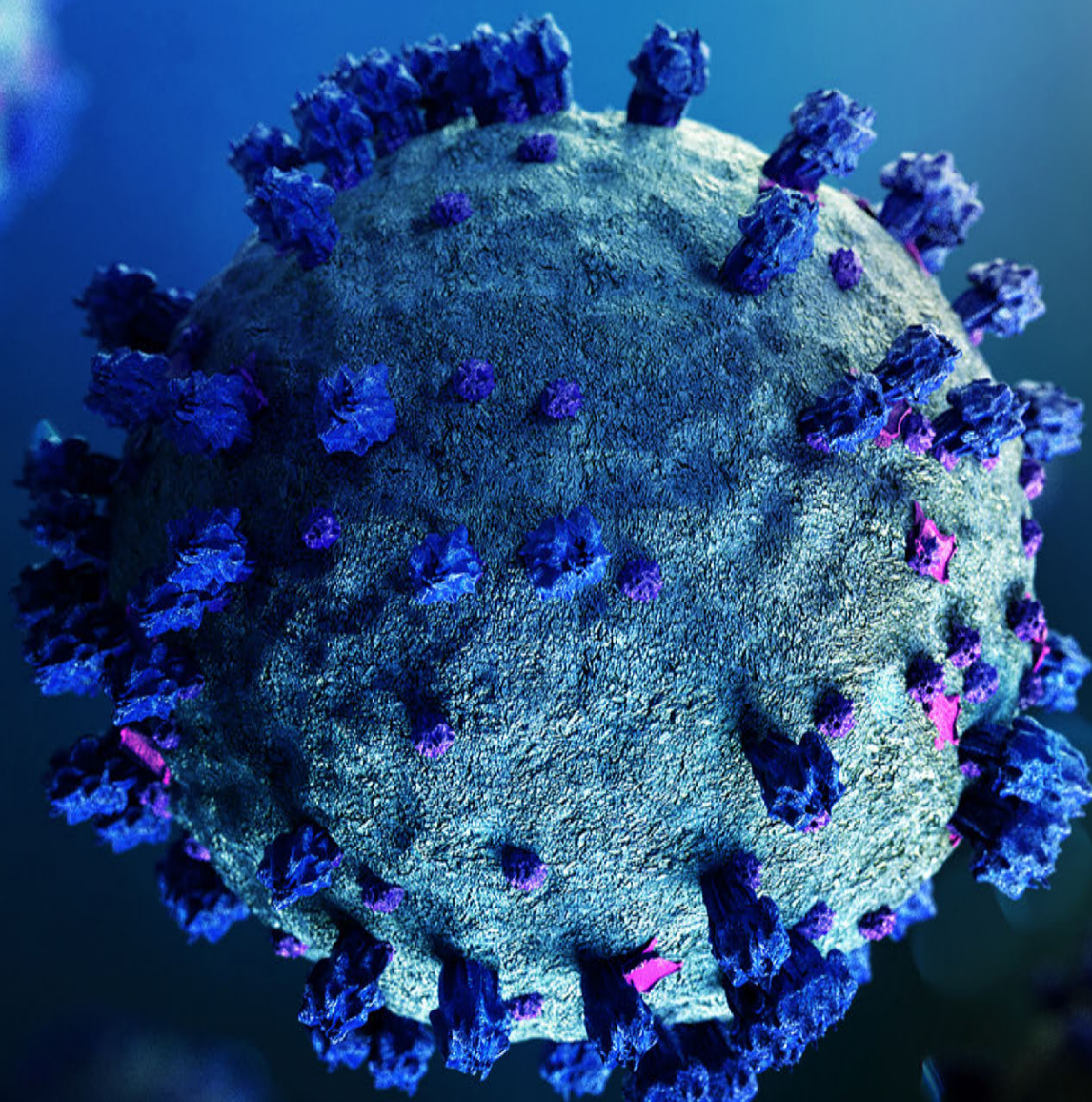


# Evaluation of the COVID-19 Genomics UK (COG-UK) Consortium

Final Report

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# Preface

This report shares the findings of an evaluation of the COVID-19 Genomics UK (COG-UK) Consortium conducted by the not-for-profit institute RAND Europe.

Section 1 outlines the background and context to the evaluation, introducing COG-UK and its aims. Section 2 provides an overview of the evaluation's aims, methods and associated caveats. Section 3 presents the COG-UK theory of change, which served as the framework for developing evaluation indicators. Section 4 discusses key findings related to the outputs, outcomes and impacts of COG-UK's activity. Section 5 discusses what influenced the consortium's evolution and outputs and provides learnings about enablers and challenges experienced in this highly

networked pathogen-genomics effort. Finally, Section 6 reflects on the learning gained and considers COG-UK's sustainability and legacy in a future pathogen-genomics landscape.

It is worth noting that the evaluation timeframe covered a period prior to the omicron variant's emergence; thus, insights on COG-UK's omicron-related activity are not part of this report.

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## Summary

### Context and evaluation aims

The COVID-19 pandemic has had an unprecedented impact on populations across the globe. As of 15 November 2021, over 9.5 million positive COVID-19 cases and over 165,000 related deaths were recorded in the United Kingdom (UK) alone.<sup>1</sup> The ability to identify individuals infected with the SARS-CoV-2 virus, which causes COVID-19, and to sequence and understand the variants of the virus that have been circulating in the UK since the onset of the pandemic have been vital in informing public health decision making and efforts to control its spread. The work of pathogen genomics experts who are part of the COVID-19 Genomics UK (COG-UK) Consortium has underpinned key sequencing and research efforts.

The COG-UK consortium was established soon after the UK went into its first lockdown of the COVID-19 pandemic in March 2020. On 1 April 2020, COG-UK received approximately £20 million in funding from the National Institute for Health Research (NIHR), the Medical Research Council (MRC) – part of United Kingdom

Research and Innovation (UKRI)<sup>2</sup> - and Genome Research Limited (operating as the Wellcome Sanger Institute). In January 2021 and April 2021, COG-UK received an additional £11.6 million from the Testing Innovation Fund and £5 million from the Department of Health and Social Care Test and Trace, respectively, to bolster their sequencing output. COG-UK is a collaborative effort between 16 academic institutions, the UK's four public health agencies (PHAs) of England, Scotland, Wales, and Northern Ireland, the Wellcome Sanger Institute, four Lighthouse Labs<sup>3</sup> and 79 National Health Service (NHS) Trusts or other organisations. COG-UK builds on the UK's strengths in pathogen genomics, population health sciences and health informatics. The consortium was set up with the aims to<sup>4</sup>:

- Provide data, analysis, tools, and research that can help guide public health decision making and policy relating to the COVID-19 pandemic;
- Advance understanding of genetic changes in the SARS-CoV-2 virus and how they relate to the spread of the virus

1 UK government (2021).

2 Grant reference number: MC\_PC\_19027

3 A network of testing laboratories launched by the UK government in March 2020 to support the fight against COVID-19 (Lighthouse Labs, 2022).

4 These were COG-UK's overarching aims as communicated to the evaluation team during the evaluation design.

and severity of COVID-19 symptoms, all of which matter for public health decision making and the development and evaluation of treatments and vaccines; and

- Support national research studies, including those that can help enable future evaluations of the effectiveness of various pharmacological and non-pharmacological interventions to prevent or treat COVID-19.

Given growing realisation of the importance of pathogen genomics for public health, the scale of investment made, and the commitment to widely sharing learning from COG-UK's experience, the consortium commissioned the not-for-profit institute RAND Europe to evaluate and learn about COG-UK's progress, evolution and impacts. More specifically, the evaluation set out to:

- Examine COG-UK's delivery against its aims in terms of its outputs, outcomes and impacts;
- Understand how processes related to governance, management and operations impacted delivery;
- Learn about enablers of progress as well as challenges experienced;
- Provide valuable formative learning for any potential future consortium phases and/or for other related efforts, including sustainability and legacy.

## Methodology

The evaluation adopted a mixed-methods approach. This involved:

- Developing an evaluation framework based on specifying a COG-UK theory of change (i.e. an understanding of what the consortium set out to achieve and how) and associated evaluation indicators;
- Collecting and analysing self-reported qualitative and quantitative data on evaluation indicators;
- Conducting in-depth semi-structured interviews with diverse stakeholders involved with COG-UK; and
- Undertaking cross-analysis, synthesis and reporting.

Data was collected between February 2021 and October 2021. Two workshops were conducted in February 2021 to specify COG-UK's theory of change and evaluation framework. Self-reported data on COG-UK's evolution, outputs, outcomes and impacts were collected for the evaluation period 1 March 2020 to 31 July 2021. Data were provided to RAND Europe in September 2021 and in-depth semi-structured interviews were conducted between April and October 2021.<sup>5</sup>

Although this evaluation provides deep and rich insights about COG-UK's experiences, there are some limitations to consider when interpreting its findings.

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5 Due to time demands on interviewees to directly engage in activities related to the COVID-19 response, the intended timeframe for interviews was extended by three months, which is why the interviews cover a somewhat longer evaluation timeframe than the self-reported data.





First, the evaluation began after the consortium had been operating for eight months. Thus, the findings presented were collected retrospectively. This means that some elements – such as developing the theory of change – depended on a degree of participants’ recollection of experiences in the consortium’s earlier phases.

Second, this evaluation’s scope and resources meant that the focus was primarily on understanding COG-UK’s delivery against its aims, identifying the factors shaping its performance, and discerning relevant lessons for the future. COG-UK unfolded in an environment without any ‘business as usual’ or control groups for comparison. Consequently, this evaluation discusses COG-UK’s contributions to the public health landscape and pandemic response, but there is no counterfactual from the UK to assess this against. Future evaluations may enrich this inquiry, perhaps considering comparators and learning from international experiences of other pathogen-genomic sequencing initiatives.

A further caveat is that an audit of the self-reported data COG-UK provided as part of this evaluation was outside the scope of this work. However, the evaluation team is confident that the diverse perspectives and experiences shared through the in-depth interviews and the specificity of the self-reported data support an objective and comprehensive analysis of COG-UK outputs and impacts as well as a detailed understanding of the diversity of influences on the consortium’s evolution and impacts.

In the following sections, we overview key insights and learning and their implications and lessons of relevance to future efforts.

### **COG-UK’s contributions to understanding and responding to the COVID-19 pandemic**

COG-UK has made diverse contributions to understanding and responding to the COVID-19 pandemic. The core outputs, outcomes and impacts of COG-UK activity are briefly summarised in Box 1 and elaborated on in the narrative that follows.

**Box 1. Key COG-UK achievements**

The consortium has **helped advance scientific knowledge about SARS-CoV-2 and helped improve methodologies** that can support high quality and efficient sequencing and pathogen genomics research and analysis.



COG-UK has also provided data and analytics that have **informed key policy and public health decisions** made in response to the COVID-19 pandemic in the UK.



The sequencing and analysis of SARS-CoV-2 genomes and the linkage of genomics data to epidemiological and patient outcomes data by COG-UK partners have **informed medical innovation efforts**, including research and evaluations of vaccine efficacy against specific variants of SARS-CoV-2 and research on the susceptibility of viral variants to therapeutics against COVID-19.



COG-UK's data, research analytics, and dissemination efforts have also **influenced how decision makers in the UK value and view the field of pathogen genomics**, as a partner in building effective public health systems.



COG-UK's resources and activities have **strengthened capacity for pathogen genomics**, which, if sustained, has the potential to significantly bolster the UK's ability to prepare and respond to future infectious disease threats.



The consortium's impacts extend beyond the UK's borders. COG-UK's approach to supporting pathogen-genomics sequencing, research and analysis, and learning from COG-UK's experience has also **influenced international SARS-CoV-2 sequencing initiatives**.





## 1. Contributions to scientific knowledge about SARS-CoV-2 and to advancing methods that support sequencing and pathogen genomics research

The sequencing of viral genomes has been essential to research and analysis efforts to understand the SARS-CoV-2 virus and its behaviour. COG-UK sequenced over 800,000 SARS-CoV-2 genomes across the UK between 1 April 2020 and 31 July 2021.<sup>6</sup> The consortium increased sequencing capacity at its sites from 5,000 to 30,000 samples per week throughout the evaluation timeframe and reduced the average cost of sample sequencing by approximately 30 per cent (from £56 to £40 blended per sample).<sup>7</sup>

Consortium members' research and analyses have advanced knowledge about the SARS-CoV-2 virus regarding variants of concern, viral behaviour, transmissibility and spread, and the impact of various public health measures. To achieve this, the consortium has been committed to openly sharing its findings and making them freely accessible since its inception. During the evaluation period for which self-reported data was provided,<sup>8</sup> COG-UK partners produced 53 publications (including 51 academic papers and 2 non-academic reports), contributing to insights that helped inform the pandemic response. COG-UK partners shared this knowledge widely through participation in 42 conferences, seminars or

training events on SARS-CoV-2 genomics.<sup>9</sup> COG-UK has also made its data widely and freely available through public-domain databases, e.g. the Global Initiative on Sharing Avian Influenza Data (GISAID), European Nucleotide Archive (ENA), and New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG).

In addition, the software tools, sequencing and analysis protocols developed by COG-UK researchers have improved methods available for public health genomics, including those beyond the COVID-19 pandemic. Similarly, COG-UK partners' efforts to help link viral sequencing and patient metadata (e.g. vaccination records, clinical, demographic and postcode information and travel history) and viral and host genome data are building a critical resource for further research of public health significance. The existing UK Cloud Infrastructure for Microbial Bioinformatics (CLIMB) data and computing infrastructure held by public health partners<sup>10</sup> was leveraged for COG-UK activities and has played a vital role in these efforts.

While these contributions are notable, the pace and scale of COG-UK outputs and contributions to scientific knowledge and methods underlying pathogen genomics will not be straightforward to sustain and apply to future public health challenges. The ability to do so will depend on securing long-term resources to support the required public health

6 COG-UK self-reported data. Quarterly data on SARS-CoV2 whole-genome sequencing, self-reported by COG-UK, based on sequencing invoices and budget spreadsheets.

7 COG-UK self-reported data. Sequencing costs per sample were not uniform across all labs due to differences in infrastructure, technology, equipment, methods and economies of scale. This cost is the cost of sequencing alone and does not include labour or any overheads.

8 From 1 April 2020 and 31 July 2021.

9 COG-UK self-reported data.

10 Funded by the MRC, CLIMB launched in 2016 as a shared computing infrastructure for the medical microbiology community. It is a collaboration between Warwick, Birmingham, Cardiff, Swansea, Bath and Leicester Universities, the MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, and the Quadram Institute in Norwich (CLIMB, 2022).

workforce and relationships between academic organisations, NHS sites and PHAs across the UK within conducive governance and management arrangements.



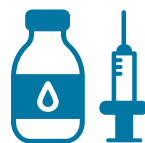
## 2. Informing key policy and public health decisions in the UK's pandemic response

COG-UK's sequencing data and analyses have helped identify variants of significance circulating in the four UK nations. The consortium's work informed policies related to border control, travel, lockdown and social distancing and improved policymaker and public understanding of links between new variants and disease severity. The consortium's pathogen sequencing has also impacted decision making in local settings, including hospitals, care homes and universities by helping to understand sources of outbreaks and transmission patterns and informing infection prevention and control and patient-safety reporting.

From the outset, COG-UK has worked closely with public health decision makers to maximise the value and impact of SARS-CoV-2 genomic data on public health. They achieved this through several routes, including: 1) participation on various committees and working groups, e.g. in Department of Health and Social Care (DHSC), Public Health England (PHE), Scientific Advisory Group for Emergencies (SAGE), and NERVTAG, 2) contributions to 36 external reports produced by policy and public health decision makers during the evaluation timeframe, 3) direct reporting to policymakers (e.g. 18 COG-UK reports to SAGE), and 4) provision of informal feedback. Throughout the pandemic, COG-UK

has worked in partnerships with actors in the public health research landscape to connect sequencing and patient metadata further and help inform future research studies and public health decision making.

The consortium supported SARS-CoV-2 genomic sequencing needs across England, Wales, Scotland and Northern Ireland using tools such as sequencing coverage reports<sup>11</sup> to help prioritise samples for sequencing and analysis. Despite significant contributions to identifying variants of concern across the four nations, COG-UK's ability to inform regional decision making in a timely manner was occasionally hampered by factors outside its direct control. Such factors included limited PHA access to the patient metadata needed to help prioritise localities from which samples should be sequenced and understand relationships between outbreaks and travel histories or vaccination records. Some of the stakeholders interviewed during this evaluation also noted possible differences in the degree of influence different PHAs had on prioritising samples for sequencing. There is an opportunity for PHAs and other partners to work together to further bolster sequencing capacity within the devolved nations in the future.



