accuracy and speed of reporting.

Financial and Human Resources

Funding for public health surveillance stems from various sources including state budgets, federal grants, and cooperative agreements. Throughout the past decade, state and local surveillance budgets have continued to decrease leading to poor data collection in certain jurisdictions. As a result, there has been increased reliance on federal grants and cooperative agreements. The primary source of funding for infectious disease surveillance is the Epidemiology and Laboratory Capacity and the Public Health Emergency Preparedness Cooperative Agreements. The CDC also offers programmatic funding for surveillance activities relating to diseases such as HIV/AIDS, tuberculosis, and sexually transmitted diseases.

Legal Provisions Relating to Public Health Surveillance

The US Constitution divides power between states and the federal government. States have authority to regulate the public's health, while the federal government's authority is restricted to specific enumerated powers. Legal provisions relating to public health surveillance can be divided into two categories: state law and federal law.

State Level. States have authority over police powers which include the power to protect and promote public health. This authority is exercised through written statutes that vary significantly between jurisdictions. All states have statutes regarding reporting of diseases, but they are not uniform, and a 2008 assessment of states found that not all Nationally Notifiable Conditions were reportable in every state.[27] Furthermore, laws related to the use, disclosure, security, and privacy of surveillance data varies from state to state.

Federal Level. Although the federal government does not possess police powers, federal laws play an important role in determining how states conduct infectious disease surveillance and use data. Particularly relevant laws include the Privacy Act of 1974, the HIPAA Privacy Rule, the Public Health Services Act, the Family Educational Rights and Privacy Act, and the Freedom of Information Act.

The Privacy Act of 1974 mandates the collection, use, and dissemination of personally identifiable information that is maintained by federal agencies. The act prohibits the disclosure of information without the written consent of the individual; however, there are 12 statutory exceptions to this rule and a court order may be made compelling the disclose of identifiable information.

The Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule became fully effective in 2004 and established a set of national standards to protect individually identifiable health

[27] Jajosky R et al., "Findings from the Council of State and Territorial Epidemiologists' 2008 Assessment of State Reportable and Nationally Notifiable Conditions in the United States and Considerations for the Future.," *Journal of Public Health Management and Practice : JPHMP* 17, no. 3 (May 1, 2011): 255–64, https://doi.org/10.1097/phh.0b013e318200f8da.

information (classified as protected health information, PHI). The Privacy Rule regulates the use and disclosure of PHI and applies to covered entities such as health plans, healthcare clearinghouses, and providers who conduct healthcare transactions electronically. Similar to the Privacy Act, the Privacy Rule prohibits the use or disclosure of PHI without the written consent of the individual. However, there are exemptions for public health, and healthcare entities are permitted to disclose PHI to authorized public health authorities.

The Public Health Service Act (PHSA) provides protection for highly sensitive data collected by the US Department of Health and Human Services. Sensitive data related to illegal conduct, intimate partner violence, or hospital-associated infection rates among others requires additional protection in order to ensure that individuals and institutions are willing to participate in a study or provide accurate information. There are two forms of protection that can be issued, an Assurance of Confidentiality and a Certificate of Confidentiality, which are both immune from compulsory disclosure.

The Family Education Rights and Privacy Act (FERPA) aims to protect the privacy of student education records and was enacted in 1974. FERPA prohibits the disclose of any personally identifiable information contained in an education record, including healthcare information, without the written consent of the individual or their guardian. There are some exceptions in the event of emergencies, but these exceptions are limited.

The Freedom of Information Act (FOIA) protects the public's right to access government records and was enacted in 1966. FOIA includes an exemption to withhold personnel and medical files that would lead to an unwarranted invasion of privacy.

2. Collection and Storage of Biological Samples

The United States does not have a centralized organization responsible for collecting and storing biosamples. The most notable organizations operating biosample storage facilities are the CDC, National Institutes of Health (NIH), and academic institutions. Biosamples and pathogens that could potentially be weaponized are often stored in biorepositories on military bases for additional security.