## 3. Informing medical innovation: testing vaccine efficacy against specific variants of SARS-CoV-2 and better understanding therapeutics

COG-UK has also provided important inputs into medical-innovation responses to the pandemic through its data and analytics. For example, the consortium's open sharing of data and insights have informed assessments of

vaccine efficacy against different viral variants. COG-UK is also working with various consortia to identify and characterise variants of concern to inform the development of the next generation of vaccines. The consortium's data on and analysis of viral mutations have helped to better understand potential treatments such as convalescent plasma therapy. As the consortium progresses its efforts to link host and viral genome data and scales-up data linkage for viral and patient metadata, there will be opportunities for further engagement with those developing and evaluating vaccines and therapeutics for COVID-19.



#### 4. Changing how decision makers view and value pathogen genomics

COG-UK has had a significant impact raising awareness about the importance of pathogen genomics as a discipline. It has increased policymaker appreciation of pathogen-genomics' value, as well as increased demand for the use of sequencing insights in public health decision making as part of the COVID-19 response. However, it remains to be seen whether increased recognition of pathogen sequencing's importance for pandemic preparedness and response will translate into increased investment and capacity for its use in other areas. Such areas might include surveillance of other infectious disease threats and public health challenges such as antimicrobial resistance where pathogen sequencing can inform medical innovation. In spring 2021, COG-UK began transitioning routine sequencing capacity for SARS-CoV-2 from research institutions to PHAs. Sequencing sites in universities and research institutes are providing a safety net for

potential surges in sequencing capacity needs. It will be important to nurture and grow this capacity in PHAs over time.



#### 5. Capacity for pathogen genomics in the UK

COG-UK has made diverse contributions to bolstering pathogen genomics sequencing and research capacity in the UK. More specifically:

- **Strengthening the workforce:** COG-UK has trained up staff across different professions (e.g. healthcare professionals, researchers, PHA staff), career-development stages and UK locations to improve sequencing, analysis and interpretation skills. The consortium estimates having trained over 800 individuals across the UK during the evaluation timeframe.
- **Physical and data infrastructure improvements:** COG-UK purchased sequencing equipment and implemented software tools that are now available at 17 sequencing sites across the UK,<sup>12</sup> providing newly increased capacity. Building upon the existing CLIMB data infrastructure, COG-UK has also used its funds to rapidly develop additional computational infrastructure (e.g. CLIMB-COVID).
- **Leadership, management and governance arrangements:** The consortium established a governance structure representing the diverse geographies and stakeholders involved in the UK public health landscape. It also established contractual arrangements, operational protocols and legal frameworks to support a four-nation, multistakeholder approach. COG-UK's collaborative approach has demonstrated

the importance of conducive governance and management support for networked public health efforts and of aligning such governance with pre-existing institutional practices. Whether such approaches can be applied and sustained beyond the COG-UK collaboration will determine this approach's feasibility for responding to future public health threats.

- **Strengthened relationships between key organisations in the public health landscape across the UK:** As a consortium of academic research partners, the Wellcome Sanger Institute, PHAs, as well as collaborators including Lighthouse Labs and NHS foundations and trusts, COG-UK has fostered collaboration between diverse professions in the interest of advancing science and informing policy. If sustained, a model of close interaction between researchers and PHAs across the devolved nations may offer a new paradigm for the future of UK public health.

Investments in equipment, methodological development and workforce skills have also supported reductions in sequencing costs per sample and improvements in sequencing and result-reporting turnaround times. On average, time from sample collection to sequencing-data upload decreased by 70 per cent across consortium sites, from 20 days in April 2020 to 6 days in June 2021.<sup>13</sup>



## 6. Impact on the international pandemic-response effort

COG-UK's data and resources are available for use by the international community. Consortium members have also advised some other countries on their sequencing and data-sharing strategies (e.g. Canada, France, Israel, the United States [US]), supported pathogen genomics efforts in 17 low-and-middle-income countries<sup>14</sup>), and shared expertise through roles in international working groups and councils (e.g. the World Health Organisation [WHO] working groups and the Global Early Warning System Action Collaborative Advisory Council).

COG-UK's experience offers lessons directly relevant to future pandemics and public health threats, with some likely to have international relevance. Examples include learning about the critical role of pathogen genomics in supporting a rapid response to pandemics and the methodological tools and protocols to use in sequencing. In addition, learning related to the logistics of collaboration between different stakeholders and the coordination of various actors may have elements applicable to diverse geographies. However, the consortium's primary focus on UK-based data may limit internationally applicable insights. This aspect merits further research to understand which aspects of COG-UK's structure and function may be adaptable to other contexts and which are more context-specific.

<sup>13</sup> COG-UK self-reported data.

<sup>14</sup> Bangladesh, Cameroon, Gambia, Ghana, India, Kenya, Malawi, Malaysia, Mauritius, Pakistan, Philippines, Saudi Arabia, South Africa, Sri Lanka, Togo, Uganda and Zimbabwe.



## Influences on COG-UK's evolution and impacts

Any effort to learn how a networked and multi-stakeholder public health genomics approach can support responses to infectious disease pandemics benefits from understanding the diversity of factors that influenced COG-UK's efforts. The consortium's evolution and impact have been affected by features internal to its structure and operations, and by a rapidly evolving and unpredictable external environment regarding both the virus evolution and evolution in the policy landscape. More specifically, key influences related to:

- **The ability to mobilise and sustain individual and institutional commitment to consortium activities, including a commitment to rapid delivery and responsiveness to increasing demand for sequencing activities.** To a large extent, this depended on individual and institutional goodwill. It was also influenced by leadership, governance and management structures and actions and by substantial investments of time and efforts to nurture productive relationships and interactions between diverse COG-UK members (see Table 1).
- **The resource environment – including financial resources, physical and data infrastructure and connectivity and human resources.** These were essential in supporting COG-UK's delivery at pace and scale (see Table 2). Critical factors enabling COG-UK to be 'fleet on its feet' included timely access to substantial funding and the ability to rapidly onboard UK sites across academic, public health and NHS

organisations and redirect staff capacity toward responding to the pandemic. Access to pre-existing data, computing and cloud infrastructure was also critical. Advocating for the need for public health genomics sequencing by leaders who came up with the idea to establish COG-UK was key to securing financial support that allowed for mobilising staff resources and requisite physical and data infrastructure in a timely manner. However, the pace and scale of activity and the demands on staff were considerable; they will be challenging to sustain in the absence of a long-term resourcing strategy for the future.

- **The ability to navigate external environmental forces, particularly those related to the speed and unpredictability with which the COVID-19 pandemic unfolded.** Both the unpredictability of viral evolution in terms of variants and their transmissibility, and evolution in the policy landscape impacted on how COG-UK carried out its activities. The urgency of the pandemic, coupled with COG-UK's resolute management, strategy, processes, partner commitment and goodwill, helped focus consortium members on the most urgent tasks and enabled agility. However, it also required continuous operation in 'fire-fighting' mode, which is unlikely to be sustainable for the longer term (see Table 3).

We elaborate on these key influences in terms of enablers and challenges in **Table 1**, **Table 2** and **Table 3**.

**Table 1. An overview of enablers and challenges related to COG-UK's ability to mobilise and sustain member commitment to consortium activity**

<b>INFLUENCE: THE ABILITY TO MOBILISE AND SUSTAIN INDIVIDUAL AND INSTITUTIONAL COMMITMENT TO CONSORTIUM ACTIVITIES</b>	
<b>Key Enablers</b>	<b>Key Challenges</b>
<p><b>Individual and institutional goodwill:</b></p> <ul style="list-style-type: none"> <li>Individual and institutional goodwill enabled COG-UK to deliver on its aims and helped manage challenges related to capacity constraints over time. Altruism and scientific intrigue underpinned individual and institutional engagement and facilitated a connected network of expertise. Institutions often provided in-kind support, e.g. access to facilities and infrastructure.</li> <li>The ability of individuals to work flexibly and adapt to changing circumstances supported the scale and pace of delivery.</li> </ul> <p><b>Supportive leadership, governance, and management:</b></p> <ul style="list-style-type: none"> <li>Dedicated central and member-site leadership, governance and management – supported by operational and logistics functions – have been key to enabling COG-UK's activities. The representation of different stakeholders and geographies in governance groups supported a four-nations approach, alongside regular meetings of the COG-UK network. Designated management, operational and logistics support helped minimise administrative demands on research staff.</li> <li>Tools and processes to support the entire consortium while minimising bureaucracy (e.g. weekly reports on the percentage of samples sequenced from each nation and weekly turnaround-time reports to inform decisions about network activities) were helpful in managing the network.</li> <li>Policies to promote inclusiveness, accountability and transparency, such as an authorship policy listing anyone contributing to producing COG-UK data as an author on outputs, helped compensate people for time spent away from other research.</li> </ul> <p><b>Overall productive relationships and interactions in the COG-UK network:</b></p> <ul style="list-style-type: none"> <li>The commitment of individuals and institutions from diverse academic, NHS, and public health organisations across the four nations of the UK was a critical enabler.</li> <li>Mobilising and deepening pre-existing relationships and building new ones around a shared vision helped nurture benevolence and trust between many COG-UK collaborators and supported rapid delivery on tasks and adaptability.</li> <li>Investing time and effort into relationship-building addressed early scepticism about the value of pathogen sequencing for the pandemic response and helped bring policymakers on board with COG-UK's vision.</li> <li>Communications infrastructure, i.e. IT platforms, supported interactions between members of a distributed network.</li> </ul>	<p><b>Challenges in matching individual and institutional capacity to demand:</b></p> <ul style="list-style-type: none"> <li>Time demands placed on individuals working at an unprecedented pace, often without direct COG-UK funding, were a significant challenge.</li> <li>Human resource capacity constraints, e.g. the numbers and types of staff available early on, were challenging to manage given rapidly increasing demands for COG-UK sequencing and analytics.</li> </ul> <p><b>Governance and management challenges:</b></p> <ul style="list-style-type: none"> <li>Implementing the consortium's governance and management arrangements was not straightforward, since COG-UK had to navigate institutions' diverse pre-existing rules and operating systems.</li> <li>Early obstacles to recruiting sufficient administrative, operational and logistics support staff led to delays in implementing some contractual arrangements and policies. These obstacles were exacerbated by COG-UK not being a legal entity.</li> </ul> <p><b>Relational challenges in an inherently complex and diverse network:</b></p> <ul style="list-style-type: none"> <li>Although rare, perceptions that power imbalances between individual PHAs occasionally influenced decision making about which samples to sequence sometimes presented a relational challenge. Some network members had different views on whether sequencing should be done centrally or locally. COG-UK developed and revised its sampling strategy over time and sought to create opportunities for partners to discuss and voice their views through various discussion forums.</li> <li>It took time to establish effective communications between researchers and PHAs to support the uptake of COG-UK insights in informing decision making; relations significantly strengthened as COG-UK evolved.</li> <li>There were some communication challenges related to the decision to move towards the gradual transition of routine sequencing from academic institutions to PHAs.</li> </ul> <p><b>Wider political developments:</b></p> <ul style="list-style-type: none"> <li>Plans and decisions related to the public health system's evolving structure and organisation introduced an additional layer of complexity to pursuing a four-nations approach that central to COG-UK strategy</li> </ul>

**Table 2. An overview of enablers and challenges related to COG-UK resources**

<b>INFLUENCE: RESOURCES- FUNDING, PHYSICAL AND DATA INFRASTRUCTURE, HUMAN RESOURCES</b>	
<b>Key Enablers</b>	<b>Key Challenges</b>
<p><b>Financial resource support:</b></p> <ul style="list-style-type: none"> <li>Timely access to substantial funding from the NIHR, MRC/UKRI and Wellcome Sanger Institute enabled COG-UK to rapidly set up operations at scale across the UK.</li> <li>Support from the Chief Scientific Advisor helped convey the need for funding a pathogen genomics network to key national-level decision makers and ensure COG-UK's timely establishment.</li> </ul> <p><b>Physical and data infrastructure:</b></p> <ul style="list-style-type: none"> <li>Pre-existing facilities and equipment helped support genome sequencing and research, while additionally purchased equipment helped bolster capacity across sequencing sites.</li> <li>CLIMB's pre-existing data infrastructure, skills and goodwill bolstered its capacity to host sequencing data from diverse and distributed sites.</li> <li>COG-UK's operational policies made it mandatory to upload sequencing data to the CLIMB data repository before payment could be authorised.</li> </ul> <p><b>Human resources:</b></p> <ul style="list-style-type: none"> <li>Diverse research, technical, administrative, management and leadership staff were fundamental to COG-UK's ability to deliver on its aims.</li> </ul>	<p><b>Financial resource challenges:</b></p> <ul style="list-style-type: none"> <li>Initial scepticism from some individuals with influence related to the value of pathogen genomics sequencing needed to be overcome. Although securing initial funding happened very promptly, overcoming some initial scepticism was relevant in relation to prioritising and targeting the utilisation of funds over time secure initial and subsequent funding. (Awareness-raising, support by influential individual champions and demonstrating early signs of value for policymakers helped in this regard).</li> <li>Challenges related to the gradual transition of sequencing activity and associated funding from academic institutions to PHAs impacted those individuals who had paused their careers to focus on COG-UK and were dependent on its financial support.</li> </ul> <p><b>Physical and data infrastructure challenges:</b></p> <ul style="list-style-type: none"> <li>Challenges with onboarding sites, securing ethical clearances and arranging for the transport of samples to respond to the surge in sequencing demand were experienced in the consortium's early stages.</li> <li>Global shortages early in COG-UK's experience hindered access to the consumables needed for sequencing.</li> <li>Efforts to optimise data sharing, flow and linkage faced some obstacles due to the lack of an integrated data platform and fragmented data systems, rules and governance across organisations in the four nations.</li> <li>Limited time and capacity to translate data into user-friendly formats to feed back to the NHS hospital sites providing samples were also experienced.</li> </ul> <p><b>Human resource challenges:</b></p> <ul style="list-style-type: none"> <li>Capacity challenges due to the scale of demand and the speed and pace at which the consortium needed to carry out sequencing, research and analyses occurred. These were primarily tackled by mobilising individual and institutional goodwill to deliver in unprecedented circumstances.</li> </ul>



**Table 3. An overview of enablers and challenges related to COG-UK’s ability to adapt to unpredictable conditions associated with the COVID-19 pandemic**

INFLUENCE: THE ABILITY TO RESPOND TO THE URGENT AND UNPREDICTABLE NATURE OF THE PANDEMIC	
Key Enablers	Key Challenges
<ul style="list-style-type: none"> <li>• COG-UK members’ readiness to adapt the extent of their focus on research versus routine sequencing activity was vital to COG-UK’s role in informing public health decision making and policy.</li> <li>• Though not without challenges, the financial resources, leadership and management ability that allowed COG-UK to rapidly bolster human-resource capacity and onboard sequencing sites underpinned COG-UK’s timeliness, relevance and impact in a rapidly changing public health landscape.</li> <li>• The urgency of the pandemic challenge focused attention on the most pressing short-term needs and mobilised support, goodwill and trust with minimal bureaucracy.</li> <li>• The novelty and experimental nature of COG-UK was conducive to agility and adaptiveness, allowing for a degree of innovation and experimentation related to governance and management approaches, and minimising bureaucracy</li> </ul>	<ul style="list-style-type: none"> <li>• The consortium’s constant flux as new people joined required a consistent focus on onboarding but also presented occasional challenges to maintaining effective communication and added to time demands on key staff.</li> <li>• COG-UK’s fire-fighting mode of operating was taxing on staff and unlikely to be sustainable for the longer term. This is an important consideration for COG-UK’s future and longer-term resourcing.</li> </ul>



## In reflection and looking to the future

COG-UK has made a significant and valuable contribution to the UK's public health genomics landscape. However, what needs to be sustained is not necessarily the network as it operated during the evaluation timeframe, but the ecosystem that has been built around it. Reflecting on the learning gained and looking to the future, COG-UK's legacy will depend on decision makers' abilities to:

- 1 Deliver public health genomics capacity guided by a clear, prioritised, long-term strategic plan:** Priorities will need to reflect and reconcile the interests of the scientific community, citizens and patients, and be aligned to the long-term priorities of governments and public health decision-makers across the four nations of the UK.
- 2 Maintain momentum, motivation and goodwill to support a network that can bring together diverse organisations across the four nations without over-reliance on goodwill alone:** Long-term funding and sustaining committed leadership will be critical. A workforce development strategy that considers novel career pathways in PHAs and academic settings will be needed, alongside an existing or novel convening structure that can ensure a coordinated national approach as well as respond to the devolved nations' unique local needs.
- 3 Ensure the involvement of all relevant actors:** COG-UK mobilised the engagement of researchers, PHAs and NHS sites across the country. As the consortium enters the next phase of its existence or morphs into a legacy structure, it may need new expertise,

e.g. bringing in private-sector partners to link genomics research with medical innovation, international expertise, patient-and-public engagement and additional involvement from the NHS to extend the role of pathogen genomics in the NHS.

- 4 Stabilise and ensure adequately funded governance, management and administrative arrangements to support networked pathogen genomics capacity in the UK:** Attention should be given to where, and how far, elements of COG-UK governance that enabled rapid delivery, minimal bureaucracy and novel practices co-existing with established institutional governance and management systems, may be adaptable to future efforts. Academic researchers will require requisite independence but governance must also support synergies and ensure a shared sense of purpose across research and sequencing services informing public health.

- 5 Advance data linkage in the public health landscape:** Access to linked data sets will be fundamental to understanding the relationship between infectious-agent genetics and behaviour on the one hand and disease severity and patient outcomes on the other. It will also underpin efforts to inform the development and evaluation of medical innovations. Wider collaboration between actors in the UK's public-health and health-data landscape will be needed.

- 6 Ensure a sustainable division of labour between diverse stakeholders in the public health genomics landscape:** Attention must be paid to ensure the sustainability of the workforce required to service routine sequencing needs in PHAs and to ensure that trained research talent is not lost from

academic settings. Considering what may be different in terms of workforce needs if COG-UK (or its legacy) were to tackle other infectious diseases or public health challenges will also matter.



**Revisit the UK's role in the global pathogen genomics landscape:**

COG-UK members' expertise impacted international public-health genomics efforts and there is further potential to develop COG-UK as a global training resource and expertise-sharing

network. At the same time, COG-UK is largely built on UK data, and a future legacy effort would benefit from an explicit focus on integrating international experiences and embeddedness in coordinated global efforts.

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## Abbreviations

BIVDA	The British In Vitro Diagnostic Association
CanCOGen	Canadian Genomics Network
CiPS	COVID-19 in Prisons Study
CIS	COVID-19 Infection Survey
CIVET	Cluster Investigation & Virus Epidemiology Tool
CLIMB	Cloud Infrastructure for Microbial Bioinformatics
CNRS	French National Centre for Scientific Research
COG-UK	COVID-19 Genomics UK Consortium
COVID-19	Coronavirus disease 2019
DHSC	Department of Health and Social Care
ENA	European Nucleotide Archive
G2P	Genotype-2-Phenotype
GDPR	General Data Protection Regulation
GenOMICC	Genetics Of Mortality In Critical Care
GISAID	Global Initiative on Sharing Avian Influenza Data
HDR-UK	Health Data Research-United Kingdom
HOCI	Hospital-Onset COVID-19 Infections
ID	Identification number
ISARIC	International Severe Acute Respiratory and Emerging Infection Consortium
ISARIC4C	Coronavirus Clinical Characterisation Consortium
MHRA	Medicines & Healthcare products Regulatory Agency
MRC	Medical Research Council
NERVTAG	New and Emerging Respiratory Virus Threats Advisory Group
NHS	National Health Service


NIHR	National Institute for Health Research
ONS	Office for National Statistics
PHA	Public health agency
PHE	Public Health England
PHS	Public Health Scotland
PHW	Public Health Wales
PI	Principal Investigator
REACT	The Real-Time Assessment of Community Transmission Study
SAGE	Scientific Advisory Group for Emergencies
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SIREN	The SARS-CoV-2 Immunity & Reinfection Evaluation Study
SOPs	Standard operating procedures
UK	United Kingdom
UK-CIC	COVID-19 Immunology consortium
UKRI	United Kingdom Research and Innovation
US	United States
VUEAG	Vaccine Update Expert Advisory Group
WGS	Whole-genome sequencing
WHO	World Health Organisation
WP	Work package

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A stylized, abstract illustration of a diverse crowd of people. The figures are represented by solid-colored shapes in shades of blue, orange, pink, and black. Many of the figures are wearing white face masks. The composition is dense, with figures overlapping, suggesting a large gathering or a public space. The overall style is modern and graphic.

# CHAPTER 1

## **Background and context**

## 1.1. A brief overview of the COVID-19 Genomics UK (COG-UK) Consortium and its aims

The COVID-19 pandemic has shone a light on the importance of pathogen genomics for public health preparedness and response to infectious disease threats. The pandemic struck many nations by surprise and has had a devastating effect on individuals, communities, and economies across the globe. As of 15 November 2021, there were over 9.5 million registered positive COVID-19 cases and over 165,000 related deaths in the United Kingdom (UK) alone.<sup>15</sup>

The ability to identify individuals infected with the SARS-CoV-2 virus – which causes COVID-19 – and to sequence and understand the virus variants circulating in the UK since the onset of the pandemic have been vital to informing public health decision making and efforts to control the virus's spread. The work of pathogen genomics experts has underpinned sequencing and research efforts.

Pathogen genomics is a scientific discipline focused on understanding the genetic code of infectious disease pathogens. The ability to do so is important for tracking transmission, identifying mutations and new variants, and informing the development of vaccines, therapies, and broader public health interventions and policies. While pathogen genomics proved valuable in tackling other infectious disease threats such as the West African Ebola outbreak from 2014 to 2016,<sup>16</sup> it is the COVID-19 pandemic that really put the spotlight on the importance of pathogen

genomics in public health preparedness and response globally.

The COVID-19 Genomics UK (COG-UK) Consortium was established soon after the UK went into its first lockdown of the COVID-19 pandemic in March 2020. COG-UK represents one of the largest pathogen genomic sequencing efforts set up in response to the pandemic globally.<sup>17</sup> COG-UK was swiftly established to support rapid and large-scale whole-genome sequencing (WGS) of the SARS-CoV-2 virus to advance knowledge about the pathogen, help understand viral transmission and evolution and provide data and analytics to inform the public health response. On 1 April 2020, COG-UK received approximately £20 million in funding from the National Institute for Health Research (NIHR), the Medical Research Council (MRC) – part of United Kingdom Research and Innovation (UKRI),<sup>18</sup> – and Genome Research Limited (operating as the Wellcome Sanger Institute). In January 2021 and April 2021, COG-UK received an additional £11.6 million from the Testing Innovation Fund and £5 million from the Department of Health and Social Care Test and Trace, respectively. The initial awards were granted to create a large-scale SARS-CoV-2 sequencing capacity within the UK and support academic research. Subsequent awards were given to help COG-UK meet the increased demand for its activities, and specifically to bolster large-scale SARS-CoV-2 sequencing capacity and equipment, and enable the transition of routine sequencing activities to the four PHAs.

15 UK Government (2021a).

16 Peacock (2020).

17 Janus (2020).

18 Grant reference number: MC\_PC\_19027.

COG-UK is a collaborative effort between 16 academic institutions, the four UK PHAs, the Wellcome Sanger Institute, and four Lighthouse Labs,<sup>19</sup> as well as 14 other sequencing collaborators and 65 other collaborators from amongst National Health Service (NHS) Foundations and Trusts and other organisations across the UK (see Annex 1 for a list of collaborators). COG-UK was rapidly established to respond to the pandemic and build on the UK's strengths in pathogen genomics, population health sciences and health informatics.<sup>20</sup> The consortium is coordinated from a central hub at the University of Cambridge but operates through a decentralised model where organisations across all four nations of the UK contribute to the consortium's sequencing, research, analysis and stakeholder-engagement activities.

In essence, COG-UK connects genomics with public health – with viral sequencing and analysis at the core of COG-UK's activity. More specifically, COG-UK's key aims at the time this evaluation was commissioned<sup>21</sup> were to:

- Provide data, analysis, tools, and research that can help guide public health decision making and policy relating to the COVID-19 pandemic;
- Advance understanding of genetic changes in the SARS-CoV-2 virus and how they relate to the spread of the virus and severity of COVID-19 symptoms,

all of which matter for public health decision making and the development and evaluation of treatments and vaccines; and

- Support national research studies, including those that can help enable future evaluations of the effectiveness of various pharmacological and non-pharmacological interventions to prevent or treat COVID-19.

The consortium is committed to sharing knowledge and promoting open science in the UK and globally so that the insights and data generated by COG-UK's activities can help support public health decision making for current and future pandemics.<sup>22</sup>

Given the growing realisation of the importance of pathogen genomics for public health, the scale of investment made and the commitment to sharing learning from the COG-UK experience widely, the consortium commissioned the not-for-profit Institute RAND Europe to evaluate and learn about its progress, evolution and impacts.

## 1.2. Reader's guide

In the following content, we first briefly overview the aims of the COG-UK evaluation, the methods used and associated caveats ([Section 2](#)). [Section 3](#) presents the COG-UK theory of change, which served as the framework for developing evaluation indicators. [Section 4](#) discusses key findings related to the outputs, outcomes and impacts of

19 A network of testing laboratories launched by the UK government in March 2020 to support the fight against COVID-19 (Lighthouse Labs, 2022).

20 COG-UK (2020a).

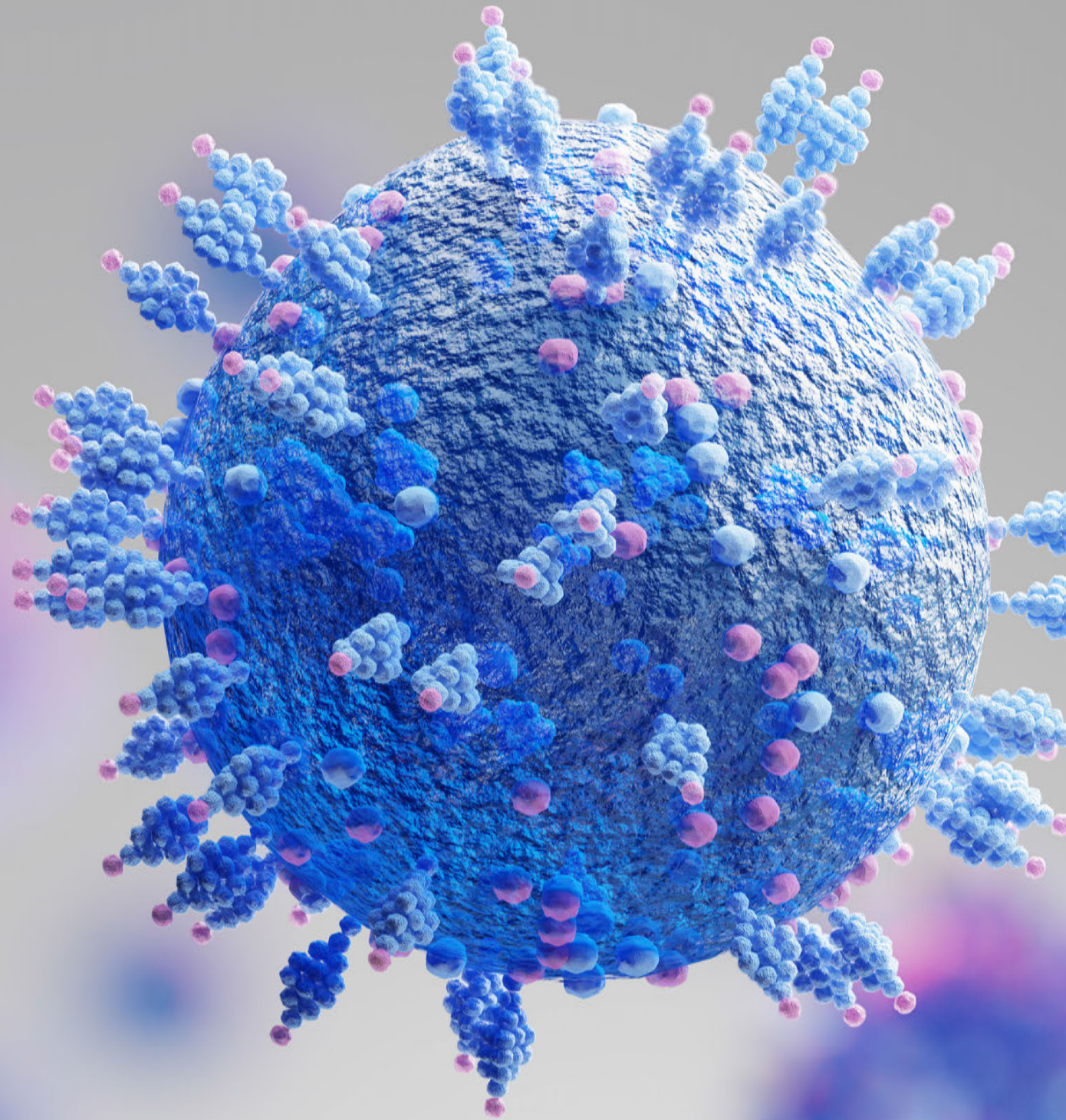
21 These aims applied to the evaluation timeframe and were communicated to RAND Europe by COG-UK when they commissioned the evaluation. The aims may change in the future to reflect the evolving COVID-19-related public health landscape. At the time of publishing this evaluation report, COG-UK was already considering adaptations for the next phase of its existence, given planned transitions of routine sequencing activity to public health agencies. This point is discussed later in this report. At the end of 2021, the consortium was also focusing on future activities related to data linkage and international collaboration.

22 COG-UK (2021a).

COG-UK's activity. References to interview-derived findings are noted parenthetically, while those derived from self-reported data are footnoted. [Section 5](#) discusses influences on the consortium's evolution and outputs and provides learnings about enablers and

challenges experienced in this highly networked pathogen genomics effort. Finally, [Section 6](#) reflects on the learning gained and considers the sustainability of COG-UK and its legacy in a future pathogen-genomics landscape.





## CHAPTER 2

# **Evaluation aims and methods**



## 2.1. Aims

The evaluation of COG-UK set out to:<sup>23</sup>

- Examine COG-UK's delivery against its aims in terms of its outputs, outcomes and impacts;
- Understand how processes related to governance, management and operations impacted delivery;
- Learn about enablers of progress as well as challenges experienced;
- Provide valuable formative learning for any potential future consortium phases and/or for other related efforts, including sustainability and legacy.

## 2.2. Methodology and caveats

The evaluation adopted a mixed-methods approach, involving:

- Developing an evaluation framework based on specifying a COG-UK theory of change and associated evaluation indicators through workshops with COG-UK representatives;
- Collecting and analysing self-reported qualitative and quantitative data on evaluation indicators;
- Conducting in-depth semi-structured interviews with diverse stakeholders involved with COG-UK; and
- Undertaking cross analysis, synthesis and reporting.

### 2.2.1. Establishing a theory of change and evaluation framework

A theory of change describes, at a high level, the critical causal pathways through which an intervention or programme uses the resources at its disposal to produce activities which lead to intended outputs and impacts. It therefore establishes key questions to inform the evaluation framework and the key data to be collected. A theory of change is recommended when evaluating complex interventions with multiple parts and non-linear causality.<sup>24</sup> Therefore, the first step in the evaluation was to work with COG-UK participants to develop a theory of change, an associated logic model (a graphical representation of the theory of change) and a set of evaluation indicators for the consortium. The COG-UK theory of change and logic model specified the initiative's desired outputs and impacts and the anticipated steps needed to achieve them according to COG-UK representatives' views (see [Section 3](#) for an elaboration of the COG-UK theory of change and logic model). This helped inform the development of evaluation indicators (see Annex 2 for an overview).

The research team drew on an analysis of COG-UK website data and conducted two online workshops with COG-UK members in February 2021 to define the theory of change and evaluation indicator framework<sup>25</sup>. The first workshop focused on developing the theory of change and associated logic model, while the second focused on specifying evaluation indicators. Participants in these workshops specified core aspects of the COG-UK theory of change in the context of key activities, desired outputs, outcomes and impacts and the inputs

23 These were COG-UK's overarching aims as communicated to the evaluation team during the evaluation design.

24 For example, see Taplin et al. (2013).

25 A total of 14 individuals representing different consortium members participated in the first workshop and 11 in the second.

available to support delivery. Participants also reflected on perceived critical success criteria. Although funding did not start until 1 April 2021, the consortium began work in March 2020. However, since this evaluation was commissioned later, participants were asked to ‘step back in time’ to consider early expectations while also reflecting on goals and approaches that needed adaptation and change over time. The latter was important as the consortium emerged as a complex intervention in a rapidly changing environment, where adaptability to changing circumstances has been seen as key to its conceptualisation and function.