CDC Division of Laboratory Systems. The CDC Division of Laboratory Systems (DLS) operates the CDC Biorepository (CBR), which was established in 1997 as a centralized resource to preserve CDC's valuable samples and provide ongoing support to CDC programs. With approximately 6.6 million biological and environmental samples, CBR strives to maintain best practices and standards, and offer sample management expertise to programs. Samples housed at the CBR have the potential to play a crucial role in public health research and population health by facilitating scientific knowledge advancement, characterization of new etiologic agents, investigation of disease causes, and development of new tests, vaccines, and treatments.

National Instititutes of Health. The NIH operates and funds various biobanks for specific purposes all around the country. Recently, the NIH launched the "All of Us" biobank initiative that aims to collect biosamples on one million or more participants over the course of the program. The All of Us Research Program is publicly funded, with resources appropriated each year by the US Congress. The 21st Century Cures Act, passed in December 2016, authorized a total of $1.5 billion over ten

years for the program. These funds, in addition to discretionary appropriations the program receives, are subject to the annual appropriations process.[28]

Academic Institutions. Academic institutions in the United States also contribute to the country's biobank infrastructure. Due to the cost of maintaining biobanks, most local and even regional health authorities are unable to sustainably collect and manage samples. This responsibility is often handed off to academic institutions who accept research grants and contracts to carry out research related to specific diseases or events in their communities or throughout the United States at a national level. The CDC also collaborates with academic institutions and awards contracts to lab to collect, test, and store bio samples. In some cases, the CDC will arrange for bio samples to be transported to CDC-operated labs. Moreover, academic institutions have their own guidelines for working with third-parties including private companies. Whereas in other countries public health and ethics are often weighted heavily in the decision-making process, the lack of overarching regulations tends to allow academic institutions to pursue opportunities for economic gain.

3. COVID-19 Response

Public Health Surveillance

According to the interviewee, the United States' surveillance system was slow to respond to the spread of COVID-19. Testing was limited to CDC labs because the CDC wanted to ensure the quality of all tests. This delayed results and limited the ability to introduce extensive testing protocols that were seen in other countries. In the meantime, the virus spread undetected in the community. Furthermore, the CDC was able to respond well to the pandemic in terms of data collection until the Trump administration issued an order ordered for the data be transferred to the White House. As a result, data analysis and public health recommendations were delayed. The CDC has since expanded its surveillance efforts to include widespread data collection, variant surveillance, serology surveillance, and data on special populations (personal comments given by US interviewers).

COVID-19 is now included on the CSTE NNC list and cases are reported to the CDC from 60 jurisdictions through the NNDSS. At the case-reporting level, individual jurisdictions collect and report data on laboratory-confirmed COVID-19 cases and probable cases based on clinical criteria and guidance from the CDC. Currently, there is both passive and active case-based surveillance consisting of reports from healthcare entities and laboratories, as well as those identified through contact tracing efforts at the local level. Each state determines the extent of the data that is collected for each case and the CDC has implemented standard systems for reporting specific data for national review.[29]

Collection and Storage of Biological Samples

The United States does not have a centralized organization overseeing the collection and storage of SARS-CoV-2 and COVID-19 biosamples. This responsibility was left mainly to academic institutions

[28] National Institutes of Health, "All of Us Research Program Backgrounder," National Institutes of Health (NIH) — All of Us, November 9, 2020, https://allofus.nih.gov/news-events/press-kit/all-us-research-program-backgrounder.
[29] Kavya Sekar and Angela Napili, "Tracking COVID-19: U.S. Public Health Surveillance and Data" (Washington, DC: Congressional Research Service, November 2, 2020), https://www.everycrsreport.com/files/2020-11-02_R46588_a58a55c0f04871f443506e5aca9fa37dab25a94d.pdf.

that had experience in handling infectious diseases. It is notable that the US Department of Defense conducted surveillance operations, although the details have not been fully disclosed at this time.

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