### 2.2.2. Collecting self-reported qualitative and quantitative data

Based on the evaluation framework, RAND Europe developed self-reporting templates to assess progress against the evaluation indicators. COG-UK’s central leadership team was responsible for coordinating data collection and providing self-reported data in a way that reflects consortium-wide delivery over the evaluation period between 1 April 2020 and 31 July 2021.<sup>26</sup> Wherever possible, the team was asked to provide source references to back the self-reported data. The RAND Europe team provided detailed guidance on completing the self-reported data (see Annex 3 for further detail on the self-reporting templates and indicators covered). The template questions related to constituent elements of the theory of change. More specifically, they captured data on indicators related to COG-UK’s activity *inputs* (e.g. funding, human resources and infrastructure), *processes* (e.g. sequencing, research and analysis activities, implementation of management and government processes,

and capacity-and-capability-building efforts), *outputs and outcomes* (e.g. sequencing outputs, research study outputs, improved methodologies for pathogen genomics and contributions to pathogen-genomic capacity in the UK), and *impacts* (e.g. advancing scientific knowledge, creating a sustainable community of practice and impacting public health decision making and policymaking). Completed self-reported data templates were returned to RAND Europe in September 2021.

### 2.2.3. In-depth stakeholder interviews

To complement the self-reported data, RAND Europe conducted 20 in-depth interviews with representatives of diverse organisations involved with COG-UK activity across academic, PHAs and NHS-related stakeholders, as well as some external stakeholders within funding, policymaking and international-expert communities. The interviews were conducted virtually between April and October 2021<sup>27</sup> using Microsoft Teams. All interviewees contributed with informed consent.

The interviews aimed to add depth and explanatory power to the self-reported data. In addition to exploring stakeholder views on the outputs and impacts of COG-UK activity, the interviews also examined influences on the consortium’s evolution and progress in the context of experienced challenges and enablers, alongside stakeholder views on COG-UK’s sustainability and legacy. See Annex 4 for the interview protocols.

Overall, RAND Europe conducted 20 interviews with representatives from the following groups: COG-UK governance and leadership (n=5), COG-UK academic or research-institution

26 Although the self-reporting templates had 1 March 2020 as the start date, the consortium largely reported activities from 1 April, when funding to support most operations commenced.

27 Due to demands on interviewees to directly engage in activities related to the COVID-19 response, the intended interview timeframe was extended by three months and is thus slightly different to the timeframe for self-reported data.

members (n=4)<sup>28</sup>; each of the UK PHAs (n=4), COG-UK funders (n=3), international experts (n=2), an NHS site (n=1),<sup>29</sup> and an external policy organisation (n=1). For a list of interview participants who consented to have their names shared, please see Annex 5. The interview sampling strategy aimed to achieve a diversity of views from various stakeholders.

#### 2.2.4. Cross analysis, synthesis and reporting

Finally, the research team brought together learning from the self-reported qualitative and quantitative data and the in-depth stakeholder interview data. The research team then triangulated insights against core elements of the COG-UK theory of change to produce a final evaluation report. The insights were discussed in meetings and iterated within the research team to deduce key themes and arrive at final messages and interpretations.

#### 2.2.5. Caveats

Some caveats must be borne in mind when interpreting the findings of this evaluation:

- Since the consortium had already been operating for eight months before this evaluation began, the current findings are primarily based on retrospectively collected data. Elements such as developing the theory of change thus depended on a degree of recollection of participants' experiences in earlier phases of the consortium's existence.
- The scope and resources for this evaluation meant that the focus was primarily on understanding COG-UK delivery against its aims, the factors shaping its performance, and the lessons learned for the future. Using

a theory of change-based framework for assessing how far change was achieved as intended is especially appropriate when there are not both 'business as usual' and intervention groups, when there is a fuzzy line between before and after and when 'before data' is incomplete. Consequently, the evaluation discusses COG-UK's contribution to the landscape but does not aim to quantify or attribute changes solely to COG-UK. Although we assess COG-UK's contribution, there is no counterfactual. The logic of inquiry is 'how far can we be confident that COG-UK delivered as intended?' and not 'can we measure the difference between what happened with COG-UK compared with what would have happened without it?'. Future evaluations may enrich this inquiry were we to consider comparators and learn from international experiences of other pathogen genomics sequencing initiatives.

- Although COG-UK provided specific documentary evidence and data-source references alongside the key analytics compiled in self-reported data, an audit of the data was outside the scope of this work.

With these methodological choices and caveats in mind, the evaluation team is confident that the diverse perspectives and experiences shared through the in-depth interviews and the specificity of self-reported data support an objective and comprehensive analysis of COG-UK's outputs and impacts and a detailed understanding of the diverse influences on its evolution and impacts. Finally, since COG-UK continues to function, future evaluations may help capture impacts and learning from activities yet to unfold.

28 One interview involved two individuals (thus four interviews were conducted amongst COG-UK academic or research-institute members, with a total of five participants).

29 One of this evaluation's aims was to understand the roles different types of partners played in COG-UK. This included an interest in the roles of academic institutions, PHAs and the NHS. NHS sites played a key role in providing samples to COG-UK. While we were only able to directly interview a representative from one NHS site, we discussed wider NHS implications across all interviews.



## CHAPTER 3

# **COG-UK's theory of change and evaluation framework**

### 3.1. What is a theory of change, and how was COG-UK's theory of change developed?

The first step in developing the evaluation framework for COG-UK was to develop a theory of change, which captures three principal elements:

- What the COG-UK consortium aimed to achieve (desired outputs and outcomes and longer-term impacts)

- How it sought to achieve desired aims (activities and processes), and
- The inputs and/or resources available to pursue desired aims (e.g. financial, physical, human).

It does so in a structured way that facilitates evaluation efforts (see Box 2 for further information about theory-of-change approaches).

#### Box 2. What is a theory of change?

- In a 'theory of change approach'<sup>30</sup> the evaluation questions are shaped by asking what an organisation or initiative is trying to achieve, why and how, as well as why and how a chosen approach is expected to support the desired outputs and impacts (i.e. what underlying assumptions does it build on?). Any subsequent implementation of evaluation activities then sets out to understand whether intended activities were implemented, whether they led to the desired results, how and why (and if not, why not?), including what the associated enablers or challenges to progress and impact have been.
- This approach helps draw out learning that can inform future practice and is often accompanied by a logic model, which helps organise the thinking integral to a theory of change in a systematic and structured way that is visually easy to follow. Together with the narratives that accompany and contextualise them, logic models can provide a guiding structure for establishing a core set of indicators based on which evaluation is implemented. These indicators should reflect multiple evaluation aims, including documenting and demonstrating achievements, learning and accountability. This approach allows for reflection, learning and future action on the evolution and performance of an initiative against its plans.<sup>31</sup>
- Experience has shown how usefully a theory of change and logic model can help organise thoughts and structure discussions. However, we are aware that they risk excessive linearity and the fallacy that, because it is 'on the map', it must also exist 'on the ground'. When using theory-of-change approaches, these risks are mitigated and managed through the nature of stakeholder engagement conducted as part of implementing the evaluation (e.g. the questions explored in stakeholder interviews).

30 A 'theory of change' is an evaluation framework that has been used in numerous contexts over many years. See: Marjanovic et al. (2012), Pawson & Tilley (1997), Washington et al. (1998) and Weiss (1995).

31 McLaughlin & Gretchen (1999).



The contents below briefly overview COG-UK's theory of change, based on workshop participants' views and background information.

## 3.2. COG-UK's theory of change

Reflecting the diversity of COG-UK's aims, its activities are varied and multifaceted but broadly fall into three activity categories:

- Research and analysis
- Capacity- and capability-building
- Implementation of management and governance arrangements to support operational delivery in a complex consortium model.

The contents below elaborate on these activities and what they set out to achieve in terms of short-and-medium-term outputs/outcomes and longer-term impacts. At the end of this section, Table 4 summarises the logic model for COG-UK.

However, while the theory of change was beneficial for orienting and guiding data collection, it was not an exhaustive list of COG-UK's accomplishments. Consequently, efforts to produce a direct correlation between the theory of change and the realised outputs, outcomes and impacts of COG-UK's activity identified via interviews and documentary evidence would overly simplify the complexity of COG-UK's evolution and outcomes. Furthermore, COG-UK was established at considerable speed to respond to the urgency of the pandemic. Although the core aims and desired areas of impact of the consortium were defined at a conceptual level, there were not tightly specified targets or milestones for many of the core areas of desired activity from

the onset. The consortium and its activities continued evolving during the reporting timeframe (and, to a limited extent, during this evaluation). This evaluation aims to take into account the unusual context of COG-UK's establishment and subsequent trajectory. The evaluation collected information on all theory-of-change dimensions through the evaluation indicators (see Annex 2) implemented via self-reported data and interview evidence (see Annex 3 and 4). The indicators described in Annex 2 map onto the constituent theory-of-change elements.

Based on the data collected, this evaluation reports on the consortium's evolution and impact by synthesising key insights into overarching themes and categories of accomplishments (see [Section 4](#)) and associated enablers and challenges (see [Section 5](#)). It also uses the evidence and insights gained to reflect on implications for COG-UK's future efforts, sustainability and legacy ([Section 6](#)).

### 3.2.1. Core activities and desired outputs, outcomes and impacts

#### 1) Research and analysis related to pathogen genomics is at the core of what COG-UK was set up to do

COG-UK research and analysis encompasses a broad range of activities. This includes collection and curation of genomic sequencing data and its linkage with other data sets (e.g. epidemiological, clinical and contact tracing data).<sup>32</sup> The consortium also set out to develop new analytical methods and tools for rapid genome analysis and to analyse sequencing data in order to facilitate improved understanding of changes in viral behaviour related to virulence or transmission and

32

Based on samples received from hospital diagnostic laboratories (subsequently sequenced by COG-UK regional labs) and from Lighthouse labs receiving swabs from non-hospitalised people or long-term care facilities (subsequently sequenced by the Wellcome Sanger Institute).

spread.<sup>33</sup> Sharing data with individuals and organisations outside the consortium and supporting data flow activities in the research, healthcare, and public health system through an open access model is a key feature of the COG-UK approach. Research and analysis activities are supported by a genome analysis infrastructure that the consortium manages activity on (e.g. UK Cloud Infrastructure for Microbial Bioinformatics [CLIMB]). From its conception, COG-UK also aimed to support national (as well as regional and local) research studies – through data, analysis, tools and other research activity – as a trusted source of insights and a collaborator in research efforts.

Research and analysis activities were conceived with multiple end-goals in mind, including advancing knowledge, building capacity and capabilities in the wider public health genomics landscape, and informing the public health response. More specifically, these activities were established to achieve a series of desired outputs, including:

- Sequencing a high number of virus genomes at pace and from a representative geography/ appropriate population to advance the knowledge base and inform public health decision making, especially in the UK.<sup>34</sup>
- Producing and openly sharing high-quality linked data outputs (in the form of databases, analytical tools, software, and analysis protocols) to deliver on efforts to build knowledge in the wider pathogen genomics and public health landscape.

- Contributing to research studies on topics of significant public health relevance and disseminating findings to inform public health decision making and policy.<sup>35</sup>

COG-UK's activities and outputs were also expected to help achieve a longer-term vision for impact. The ability for longer-term impacts to materialise is, of course, not fully in COG-UK's control, as it depends on political, economic, scientific, epidemiological and behavioural developments in the wider landscape. Some of the desired impacts depend more on the external context than others, but all link closely to and build on the types of outputs that will stem from COG-UK's activity.

In terms of longer-term outcomes and impacts, COG-UK since its conception sought to:

- Improve the global scientific knowledge of genetic changes in the SARS-CoV-2 virus and their relations to spread, transmission and symptom severity. This matters for public health decision making and the development of treatments and vaccines and for evaluating the effectiveness or impact of policy and pharmacological interventions.
- Achieve real-world utility and impact on public health and policy decision-making and actions related to the COVID-19 response, and to the management and control of the COVID-19 pandemic. This includes helping decision makers access timely, high-quality data. Achieving this impact was seen to depend partially on the relevance, quality and communication

33 Examples include genomic analysis, bioinformatics, linking genome sequencing and analyses to transmission and outbreak analysis, mutational analysis and tracking through monitoring of prevalence, geographic distribution and significance.

34 Achievement of this output was envisaged by reducing sequencing times (due to increased national capacity), sequencing appropriate samples (rather than random ones) and implementing a framework for guiding this type of activity (e.g. how sample turnaround times are managed).

35 The national studies were expected to contribute knowledge to diverse public health topics such as infection prevention and control measures to reduce spread; studies to understand infection rates, transmission and outbreaks; mutational analysis and its relation to spread and symptoms; and/or research on re-infection, immunity and vaccine trials.

of COG-UK's outputs and insights and on decision makers' receptiveness and ability to act on the acquired knowledge and insights.

- Achieve longer-term impact on the vaccine-innovation landscape so that sequencing is recognised as a critical component to vaccine development, ensuring that sequencing and COG-UK (or its legacy) are at the forefront of shaping vaccine programmes in the future.

## **2) A second key pillar of COG-UK's activity was to implement activities focused on longer-term capacity-and-capability-building in the public health genomics landscape**

COG-UK also has a vital role in long-term capacity-and-capability-building in pathogen genomics and public health service delivery in the UK. As part of its remit, the consortium set out to contribute to building a national COVID-19 genomic surveillance system and capacity to help PHAs identify and respond to future outbreaks at pace. This includes efforts to bolster sequencing capacity and analysis tools to enable public health authorities to monitor viral mutations (including in relation to informing vaccine development and evaluation) and to support wider research and public health aims.

The consortium sought to operationalise this remit through investment in people (education and training of the workforce), research on priority topics, sequencing-site infrastructure, data infrastructure (e.g. bioinformatics analysis tools and cloud-based solutions), equipment for sequencing high sample volumes in short periods, investment in supporting rapid data flows and wider communications about consortium-driven insights and learning.

COG-UK also sought to contribute to capacity building through creating and nurturing lasting collaborations across different stakeholders, both within and between the four UK nations. The strategy for achieving this was rooted in

supporting joint working between academia and/or research organisations, PHAs and NHS Foundation Trusts. This helped mobilise skills, expertise, and infrastructure (e.g. sequencing labs) to enable sequencing at an unprecedented scale and pace, as well as cutting edge research and support for public health decision-making.

Communication, awareness-raising and sharing of expertise with decision makers in the healthcare system were also seen as central to COG-UK's efforts to build capacity for understanding and engaging with public health genomics among policymaking communities, regulators and PHAs.

The key desired outputs from COG-UK's efforts to build capabilities and capacity included:

- Strengthened national sequencing, analysis and surveillance capacities and capabilities for COVID-19.
- A networked system across the UK involving academics/researchers, PHAs and NHS stakeholders working together (rather than in silos) to help PHAs identify and respond to future outbreaks and monitor mutations. Achieving a dynamic network was seen by COG-UK stakeholders as key to ensuring a connected community linking genomics with public health decision making.
- Demonstrable usefulness and value of COG-UK's capacity and capability contributions to a wide pool of decision makers in the public health genomics and service-delivery landscape, i.e. value to those in and outside the consortium.

In terms of longer-term outcomes and impacts from capacity and capability-building efforts, COG-UK set out to:

- Ensure that the consortium activities and the capability and capacity it builds nationally can help enable future evaluations of the effectiveness of both pharmacological and non-pharmacological

COVID-19 interventions informed by genome analysis.

- Achieve a long-term impact on establishing sustainable communities of practice and a national pathogen-genomics platform (i.e. a dynamic and evolving rather than a static network of connected individuals and organisations). Such a platform could be mobilised for future epidemics and/or pandemics (COVID-19 related or other). In this context, the COG-UK network could potentially lead to a sustainable pathogen-genomics-and-public-health platform for the future.
- Leave a legacy in terms of contributing to a UK landscape where public health genomics research and public health service delivery are more closely integrated (e.g. where learning from COG-UK as a model impacts on the integration of sequencing activity, infrastructure, and tools into relevant national PHAs and/or where activities are coordinated better than in the past).<sup>36</sup>
- Achieve global impact in terms of connecting genomics and public health, e.g. by helping inform vaccine policy and building skills in the global research and public health workforce.

### **3) Implementing management and governance processes that could support operational delivery was also a key aspect of COG-UK's existence as a complex and multifaceted consortium**

At the time of inception, COG-UK chose to invest in a management and governance infrastructure that could support operational delivery in a complex consortium model

involving multiple diverse partners and aims. Establishing this infrastructure was a novel process that needed to bring together diverse partners spanning academia, the NHS and PHAs and ensure appropriate oversight, member-support arrangements, operational protocols and frameworks for different activities. Among workshop participants helping define the theory of change, orchestrating and managing relationships and engagement within the consortium were seen as a core function of COG-UK's management, and essential for ensuring that the benefits of engaging diverse regional partners, multidisciplinary expertise and diverse stakeholders are reflected in consortium activities and outputs. Part of the management and governance arrangements was also to support communication, awareness-raising and public relations activity (e.g. with the wider research community, media/journalists, the lay public, decision makers and other stakeholders). This pursuit was seen as important to achieving impact and ensuring clarity on the scope and remit of COG-UK activity.<sup>37</sup>

Although the consortium's management-and-governance arrangements were primarily established to support the delivery of its aims, COG-UK also envisaged a series of concrete operational outputs which could support both COG-UK activity and other consortium-based efforts in the future. Examples include standard operating procedures (SOPs) for feeding research insights and data to decision makers, legal frameworks for collaborative consortia involving many different types of actors, and financial management protocols for activities not necessarily traditional for academic ways of operating. Workshop participants saw these types of outputs as having scope to enable

<sup>36</sup> Peacock (2020).

<sup>37</sup> For example, relating to a perceived need to specify how much COG-UK is primarily a research initiative and how much it aims to support public health service delivery (i.e. conducting sample sequencing and analysis in response to policymaker and PHA requests).

COG-UK activities and as an output in and of themselves – with potential utility in future pathogen-genomics efforts.

### 3.2.2. Inputs to support desired goals

For COG-UK to conduct its activities, diverse resources (e.g. financial, physical, human, relational) needed to be made available to pursue desired aims. The contents below summarise the funding support, governance-and-management structures, human-and-relational resources, and equipment/physical infrastructure that supported and fed into COG-UK activity:

#### 1) Funding:

Financial resources were a pre-requisite for COG-UK activities. As introduced earlier, and during the timeframe for this evaluation, on 1 April 2020, COG-UK received an initial £20,790,000 award from the NIHR, the MRC (part of UKRI<sup>38</sup>), and Genome Research Limited (operating as the Wellcome Sanger Institute). COG-UK received an additional £11,600,000 of funding from the Testing Innovation fund in January 2021 and another £4,999,000 from the DHSC Test and Trace in April 2021. COG-UK's initial funding award was to create a large-scale SARS-CoV-2 sequencing capacity and support academic research, including the provision of data and metadata to the COG-UK database. Subsequent funding was given in response to increased demand for COG-UK's activities, and specifically to bolster large-scale SARS-CoV-2 sequencing capacity and equipment and enable the transition of routine sequencing activities to the PHAs (a process

which began in the Spring of 2021, discussed in [Section 4](#) and [Section 5](#) of this report).

#### 2) Governance, management and operational infrastructure:

COG-UK's activities are framed by a governance infrastructure, legal framework and operational framework intended to support delivery of the consortium's aims. These consist of:

- The core leadership team (Executive Director and Chair, Director of Data Sciences, Associate Director and Director of Operations, and two Deputy Directors) that oversees the consortium's management, business planning and governance.
- A governance and advisory group that provides counsel and is an oversight and monitoring body.
- A steering group that provides strategic support to COG-UK and undertakes reviews of publications and analysis proposals, making decisions on those.
- Management and administration, including a logistics team (Logistics Manager, Logistics Assistant, Operations Manager, and Scientific Project Manager), and project management, communications and administration support overseeing consortium administration, internal policies, project management, publications activity, and communications.
- Operational working groups that cover aspects such as research and wider consortium operational support, data-sciences activity and operational aspects of partnership working.<sup>39</sup>

38 Grant reference number: MC\_PC\_19027.

39 Eight operational working groups were initially established, covering: Modelling, Phylogenetics and Display, Sample Logistics, Metadata and Patient Linkage/Epidemiology/Health Informatics, Sequencing, Data/Bioinformatics, Clinical Virology, Mutations Research, and Wastewater. However, the 'Modelling, Phylogenetics and Display' and 'Clinical Virology' working groups are no longer active at the time of publishing this report. Working groups were established with a defined scope, and some groups ceased to exist once they had delivered on the scope of their defined aims. These evolved to reflect the evolving priorities of the consortium projects in line with COG-UK's role and objectives in the pandemic response.



- An operational framework with specialist working groups, sequencing centres and sampling sites that supports delivery on consortium activities, including various logistical, regulatory and laboratory protocols, workflows and tools. The COG-UK Consortium Agreement provides a legal framework for cooperation and data sharing between 21 partners (with Cambridge University as the leading party) that sets out operational, commercial and organisational aspects and governs data flows between partners.

### **3) Human resources and pre-existing relationships:**

Human resources inputs comprise of scientific, management and operations, and policy experts within delivery partners working across academia, the four UK PHAs and the NHS. Multidisciplinary researchers work on various aspects of COG-UK's activity, supported by operational, management, governance and leadership staff. While some staff are COG-UK funded, the consortium also relies heavily on volunteers. Based on data shared by COG-UK, the consortium funded 27 research and technical staff and 17 administrative and management staff as of July 2021.<sup>40</sup> COG-UK estimates that more than 800 additional individuals have volunteered their time to COG-UK. Though not all volunteers were

involved from the beginning, they have been essential inputs into the consortium's delivery.<sup>41</sup>

Pre-existing relationships and networks were also a key input, helping mobilise goodwill across different staff types and organisations. COG-UK emerged from relationships between UK pathogen-genomics-and-sequencing academics, including UK academics with secondments to PHAs, individuals involved with CLIMB (which enabled the rapid creation of the COG-UK computing infrastructure)<sup>42</sup> and the ARTIC Network (an international network of academics and public health researchers enabling sequencing in remote and resource-limited locations that was key to the early release of SARS-CoV-2 sequencing protocols).<sup>43</sup>

### **4) Equipment and technical infrastructure:**

COG-UK secured access to data sequencing and analysis infrastructure, made available through the Wellcome Sanger Institute, regional laboratories and sequencing hubs, and the CLIMB bioinformatics infrastructure to input into consortium activities. Although not all infrastructure was available initially, it was a critical input resource for enabling research, analysis, capacity and capability-building efforts. For a list of sequencing equipment across the consortium, see Annex 6.

The COG-UK theory of change is overviewed in Table 4 (next page).

40 Based on a headcount over the evaluation timeframe, not the full-time equivalent (FTE), and derived from self-reported data. Note that as the Wellcome Sanger Institute manages its budget separately, these counts do not include Sanger Institute staff.

41 The consortium primarily based this on authorship lists of various documents. This number represents a headcount over the evaluation timeframe, not the FTE, and is derived from self-reported data.

42 Funded by the MRC, CLIMB launched in 2016 as a shared computing infrastructure for the medical microbiology community. CLIMB is a collaboration between Warwick, Birmingham, Cardiff, Swansea, Bath and Leicester Universities, the MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, and the Quadram Institute in Norwich.

43 ARTIC comprises scientists from the universities of Edinburgh, Birmingham, Cambridge, Oxford, KU Leuven, UCLA and the Fred Hutchinson Cancer Centre. The ARTIC group have experience in previous outbreak situations, including the West African Ebola virus epidemic of 2013–2016.

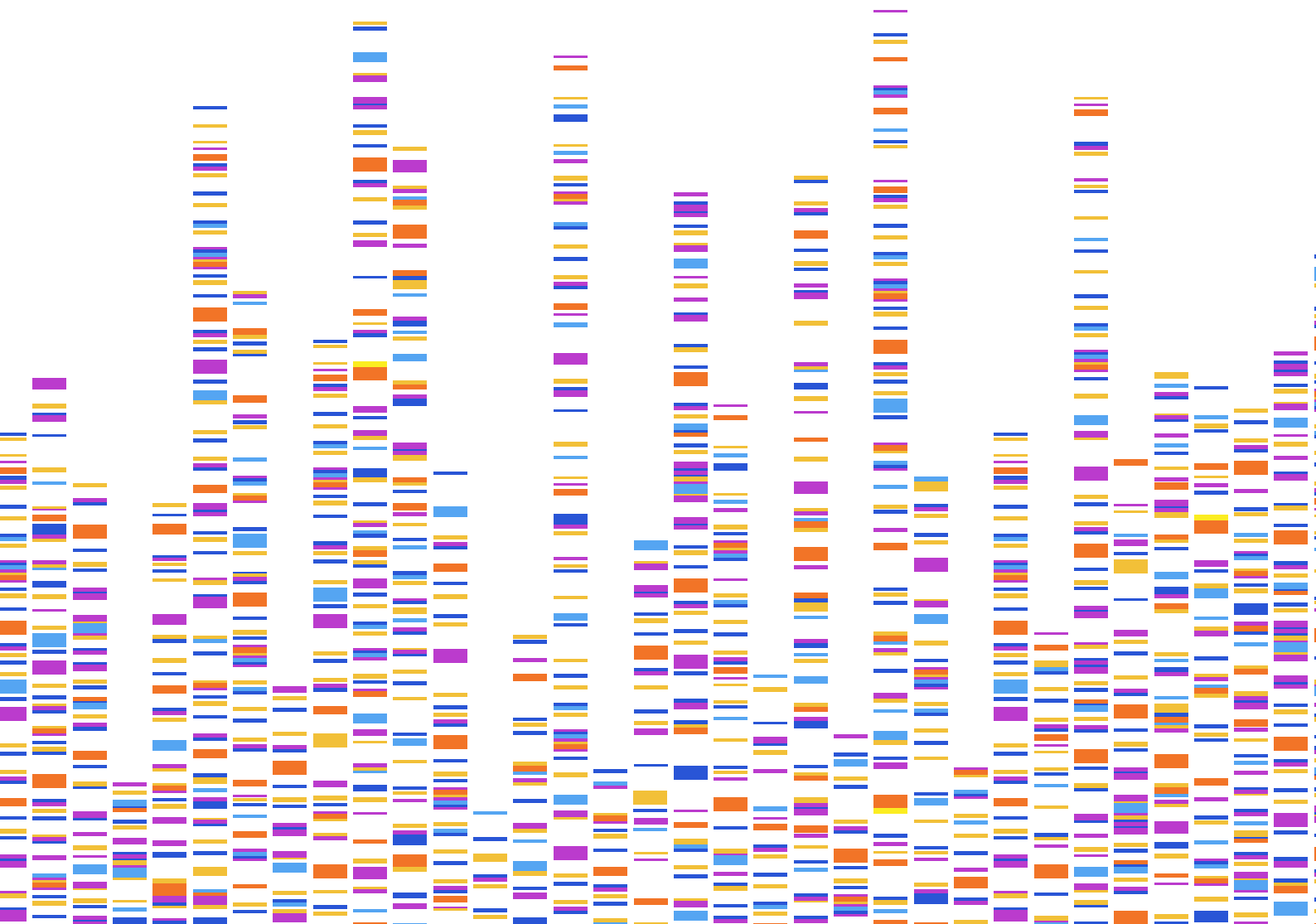
**Table 4. COG-UK Theory of Change**

INPUTS	PROCESSES/ACTIVITIES	DESIRED OUTPUTS AND OUTCOMES	DESIRED IMPACTS <sup>44</sup>
<p><b>Funding support</b></p> <ul style="list-style-type: none"> <li>DHSC NIHR (National Institute of Health Research), UKRI- MRC and the Wellcome Sanger Institute: £20 million (April 2020) and DHSC Testing Innovation Fund: £16.6 million (£11.6 million in January 2021 and £4.6 million in April 2021).</li> </ul> <p><b>Governance, management, and operations</b></p> <ul style="list-style-type: none"> <li>Core leadership team, governance and advisory group, steering group, management and logistic teams.</li> <li>Operational framework with specialist working groups, sequencing centres, sampling sites, and logistical, regulatory and laboratory protocols, workflows and tools.</li> </ul>	<p><b>Research and analysis activity</b></p> <ul style="list-style-type: none"> <li>Collection and curation of data (e.g. genomic sequencing data and its linkage with other data sets such as epidemiological, clinical, and contact tracing data).</li> <li>Sharing of datasets and support for data flow activities in the research, healthcare, and public health system.</li> <li>Conducting analysis and sharing findings (e.g. genomic analysis, bioinformatics, linking genome sequencing and analyses to transmission and outbreak analysis, mutational analysis and tracking through monitoring of prevalence, geographic distribution, and significance).</li> <li>Developing and sharing analytical tools and methods for rapid genome analysis and managing analysis infrastructure (e.g. CLIMB bioinformatics infrastructure).</li> <li>Collaboration on research studies that aim to inform public health decision making and policy (as part of collaborative national studies or local and regional ones).</li> </ul> <p><b>Capacity and capability building in the system</b></p> <ul style="list-style-type: none"> <li>Building a national COVID-19 genomic surveillance system and capacity to help PHAs identify and respond to outbreaks at pace, to monitor viral mutations. Doing so through investment in             <ul style="list-style-type: none"> <li>Education and training to enhance skills</li> <li>Sequencing site infrastructure</li> </ul> </li> </ul>	<p><b>Research-and-analysis related</b></p> <ul style="list-style-type: none"> <li>A high number of virus genomes are sequenced at pace and from a representative geography/ population (target of 180,000 applied to evaluation timeframe).</li> <li>High quality linked data outputs are produced and shared in the form of databases or other resources to inform public health decision making.</li> <li>Genomic sequencing data and analyses are shared with eligible applicants via open access .</li> <li>Genomic sequencing methods, analytical tools and software, and analysis protocols are developed and shared to enable use by academics, public health agencies, and NHS organisations.</li> </ul>	<p><b>Advancing the knowledge base</b></p> <ul style="list-style-type: none"> <li>Increased understanding of genetic changes in the SARS-CoV-2 virus and their relations to spread, transmission, and severity of symptoms.</li> </ul> <p><b>Real-world utility and impact</b></p> <ul style="list-style-type: none"> <li>COG-UK activities and outputs impact on public health and policy decision making and response, management, and control of the COVID-19 pandemic in a timely manner.</li> <li>Evaluations of the effectiveness of various pharmacological and non-pharmacological interventions integrate genomic sequencing in the future, informed by COG-UK (or its legacy) genomic analysis activity (applied to COVID-19 and other disease areas).</li> <li>COG-UK (or its legacy) is a critical partner in shaping vaccine development programmes in the future.</li> </ul> <p><b>Sustainable communities of practice- a national pathogen genomics network</b></p> <ul style="list-style-type: none"> <li>A sustainable community of practice supports a dynamic and adaptable</li> </ul>

INPUTS	PROCESSES/ACTIVITIES	DESIRED OUTPUTS AND OUTCOMES	DESIRED IMPACTS <sup>44</sup>
<ul style="list-style-type: none"> <li>The COG-UK Consortium Agreement as the legal framework for cooperation and data sharing.</li> </ul> <p><b>Human resources (managerial, scientific, and policy expertise) and relationships</b></p> <ul style="list-style-type: none"> <li>Leadership team and delivery partners working across the NHS, academia and/or research and the four PHAs.</li> <li>Multidisciplinary research teams.</li> <li>Operational staff.</li> <li>Pre-existing relationships and networks.</li> </ul> <p><b>Equipment and technical infrastructure</b></p> <ul style="list-style-type: none"> <li>Wellcome Sanger Institute's sequencing and analysis facilities.</li> <li>Regional laboratories and sequencing hubs.</li> <li>CLIMB bioinformatics infrastructure.</li> </ul>	<ul style="list-style-type: none"> <li>technical equipment</li> <li>data infrastructure and data flows</li> <li>external communications with research, healthcare, public health, and policy communities.</li> <li>Building capabilities and demand for evaluations of the effectiveness of pharmacological and non-pharmacological interventions to be informed by COG-UK sequencing activity.</li> <li>Creating and nurturing lasting collaborations across different stakeholders (academia and/or research, PHAs, and NHS organisations) locally and between the four nations to support future preparedness and response.</li> <li>Building capability amongst decision makers in the healthcare system to act on data and evidence enabled by COG-UK communications activity and sharing of expertise (e.g. via reporting to SAGE, MHRA, PHAs, NHS decision makers, sharing insights through other means).</li> </ul> <p><b>Implementing supportive management and governance processes</b></p> <ul style="list-style-type: none"> <li>Establishing governance and management arrangements and operational frameworks and protocols to enable partner engagement across different types of consortium members and activities: research, NHS, PHAs.</li> <li>Orchestrating and managing relationships across the consortium.</li> <li>Communications, awareness-raising, and public relations activity to support impact and manage expectations about COG-UK-driven research and analysis versus demand-driven service-support activity.</li> </ul>	<ul style="list-style-type: none"> <li>National, regional, or local research studies conducted with COG-UK improve scientific knowledge and provide important insights for public health decision making and policy.</li> </ul> <p><b>Capacity-and-capability related</b></p> <ul style="list-style-type: none"> <li>UK pathogen-genomics sequencing and analysis and surveillance-system capacity are improved in a connected/networked system.</li> <li>The expertise gained by staff contributing to COG-UK activity and the outputs of their work are valued and deemed useful by decision makers (policymakers, PHAs, NHS organisations). COG-UK is acknowledged for the insights and expertise it shares.</li> <li>Operational outputs produced by COG-UK (e.g. standard operating protocols, legal frameworks, financial management protocols) are applicable and adaptable to other efforts and initiatives.</li> </ul>	<p>pathogen genomics platform that can be mobilised for future pandemics/public health threats to support sequencing, analysis, surveillance, outbreak monitoring needs (COVID-19 or others).</p> <ul style="list-style-type: none"> <li>An improved and sustainable pathogen genomics data and physical/technical infrastructure in the UK (e.g. bioinformatics infrastructure, data repository infrastructure, modern sequencing equipment) as a global example of excellence is created.</li> <li>Learning from COG-UK as a model impacts the integration of sequencing activities, infrastructure, and tools into relevant national PHAs.</li> <li>Learning from the COG-UK experience enables better future logistics and operational preparedness for integrating genomics research with service support in a public health response (e.g. via improved understanding and requisite protocols and governance arrangements).</li> <li>COG-UK achieves global impact (e.g. on shaping vaccine policy, building skills in the global research and public health workforce, influencing international pathogen genomics research and sequencing initiatives) and is active in global networks/collaborations.</li> </ul>

## CHAPTER 4

# **COG-UK contributions to the COVID-19 pandemic response: outputs, outcomes and impacts of COG-UK activities**



As introduced in [Section 1](#), COG-UK set out to make diverse contributions to the COVID-19 pathogen-genomics landscape and the pandemic response in the UK. In the contents that follow ([Section 4](#)), we provide an overview of the key outputs, outcomes and impacts of COG-UK's activity during the evaluation reporting timeframe (1 March 2020 to 31 July 2021). These relate to:

1. Contributions to advancing scientific knowledge about SARS-CoV-2 and the methods that support pathogen genomics research;
2. Informing key policy and public health decisions in the UK's pandemic response;
3. Providing information used to test vaccine efficacy against specific variants of SARS-CoV-2 and better understand therapeutics to treat COVID-19;
4. Impact on how policymakers in the UK view and value pathogen genomics;
5. Strengthening capacity for pathogen genomics in the UK through a collaborative approach; and
6. Impact on the international pandemic-response effort.

Box 3 summarises the key contributions of COG-UK in each of these six areas.

### **Box 3. COG-UK achievements in key areas of impact – key learning points**

#### **1. Contributions to scientific knowledge about SARS-CoV-2 and to advancing methods that support sequencing and pathogen genomics research:**

- The sequencing of viral genomes has been essential to research and analysis seeking to understand the SARS-CoV-2 virus and its behaviour. COG-UK sequenced over 800,000 SARS-CoV-2 genomes across the UK between 1<sup>st</sup> April 2020 and 31<sup>st</sup> July 2021.
- COG-UK research and analyses made significant contributions to knowledge about the SARS-CoV-2 virus, variants of concern, viral behaviour, transmissibility and spread, and to understanding the impact of diverse public health measures. The consortium also made key contributions to advancing the methodologies used in pathogen-genomic sequencing and analysis. Insights were widely disseminated through academic publications and conferences.
- Efforts made by COG-UK partners to help link viral sequencing and patient metadata are building up a critical resource for further significant public health research. The CLIMB data and computing infrastructure has played a key role in these efforts.

#### **2. Informing key policy and public health decisions in the UK's pandemic response:**

- COG-UK's sequencing data and analyses helped identify variants of significance across the UK, informed policies related to border control, travel, lockdown and social distancing, and helped improve policymaker and public understanding of links between new variants and disease severity.
- The consortium's pathogen sequencing has also impacted decision making in local settings, including hospitals, care homes and universities (e.g. informing infection prevention and control).
- The consortium supported needs across the four nations using tools such as sequencing coverage reports to help prioritise samples for sequencing. Despite significant contributions to identifying variants of concern across the four nations, the ability to inform regional decision making in a timely manner was occasionally hampered by factors outside COG-UK's direct control.
- COG-UK worked closely with public health decision makers to maximise the impact of its work. COG-UK members took part in various committees and working groups, contributed to external reports and directly reported to policymakers.



### **3. Testing vaccine efficacy against specific variants of SARS-CoV-2 and better understanding therapeutics:**

- COG-UK's open sharing of data and insights provided input into assessments of vaccine efficacy against different viral variants. COG-UK is also working with others, such as the Genotype-2-Phenotype consortium and Oxford Vaccine Group, to identify and characterise variants of concern in a way that can inform the development of the next generation of vaccines. The consortium's data and analysis of viral mutations have also helped to better understand potential treatments under investigation.

### **4. Changing how decision makers view and value pathogen genomics:**

- COG-UK has had a significant impact on raising awareness about the importance of pathogen genomics as a discipline, increased policymaker appreciation of its value, and increased demand for the use of sequencing insights in public health decision making.

### **5. Capacity for pathogen genomics in the UK:**

- COG-UK made diverse contributions to pathogen-genomic sequencing and research capacity in the UK. The consortium trained over 800 staff across different professions and stages in career development to improve sequencing, analysis and interpretation skills. COG-UK also purchased sequencing equipment and implemented software tools that are now available in 17 sequencing sites across the UK. Building upon the existing CLIMB infrastructure, COG-UK also used its funds to rapidly develop additional computational infrastructure. The consortium established a governance structure representative of diverse geographies, as well as contractual arrangements, operational protocols and legal frameworks to support a four-nation, multistakeholder approach. COG-UK also bolstered the strength and scale of collaborative relationships between academia/research institutes, public health agencies, the NHS and Lighthouse Labs in the interest of advancing science and informing policy.

### **6. Impact on the international pandemic response effort.**

- COG-UK data and resources are readily available for use by the international community, and consortium members have advised some other countries on their sequencing and data-sharing strategies. COG-UK members have also supported international efforts through representation on international working groups and councils and collaborating with international organisations, many from low-and-middle-income countries.
- COG-UK's knowledge and experience offer lessons of direct relevance to future pandemic and public health threats in the UK and potentially globally.

#### **4.1. Contributions to the scientific knowledge base on SARS-CoV-2 and to advancing methods that can support high-quality and efficient pathogen genomics research.**

Viral genome sequencing has been a prerequisite for better understanding the SARS-CoV-2 virus and its behaviour and COG-UK rapidly increased sequencing

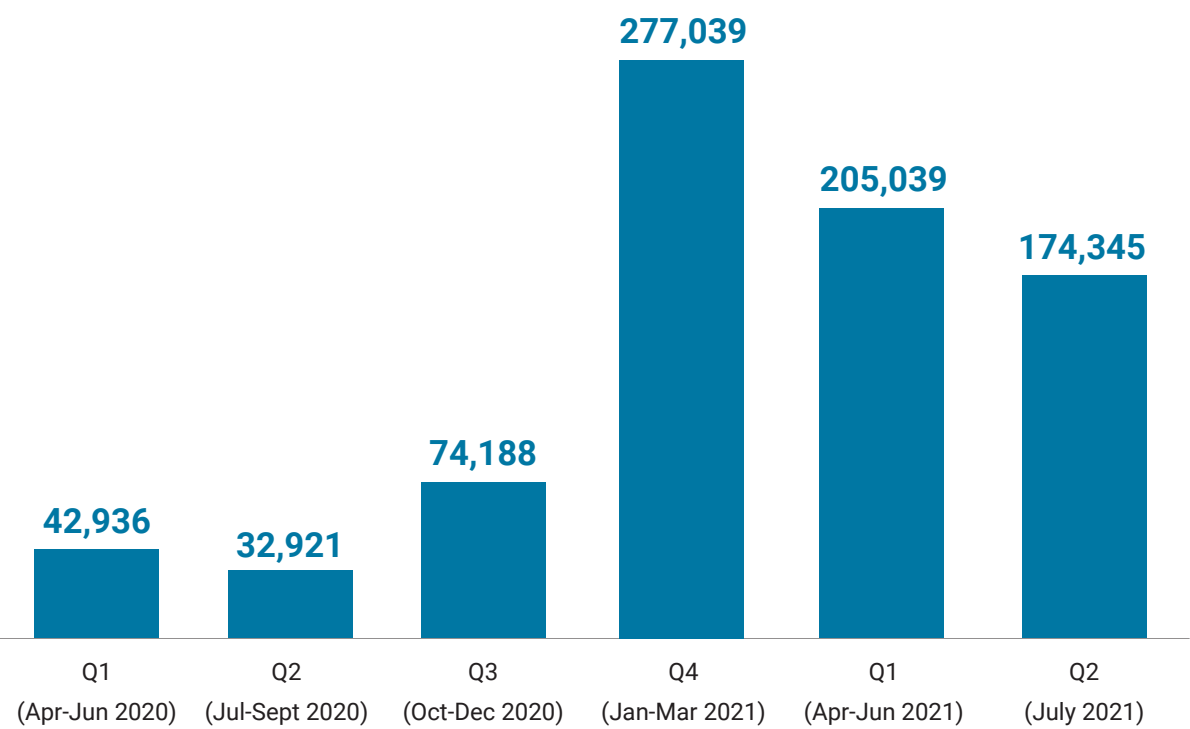
capacity to keep up with demand.

COG-UK's contributions to the knowledge base about SARS-CoV-2 are underpinned by the consortium's ability to rapidly sequence viral genomes. Although COG-UK initially set out to sequence 180,000 SARS-CoV-2 genomes between 1 April 2020 and 30 September 2021, the scale of sequencing increased over time: they were able to sequence more than 800,000 genomes between 1 April 2020 and 31 July

2021 across 17 sequencing sites.<sup>45</sup> On average, approximately 5,000 SARS-CoV-2 samples were sequenced per week in April 2020, 8,000–10,000 samples per week in December 2020, and up to 30,000 samples per week in February 2021.<sup>46</sup> During this timeframe, the consortium responded to peaks and troughs in sequencing demand due to changes in the transmissibility of variants circulating in the

UK. Figure 1 illustrates changes in SARS-CoV-2 whole-genome sequencing volume over time across the 17 sequencing sites, showing that sequencing peaked in the January–March quarter of 2021 (with 277,039 samples sequenced across the UK). See Annex 7 for details on sequencing volume by consortium sites across the UK.

**Figure 1. Number of SARS-CoV-2 whole genomes sequenced over time across 17 COG-UK sequencing sites<sup>47</sup>**



45 COG-UK self-reported data. Quarterly data on SARS-CoV2 whole-genome sequencing, self-reported by COG-UK, based on sequencing invoices and budget spreadsheets.

46 COG-UK self-reported data. Quarterly data on SARS-CoV2 whole-genome sequencing, self-reported by COG-UK, based on sequencing invoices and budget spreadsheets.

47 Between Q1 and Q3 2020, the Wellcome Sanger Institute only reported the total number of samples sequenced (47,581) rather than by quarter. Because the latter was not available for this period, we used the average number of samples sequenced across all three quarters for this graph (i.e. 15,860 or 15,861 samples sequenced per quarter). However, it is more likely that sequencing capacity increased at Wellcome Sanger Institute over time and was not equal across these periods.

The increase in sequencing capacity was achieved by shifting existing capacity from research activities within the consortium to support routine sequencing that informs public health decision-making. This was done by expanding the number of new sequencing sites and securing additional funding to support sequencing capacity.<sup>48</sup> Rapidly mobilising individuals willing to come together and dedicate their time to sequencing and doing so in a coordinated way is also key to achieving COG-UK's sequencing throughput [Int. 9, 11, 14,].

**COG-UK's research has played an important role in advancing scientific knowledge about SARS-CoV-2 in the UK and globally. Over the evaluation timeframe, the consortium contributed 53 publications about the virus and pandemic and disseminated knowledge as part of at least 42 events on SARS-CoV-2 genomics.**

During the evaluation timeframe, COG-UK conducted research that helped understand the SARS-CoV-2 virus, its behaviour and spread, and the impact of various public health measures [Int. 1, 3, 8, 10, 15]. The consortium's contributions included answering important research questions and informing service delivery [Int. 6, 10]. Sequencing activity was crucial for informing many research questions and analyses. As illustrated by one interviewee:

*'It's the sequencing and understanding which areas of the sequence are likely to cause health issues, such as increasing infectivity... If the sequencing is changing in an area [of the sequence] that people know that the virus would be using that area to enter a cell... It's the sequencing and then the modelling of that sequencing*

*onto the biology of the virus that's really crucial.'* [Int. 4]

During the evaluation timeframe, COG-UK members have been involved in nine core national studies to identify which SARS-CoV2 variants were circulating in the UK population over time and understand COVID-19 disease prevalence in the community (see Table 5). In addition, COG-UK was (and continues to be) involved in other collaborations, as summarised in Table 6.

The consortium's research work has resulted in 53 publications (51 academic journal papers and 2 reports), representing important contributions to scientific knowledge. These outputs cover a range of topics, including:

- Understanding the properties of SARS-CoV-2 variants and mutations (n=19);
- Knowledge related to the introduction, transmission and prevalence of SARS-CoV-2 in the population (e.g. in UK regions, internationally or in specific settings such as care homes) (n=12);
- The immunobiology of SARS-CoV-2, including understanding immune escape, T-cell immunity, viral recombination, and transmission from humans to animals (n=6);
- The development of sequencing protocols and computational tools or infrastructure (n=6);
- Genomic surveillance (n=3);
- Research related to diagnostic testing (n=2);
- Research on the impact of travel restrictions or social distancing policies on SARS-CoV-2 transmission (n=2);
- Other topics, such as research on the mechanism of action of remdesivir (n=1), a

48

COG-UK reported £11.6 million received from the Department of Health and Social Care Testing Innovation Fund (funding start date: January 2021).

clinical trial protocol (n=1), and a description of the COG-UK consortium (n=1).

For a list of publications and reports, please see Annex 8.

COG-UK has also disseminated its work as part of at least 42 conferences, seminars or training events on SARS-CoV2 genomics.<sup>49</sup> For a list of events, please see Annex 9.

**Table 5. COG-UK Consortium Core Research Studies**

Study name	Brief Description
The COG-UK HOCI (Hospital-Onset COVID-19 Infections) study <sup>50</sup>	The COG-UK HOCI study investigates how integrating rapid, real-time COVID-19 genomic sequencing can impact decision making by infection control teams to prevent the spread of the SARS-CoV-2 virus in NHS hospitals.
The Oxford Vaccine trial <sup>51</sup>	The 'Investigating a vaccine against COVID-19' study aims to assess whether the ChAdOx1 nCoV-19 vaccine can protect healthy people from COVID-19, providing information on the vaccine's safety and ability to generate protective immune responses to SARS-CoV-2.
The Novavax Vaccine trial <sup>52</sup>	The Novavax trial is a blinded clinical trial of the NVX-CoV2373 vaccine.
The CiPS (COVID-19 in Prisons) Study <sup>53</sup>	The CiPS study tests staff and inmates at 28 prisons across England.
The Vivaldi study <sup>54</sup>	Led by UCL, the Vivaldi study is a collaboration with Four Seasons healthcare, a large care home chain, and the Department of Health and Social Care. The study aims to determine how many care-home staff and residents have been infected with COVID-19 and inform decisions around the best approach to COVID-19 testing in the future.
The GenOMICC (Genetics Of Mortality In Critical Care) study <sup>55</sup>	GenOMICC is an open, collaborative, global community of doctors and scientists working to understand and treat critical illness. Partners in the study have been recruiting patients since 2016 to study emerging infections (SARS/SARS-CoV-2/MERS/flu), sepsis, and other forms of critical illness. It is the largest study of its kind anywhere in the world. As part of this study, COG-UK also collaborates with ISARIC4C (the Coronavirus Clinical Characterisation Consortium).
The Real-time Assessment of Community Transmission (REACT) Study <sup>56</sup>	REACT is a series of studies using home testing to improve understanding of how the COVID-19 pandemic is progressing across England.

49 Self-reported data from COG-UK, representing a selection of events attended predominantly by the COG-UK core team. Note that since there was no requirement for all members to update central management about events they attended and contributed to, this is unlikely to be a comprehensive list.

50 COG-UK (2020d).

51 The Oxford Vaccine Trial (2022).

52 Novavax (2022).

53 UK government (2021b).

54 UCL (2021).

55 Leeds Teaching Hospitals NHS Trust (2021).

56 Imperial College London (2021).

Study name	Brief Description
The Office of National Statistics (ONS) COVID-19 Infection Survey (CIS) <sup>57</sup>	This study's overall purpose is to estimate how many people of different ages across the UK have already had COVID-19, even if they do not know they had it.
The SARS-CoV-2 Immunity & REinfection EvaluationN (SIREN) Study <sup>58</sup>	The SIREN study investigates the impact of detectable anti-SARS-CoV-2 antibodies on the incidence of COVID-19 in healthcare workers.

**Table 6. COG-UK Other Research Collaborations<sup>59</sup>**

Study name	Brief Description
The G2P (Genotype-2-Phenotype) consortium	Led by Imperial College London, G2P involves scientists from ten research organisations in the UK who study how changes in virus genes affect the virus's observable characteristics. COG-UK has worked with G2P to enable experimental validation of the biology of variants, particularly Alpha and Delta.
The UK-CIC (COVID-19 Immunology) consortium	Led by the University of Birmingham, UK-CIC brings together immunology centres of excellence to research how the immune system interacts with COVID-19 to develop better diagnostics, treatments and vaccines. COG-UK has worked with CIC in variant characterisation.
HDR-UK (Health Data Research United Kingdom)	The COG-UK consortium is a member of the HDR UK Research Alliance, working to unify the use of health data across the UK, support the UK's response to COVID-19 and make COG-UK datasets securely available for researchers to request access via the HDR Innovation Gateway.
The MHRA (Medicines & Healthcare products Regulatory Agency)	COG-UK has worked with the MHRA to provide information on mutations and variants.
BIVDA (The British In Vitro Diagnostic Association)	COG-UK have worked with BIVDA to provide advice on COVID-19 diagnostics.
GISAID (Global initiative on sharing all influenza data)	COG-UK have worked with GISAID to ensure timely and open international sharing of all COG-UK data.

<sup>57</sup> ONS (2021).

<sup>58</sup> NHA Health Research Authority (2020).

<sup>59</sup> Note: This table lists COG-UK collaborators by stakeholder type. Given the high number of individual stakeholders (with each stakeholder collaborating with numerous others both internal to and external to the consortium) it is not possible to document all individual collaboration relationships in detail. In most cases, the geographical spread is indicated by stakeholder name.

**The consortium has advanced methods used in public health genomics, producing software tools and sequencing and analysis protocols that may be applicable beyond the COVID-19 pandemic.**

COG-UK has made significant contributions to advancing knowledge on public health genomics research methods, including bioinformatic tools and protocols used for both sequencing and analysis [Int. 1, 8, 9]. Throughout the pandemic, the consortium implemented a programme of continuous improvement to enhance methodologies used in sequencing and data analysis in a way that maintains COG-UK's high-quality sequencing capability while making the process cheaper and more efficient [Int. 10]. Although this remains to be seen, the tools and methodological resources produced have the potential to be adapted to other pathogen genomics efforts in the future.

**COG-UK's contributions to data linkage in the public health system, including the development of UK-wide datasets linking SARS-CoV-2 and patient metadata, are a critical resource for advancing understanding of the virus and its behaviour and impacts.**

COG-UK has developed a single, UK-wide SARS-CoV2 dataset that is linked to patient metadata from PHAs, patient cohorts and electronic health records. This dataset has enabled a range of critical biological and public health questions to be addressed. For example, COG-UK's genomics data link to the Genetics of Mortality in Critical Care (GenOMICC) patient cohort, enabling COG-UK

to identify approximately 1,800 linked host and viral genomes.<sup>60</sup> COG-UK's genomic data also link to the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and the Office of National Statistics (ONS) patient cohorts.

**COG-UK is committed to open science and has made its outputs widely available in the public domain to facilitate knowledge transfer.**

All COG-UK outputs are freely available in the public domain, including its sequencing data, protocols<sup>61</sup> and analytic tools,<sup>62</sup> to allow worldwide access and use. In doing so, COG-UK aims to add transferable knowledge and value that will last beyond the current COVID-19 pandemic [Int. 8]. According to one interviewee:

*'It's very rare for people to just be like "I've done this work, here you go, use it. Use to further the knowledge and the understanding of this area"... Here, there's such a giveaway culture of true public good.'* [Int. 8]

Throughout the evaluation timeframe, all COG-UK data have been uploaded as rapidly as possible to the Global Initiative on Sharing Avian Influenza Data (GISAID) database and the European Nucleotide Archive (ENA). These data are readily available for international scientific communities to use in virology, immunology and bioinformatics research and the design and development of vaccines, therapeutics and diagnostics. As of 28 July 2021, 694,252 SARS-CoV-2 genomic sequences had passed quality checks and been made publicly available.<sup>63</sup>

60 Estimate provided by COG-UK self-reported data.

61 COG-UK (2021e).

62 COG-UK (2021f).

63 COG-UK (2022b).



## 4.2. Contributions to informing key policy and public health decisions in the UK's pandemic response

**COG-UK's sequencing data and analytics have been used to inform policies related to border control, travel, lockdown, and social distancing.**

COG-UK's sequencing data, research and work to link sequencing information with clinical metadata have informed ongoing policy decisions throughout the pandemic related to UK policy on border control, international travel and quarantine [Int. 4, 7, 10]. Research has also helped increase policymaker and public understanding of the disease-severity risk posed by new variants [Int. 1, 15]. As illustrated by an expert consulted for this work:

*'We [COG-UK] have been able to generate data that has had numerous effects on policy and intervention decisions. We generate the data on which variants are tracked, and we generate the data on which vaccine efficacy is really considered, and we've generated a raft of data that's informed many policy decisions.'* [Int. 10]

More specifically, COG-UK genomics data have been used to alert the UK government and policymakers to the presence of new variants in the country, including variants of concern (i.e. with greater transmissibility or severity of illness) and variants under investigation and circulating in the UK [Int. 3, 10]. Genomics data produced by the consortium, combined with in-depth patient metadata from PHAs or research efforts,

have helped understand the spread of new variants, their location within communities, and the association between variants and disease severity. For example, by linking genomic data to patient data, it was possible to analyse a spike protein mutation (D614G) and its association with disease severity and patient outcomes early in the pandemic.<sup>64</sup> These data types have been fundamental to informing the UK's policy response to the pandemic [Int. 1, 4, 8, 10], including outbreak management across the four PHAs in the UK (e.g. identifying outbreaks, understanding if an outbreak is due to single or multiple introductions of SARS-CoV-2 and identifying opportunities to interrupt transmission chains).

According to another interviewee who represents an external stakeholder:

*'We owe a huge debt to COG-UK and learned an immense amount about COVID and things that definitely informed public health decision making.'* [Int. reference withheld to preserve anonymity]

COG-UK's research has contributed to government decision making since early in the pandemic. For example, work by COG-UK members at the University of Oxford in England,<sup>65</sup> the University of Edinburgh, the University of Glasgow and St. Andrew's University in Scotland,<sup>66</sup> alongside work by Cardiff University in Wales using COG-UK genomic sequencing data,<sup>67</sup> helped enable an early understanding of the origins of SARS-CoV-2 introduction to the UK and helped to inform border-control policies [Int. 4, 10].<sup>68</sup> Another study by COG-UK members at the

64 COG-UK self-reported data.

65 Du Plessis et al. (2021).

66 Lycett et al. (2021).

67 Connor et al. (2020).

68 Lycett et al. (2021).

University of Cambridge generated evidence on the impact of travel restrictions into the UK during summer 2020.<sup>69,70</sup>

Specific to COG-UK's impact on social-distancing and mixing policies, the discovery of the B.1.1.7 variant (also known as the 'Alpha'

variant) informed a change in government policy. The discovery led to the introduction of more restrictive social mixing measures during Christmas 2020 and January 2021 [Int. 1, 9, 11, 12, 14], as elaborated in Box 4.

**Box 4. Outputs and impact in action: Discovery of B1.1.7 (alpha variant) and its impact on social mixing policy over Christmas 2020<sup>71</sup>**

The context: Until mid-December 2020, there were plans for the UK to relax its rules on social distancing to allow family and friends to come together and celebrate Christmas in 'bubbles' (i.e., groups of people from two to three households [depending on the nation] could mingle together indoors for up to five days). However, routine surveillance that same month identified rapidly rising SARS-CoV-2 cases in Kent and the surrounding Southeast England area. A new SARS-CoV-2 variant that was 50 per cent more transmissible than prior variants was identified as responsible for the surge in cases and became known as the 'alpha' variant (B.1.1.7). In response, the UK Government reduced the period permitting Christmas 'bubbles' to just Christmas Day throughout most of the UK. It also placed much of Southeast and Eastern England into a higher restriction tier: residents could only celebrate with their households and pre-existing support bubbles (i.e. households that people living alone could meet with indoors for social support). It is widely believed that these changes helped slow transmission and reduce the number of UK infections, hospitalisations and deaths. Other countries started closing their borders to the UK, which may have slowed transmission in these countries.

**COG-UK's contribution to government policy on social mixing over Christmas 2020:** COG-UK produced the sequencing evidence and analytics that informed the UK government's decision to change the Christmas 2020 social-distancing restrictions. This knowledge enabled UK policymakers to take decisive action that is believed to have saved lives. COG-UK sequencing partners and central and coordinating teams themselves cancelled Christmas plans and returned to laboratories to support demand for sequencing over Christmas 2020.

The type of sequencing conducted (i.e. decisions about which samples to sequence) and communication with key UK government agencies and international agencies such as the World Health Organisation (WHO) were important for timely action. COG-UK's leadership team had argued throughout the pandemic in favour of UK-wide sequencing of randomly selected samples, although some other stakeholders advocated concentrating resources on targeted sampling. Interviewees shared that COG-UK's decision to sequence samples from across the UK helped them identify and understand the alpha variant in a timely manner. COG-UK's communication links with WHO and others ensured the rapid dissemination of knowledge, allowing UK and international stakeholders to take prompt action. In addition, COG-UK researchers' interactions with UK PHAs facilitated analysis of the sequencing data in combination with the epidemiological information gathered by PHAs, which helped identify the B.1.1.7 as a key variant of concern.

69 Aggarwal et al (2021).

70 COG-UK (2021c).

71 Self-reported consortium data supported by interview insights [Int. 1,3,8].

According to one interviewed expert, COG-UK's work also enabled the rapid detection of the Delta variant introduced by people travelling from abroad in Spring 2021, which informed the UK's subsequent travel policies [Int. 9]. The expert also noted that it would have been difficult to distinguish the cause of viral spread without genetic sequencing information or determine whether it was due to a new and more transmissible SARS-CoV-2 variant rather than social behaviour. This understanding was vital in informing policy action [Int. 9]. Knowledge about this variant of concern likely contributed to a policy decision to delay the originally planned easing of restrictions by four weeks, from 21 June to 16 July 2021.

**COG-UK has demonstrated that pathogen-sequencing data and resources can significantly impact public health interventions in specific settings, including hospitals, long-term care facilities and universities.**

COG-UK has contributed data, analytics and tools to support SARS-CoV-2 research and outbreak investigations in diverse settings, including hospitals, long-term care facilities and universities. For an illustration of these activities, see Box 5.

### Box 5. Outputs and impact in action: COG-UK activities to support public health interventions in local settings<sup>72</sup>

#### Hospital setting:

- COG-UK's contributions to research on implementing real-time SARS-CoV-2 genomic sequencing in a hospital setting demonstrated an impact on infection-control interventions and patient-safety reporting for healthcare-associated COVID-19.<sup>73</sup> In the HOCl study, COG-UK is investigating the impact of integrating rapid, real-time COVID-19 genomic sequencing on infection-control team decision making to prevent the spread of SARS-CoV-2 in NHS hospitals.
- COG-UK's sequencing capacity and software tools have also been used to investigate and understand local outbreaks of COVID-19 in hospital settings. For example, very early on in the pandemic, COG-UK developed the CIVET tool (Cluster Investigation & Virus Epidemiology Tool), which became the key software tool used for a serious incident investigation in a Northern Ireland Hospital Trust [Int. 5]. COG-UK's capacity to conduct viral-genome sequencing helped identify the cause of the hospital's COVID-19 outbreak by providing information on the genetic makeup of the responsible variant.

#### Community-based healthcare setting:

- Rapid implementation of SARS-CoV-2 sequencing was used to investigate healthcare-associated COVID-19 cases and transmission between hospital and community-based healthcare settings, demonstrating the utility of real-time genomics surveillance to inform infection-control interventions.<sup>74</sup>
- A COG-UK review of the role of genomics in understanding COVID-19 outbreaks identified that staff and residents in long-term care facilities were usually infected with identical SARS-CoV-2 genomes and outbreaks were primarily due to a single or few introductions rather than a series of seeding events from the community.<sup>75</sup>

#### University setting:

- With funding from COG-UK, researchers from the University of Cambridge assessed transmission of SARS-CoV-2 amongst students and staff to understand drivers and patterns of viral transmission. This research helped inform local infection-control measures and understand their impact as well as the impact of national lockdown policies.<sup>76</sup> Findings from the COG-UK research and analyses were used to inform advice on disease-control measures in Higher and Further Education settings.<sup>77</sup>

The consortium supported sequencing needs across the four nations using tools such as sequencing-coverage reports to help prioritise samples for sequencing. However, progress was occasionally impeded due to factors outside COG-UK's direct control.

Despite widespread recognition of COG-UK's contribution to public health and policy-level decision making [Int. 1, 3, 4, 7, 9, 10, 11, 12, 14 and 15], one interviewee suggested that more could have potentially been achieved to help prevent the severity of outbreaks in

72 COG-UK self-reported data.

73 Meredith et al. (2020).

74 Meredith et al. (2020).

75 Aggarwal et al. (2020).

76 Aggarwal et al. (2021c).

77 Aggarwal et al. (2021b).

some of the devolved nations<sup>78</sup>. While the context within which COG-UK was operating was rapidly changing and the scale of demand for sequencing activity high [Int 10], one interviewee felt that PHE had a bigger influence on which samples were sequenced than PHAs in some of the devolved nations. The interviewee thought this led to a period where some of their samples ended up further back in the queue, leading to a delay in timely identification of a new variant of concern in a devolved nation<sup>79</sup>.

According to the self-reported data, COG-UK's sampling strategy was initially impacted by other factors as well. Such factors included lack of access to metadata by PHAs, which made sample identification and targeting sequencing more difficult in the early stages of the consortium's work. This was due to the time it took to implement the data-sharing agreements that needed to be in place to allow access to sample-related metadata. COG-UK's Health Informatics Working Group supported improvements in data linkage as the consortium matured. However, a diversity of sample sequencing relative to numbers of COVID-19 positive cases persisted over time between some devolved nations, pointing to an opportunity to further bolster PHAs and sequencing capacity within the devolved nations in the future (see Annex 7, Table A7-2).

COG-UK developed a strategic operational plan, including the production of weekly sequencing-coverage<sup>80</sup> reports to facilitate coverage monitoring and identify low-coverage areas

requiring attention and action.<sup>81</sup> The consortium reported that the average UK coverage was 24 per cent between April 2020 and July 2021, ranging from a minimum coverage of 3 per cent in December 2020 to a maximum coverage of 68 per cent in May 2021.<sup>82</sup>

According to self-reported data, the consortium's sampling strategy was responsive to changing PHA priorities as demand for genomic sequencing and the need for information about SARS-CoV-2 variants changed across the UK. For example, significant time, resources and sequencing capacity was used to identify the location of retrospective outbreak samples, retrieve samples from storage, and sequence them in the summer of 2020. Similarly, the sequencing of samples from hospitals and long-term care facilities were prioritised in the pandemic's early stages, while the sequencing of imported cases and supporting surveillance studies – including the ONS COVID Infection Survey and Real-time Assessment of Community Transmission (REACT) – were prioritised later in 2020. Accordingly, resources were reallocated to these efforts and shifted away from other activities (e.g. research).

**From the outset, COG-UK has worked closely with public health decision makers to maximise the value and impact of the consortium's work.**

COG-UK participants actively work with public health and policy decision makers via participation on various committees and working groups, contributions to briefs

78 Interviewee reference withheld to preserve anonymity.

79 Interviewee reference withheld to preserve anonymity.

80 'Coverage' is defined as the percentage of positive PCR samples sequenced and reflects virus prevalence and network sequencing output, with coverage rising when prevalence rates are low.

81 See coverage reports here: <https://www.cogconsortium.uk/news-reports/coverage-reports/>

82 COG-UK aimed to achieve at least 10 per cent coverage. Full coverage was not possible due to a proportion of samples containing insufficient virus (CT value above 30), contamination or missing metadata.

and reports produced by policy and public-health decision makers, widescale sharing of COG-UK's insights through direct reporting to policymakers, and provision of informal

feedback. Box 6 provides a snapshot of the diverse ways the consortium has engaged with and disseminated learnings to key decision makers as a route to impact.

**Box 6. Outputs and impact in actions: Diverse ways COG-UK engages with and disseminates learning to key decision makers in the UK<sup>83</sup>**

**Participation in committees and working groups:**

- COG-UK's members sit on diverse DHSC and PHE groups to provide expert advice and information to help inform decisions related to the pandemic response. COG-UK also works together with PHE and NHS Track & Trace. As part of the PHE Variants Technical Group Meeting, COG-UK provides scientific and operational input on variants of concern and interest.
- The consortium also has representatives on several Scientific Advisory Group for Emergencies (SAGE) sub-groups, including the PHE serology working group, the Social Care working group, the Ethnicity subgroup, the Hospital Onset COVID-19 working group, and the New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG). COG-UK members have also been involved in and contributed data to several reports from NERVTAG, including a joint COG-UK-NERVTAG summary statement on the evidence for genetic change in SARS-CoV2 and effects on phenotype.<sup>84</sup>

**Contributions to report and briefings:**

- COG-UK members contributed data to a series of PHE technical briefings on SARS-CoV2 variants of concern and variants under investigation.<sup>85</sup> Consortium members advised the UK government on the standards included in the legislation for commercial sequencing and data flows as part of the test-to-release programme.
- The consortium's insights have input into 36 external reports produced between 1 March 2020 and 31 July 2021 by SAGE, the Children's Task and Finish Group (TFC), NERVTAG, and PHE (for a full list of reports, see Annex 10: 'List of reports').

**Direct reports to policymakers:**

- During the evaluation timeframe, COG-UK submitted 18 formal reports to SAGE on the consortium's progress and preliminary-and-updated analyses of data at local, regional and national levels.<sup>86</sup> These reports have provided early insights on outbreaks in specific settings (e.g. hospitals, care homes and universities), on patterns of introduction and transmission of SARS-CoV-2 variants in the UK, and patterns of the evolution of SARS-CoV-2 mutations.

**Informal feedback:**

- Either as individuals or groups, COG-UK members have provided informal feedback to requests from SAGE, GO-Science and the Chief Scientific Advisor/Chief Medical Officers on numerous occasions. They fed back on topics including reinfection, genomics to estimate outbreak size, SARS-CoV-2 infections in mink, and transmission in prisons.

83 COG-UK self-reported data.

84 Scientific Advisory Group for Emergencies (2020).

85 Public Health England (2021).

86 COG-UK (2020b).



According to self-reported data, COG-UK members have also provided advice and expertise, collaborating with researchers in 28 countries (including 17 low-and-middle-income countries<sup>87</sup>) to support sequencing efforts.

**The consortium is also taking steps to ensure that sequencing data are sustainably interconnected to facilitate their use in research and to inform public health and policy decision-making.**

COG-UK and HDR-UK have worked in partnership to further ensure that linked COG-UK genomics data and associated linked patient and other data (e.g. genomics) are made even more accessible to UK researchers to generate new research.<sup>88</sup> Many insights from such research are likely to also be relevant for informing public health decision-making.

### **4.3. Contributions to testing vaccine efficacy against specific variants of SARS-CoV-2 and better understanding therapeutics to treat COVID-19**

**COG-UK data and insights have been made freely available to the global research-and-innovation community to use in efforts to understand vaccine effectiveness and to inform the development of next-generation vaccines.**

COG-UK's sequencing data have been important as part of the vaccine response, particularly in terms of efforts to understand and evaluate how well vaccines work against specific variants [Int. 2, 5, 10]. As mentioned

earlier, COG-UK has made nearly 700,000 SARS-CoV-2 genomic sequences publicly available<sup>89</sup> and, based on the consortium's self-reported data, these sequences are regularly mined by vaccine developers. The consortium's policy of openness and widescale data-sharing from the outset has helped enable groups developing and evaluating COVID-19 vaccines to understand vaccine effectiveness [Int. 7, 10, 11, 14]. There was a time during the pandemic when COG UK's SAR-CoV-2 genomes constituted 50 per cent of the total SARS-CoV-2 genome sequences on the international GISAID sequencing database. According to COG-UK's Executive Director, COG-UK's SARS-CoV-2 genomes made up a quarter of the genomes on GISAID as of November 2021 as other countries over time also enhanced contributions to the database.<sup>90</sup>

As highlighted by one expert:

*'Sequencing has become the key partner to vaccine development and keeping vaccines working.'* [Int. 10]

Using COG-UK's sequencing data, vaccine developers recognised the beta variant first identified in South Africa as a variant against which they should (and did) develop a vaccine [Int. 10]. If a vaccine does not fully prevent infection, sequencing data can also help show which variant can evade the immune system and the characteristics enabling it to do so. Thus, ongoing and future sequencing can inform future efforts to re-engineer or improve vaccines. According to a stakeholder consulted as part of this evaluation, it would have been challenging without such sequencing data for vaccine developers to predict where the next

87 Bangladesh, Cameroon, Gambia, Ghana, India, Kenya, Malawi, Malaysia, Mauritius, Pakistan. Philippines, Saudi Arabia, South Africa, Sri Lanka, Togo, Uganda and Zimbabwe.

88 COG-UK self-reported data.

89 COG-UK self-reported data. From Majora, COG-UK Public Dashboard.

90 Peacock (2021).

round of SARS-CoV-2 vaccine development should be directed [Int. 10].

*'If you had no sequence data, it would be quite difficult to know what you'd need to direct your next round of vaccines to... Whereas now we know that, for example, the variant first detected in South Africa – the Beta variant – is one that vaccine developers have developed a new vaccine for already.'* [Int. 10]

COG-UK has also been working closely with the Genotype-2-Phenotype consortium to support the virological investigation of variants of interest and concern with implications for vaccine development and has collaborated with the Oxford Vaccine Group and Novavax NVX-CoV2372, providing sequencing data to their vaccine clinical trials.<sup>91</sup> In addition, they have engaged with Pfizer on vaccine development.<sup>92</sup>

The consortium has also provided (and continues to provide) input into several of the UK groups working on various aspects of ongoing vaccines development, evaluation, and/or regulation, informing the next generation of vaccines to help improve vaccine efficacy. Examples include the Medicines and Healthcare products Regulatory Agency (MHRA), the British *In Vitro* Diagnostic Association (BIVDA), and the Department of Health and Social Care (DHSC) Vaccine Update Expert Advisory Group (VUEAG)[Int. 10].

**COG-UK data have also been used to understand SARS-CoV-2 susceptibility to treatments for COVID-19, with the potential to inform the development**

**of novel therapeutics that target viral molecules.**

COG-UK data and methodology have also been used to study SARS-CoV-2 susceptibility to COVID-19 therapeutics. For example, in a case study of an immunocompromised individual treated with convalescent plasma therapy, researchers observed a series of viral mutations that altered susceptibility to neutralisation via antibodies within the convalescent plasma.<sup>93</sup> SARS-CoV-2 genomics data have the potential to play a role in the development of other COVID-19 therapeutics where the drug target is a virus molecule (e.g. inhibitors of SARS-CoV-2 RNA-dependent RNA polymerase, such as Remdesivir). Such work can be facilitated by the COG-UK Mutation Explorer.<sup>94</sup>

#### **4.4. Contributions to how policymakers in the UK view and value pathogen genomics**

**COG-UK has significantly impacted how policymakers in the UK view and value pathogen genomics by raising awareness about its importance for public health and increasing demand for its use in decision making.**

COG-UK's efforts have helped raise awareness about the value of pathogen genomics and demonstrated the power and importance of pathogen genome sequencing and research in managing infectious disease pandemics and informing public health decisions [Int. 1, 4, 7, 9,11,14]. As one interviewee emphasised:

91 COG-UK self-reported data.

92 Professor Sharon Peacock, Executive Director of COG-UK, has served as an ad hoc member of Pfizer's mRNA Scientific Advisory Panel, Infectious Disease Vaccines Subcommittee and Pfizer's Coronavirus External Advisory Board.

93 Kemp et al. (2021).

94 COG-UK (2022a).

***‘As bad as COVID-19 has been, it did give an exemplar for what these technologies and informatics can actually do and provide to decision makers.’ [Int. 20]***

Before the pandemic, sequencing was used primarily in reference labs in the UK to detect and manage small outbreaks of, for example, foodborne pathogens such as *Escherichia coli* [Int. 10]. With the COVID-19 pandemic, SARS-CoV-2 sequencing became central to public health policy in the UK; there is now widespread demand for sequencing from the micro-level (such as within individual hospitals) to the national government level [Int. 9]. How much this will apply to other viruses in the future – or indeed to other public health challenges, such as antimicrobial resistance – remains to be seen. However, the COVID-19 experience is likely to increase demand for pathogen genomics in the future across diverse infectious diseases [Int. 1, 4, 10].

Mutation identification and analysis can help identify many different types of viral outbreaks. However, in the early stages of the pandemic, the mutation rate of COVID-19 was thought to be relatively low. It took time and the emergence of more transmissible strains and their identification and characterisation using data generated by COG-UK and others for public health decision makers and policymakers to become aware of the value of sequencing [Int. 1]. COG-UK also showed that pathogen genomics could be used to estimate the prevalence and spread of the virus in the population. Furthermore, the data they produced has closely reflected the public health epidemiological data from NHS Test and Trace [Int. 7]. As one interviewee flagged:

***‘We now have an exemplar that is a real kind of door opener, if you like, to have conversations around...other diseases and the role of population-level genomic surveillance and its importance.’ [Int. 20]***

According to some COG-UK members, there has been a profound change in the perception of genomics data’s role in public health overall [Int. 1, 4, 7, 10, 11, 14]. A greater appetite has emerged for setting up a genomics sequencing initiative for other pathogens and integrating greater public health genomic-sequencing capacity into the PHAs. According to one interviewee, PHAs across the country are now more enthusiastic about pathogen-genome sequencing and see it as the tool to explore future outbreaks; they are more eager to ensure that capacity and expertise developed through the experience of responding to the COVID-19 pandemic are retained [Int. 2].

#### **4.5. Contributions to improved capacity for pathogen genomics in the UK**

**COG-UK has significantly contributed to enhancing the skills, workforce, infrastructure, networks and relationships needed to support pathogen-genomic sequencing in the UK. If sustained, this capacity could significantly bolster the UK’s ability to use pathogen genomics in other disease areas in the future.**

COG-UK’s ability to rapidly bring together and focus pre-existing sequencing-and-research capacity and collaboration and build on it by including new collaborators who were not previously linked was widely recognised as one of the consortium’s key achievements [Int. 1, 3-12]. As two experts highlighted:

***‘[COG-UK] changed the paradigm for how people work together. It brought together academics with public health agencies, together with people in the NHS and testing labs. That hasn’t really been done before.’ [Int. 10]***

***‘People who in some sense are friendly but maybe competitive all realised we***

***must be everyone in the same boat rowing in the same direction.’ [Int. 12]***

The consortium connected many of the key individuals and institutions involved with genomics across the UK [Int. 2, 8, 11]. At its inception, COG-UK was composed of 17 unique sequencing sites with a total of 134 genomic sequencing machines.<sup>95</sup> COG-UK was initially set up to conduct public health virology and epidemiology research. However, given the public health system’s demand for sequencing support, the consortium spent the first 18 months of the COVID-19 pandemic delivering a sequencing function as a public health service. Some interviewees reflected on how people have worked together at speed and under considerable pressure, putting aside individual egos and professional protectionism to pursue the common mission of using pathogen-genomic sequencing and research to help respond to the pandemic [Int. 7, 8]. Some experts suggest that compared to universities’ relative agility, conventional structures available through PHAs would have faced greater challenges establishing the same research and development provision as quickly [Int. 5]. However, the transition of sequencing capacity to PHAs began in Spring 2021 and should help enhance sequencing capacity within PHAs for the future, as discussed in [Section 5](#) of this report. As illustrated in one interviewee’s comment:

***‘Within a very, very short period of time in response to what is certainly – in my lifetime the most significant public health crisis that the world has had to deal with, COG-UK has managed to pull together an incredibly well-connected network***

***of experts from academia, from the NHS, from public health authorities, and brought it all together in a well-connected network that has had just a massive impact on our understanding of the disease.’ [Int. 3]***

According to some experts, bringing together such diverse pathogen-genomic expertise was a novel undertaking. Therefore, the model of academics working and attending meetings in collaboration with PHAs was seen as particularly novel [Int. 6, 10, 11]. Providing it is sustained, this type of interaction may enable a new paradigm for the future of UK public health based on collaboration across professions [Int. 10].

COG-UK’s activities have also contributed to a step-change in pathogen genomics capacity across the four UK nations [Int. 1, 2, 5, 7]. Although there is further capacity-building and capacity-sustaining work ahead, several interviewees emphasised highly collaborative ways of working and knowledge-and-data sharing from early in the pandemic across the four nations within COG-UK [Int. 2, 5, 10, 11]. According to one interviewee, one of the devolved nations<sup>96</sup> would not have been able to participate in public health genomics during the pandemic without the networks COG-UK created; indeed, the interviewee believes this will outlive COG-UK<sup>97</sup>. Although funding is always a challenge, two experts noted that COG-UK helped leverage funding for the devolved nations to develop their own public health genomics systems [Int. 2, 16].

COG-UK also developed operational, governance and management arrangements to support a highly networked and

95 Figure provided by COG-UK in self-reported data; note that the count does not include numerous liquid-handling robots.

96 Name withheld to preserve confidentiality.

97 Interviewee reference withheld to preserve anonymity.

multi-stakeholder approach to public health genomics research, analysis and sequencing support for the public health system [Int. 1]. For example, the legal frameworks, standard operating protocols and financial-management protocols helped implement the networked model. They could be helpful tools for future networked public health genomics efforts that bring together diverse organisations across different UK regions [Int. 10].

By and large, COG-UK participants from the devolved administrations have been vocal in their support for continuing a four-nation public health genomics approach in the future. They note the synergistic value of a collective approach to building sequencing capacity, securing funding and sharing expertise [Int. 6]. However, although rare, there have been some divergent views on the effectiveness of relationships between different actors involved with COG-UK [three interviewees commented on this]<sup>98</sup>, particularly regarding

the relative power and influence of PHE versus some of the devolved nations' PHAs [one interviewee commented on this <sup>99</sup>]. COG-UK also experienced divergent views on whether more sequencing should have been undertaken locally (so that the devolved nations could control their own data) or centrally at the Wellcome Sanger Institute [Int 9, 14]. These and other associated challenges are explored further in [Section 5.1.3](#) on collaborative relationships.

Box 7 provides an overview of different types of capacity contributions. These include building a skilled workforce, physical infrastructure (e.g. equipment and facilities), data infrastructure (e.g. cloud computing), leadership, management-and-governance arrangements, and strengthening networks and relationships within and between academics, the NHS and public health decision makers and policymakers.

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98 Interview references withheld to preserve anonymity.

99 Interviewee reference withheld to preserve anonymity. Includes interviewees from different stakeholder groups.

### Box 7. Outputs and impacts in action: COG-UK capacity-building contributions<sup>100</sup>

**Workforce and skills:** Existing staff at academic and research-partner organisations were re-trained as needed to support sequencing efforts, and consortium funding was used to hire new staff. COG-UK newly trained numerous postgraduate staff in handling, preparing and analysing genetic material and interpreting and reporting genomic sequencing data such as CIVET (Cluster Investigation & Virus Epidemiology Tool). Staff receiving such training represent various roles, including clinicians, biomedical scientists, nurses, health-protection teams, infection control teams, diagnostic laboratory scientists/technicians and local PHA teams. More than 160 sequencing staff/volunteers and more than 650 clinicians benefited from training.<sup>101</sup> This newly trained workforce is a crucial asset of COG-UK and will be an important part of its legacy, continuing to support pathogen genomics in the future. In addition, COG-UK members share their work at COG-UK's internal seminars, which began in September 2020. A total of 12 meetings were held during the evaluation period, with three presenters at each meeting drawn from across the consortium. A question-and-answer session followed presentations, enabling discussion and knowledge exchange. On average, 40 people attended each seminar.

**Physical infrastructure (equipment, facilities):** There are a total of 17 sequencing sites and 134 sequencing machines across the COG-UK consortium. COG-UK's sequencing capabilities increased over time as consortium partners expanded capacity and shifted resources from research to service delivery to meet changing demand for sequencing through different stages of the pandemic. COG-UK has supported the expansion of existing infrastructure by purchasing equipment for the network with COG-UK funding. This equipment is now in place in sequencing labs across the UK, providing increased capacity for SARS-CoV-2 genomic sequencing.

**Leadership, management and governance arrangements:** The consortium established a governance structure representing diverse geographies and stakeholders involved in the public health landscape and contractual arrangements, operational protocols and legal frameworks to support a four-nation, multi-stakeholder approach. The ability to sustain conducive governance and management support for future networked public health efforts and align them with pre-existing institutional level practices will determine the ability to mobilise relationships, the activities needed to integrate public health genomics research in other clinical areas and the response to future threats.

**Data infrastructure:** Building upon the existing UK Cloud Infrastructure for Microbial Bioinformatics (CLIMB), COG-UK has used its funds to rapidly develop additional computational equipment (CLIMB-COVID). CLIMB received a £1.2 million funding boost from UK Research and Innovation (UKRI) in January 2021, which helped support and expand computing capabilities (e.g. computing power, storage and analysis tools). These resources are available to microbiologists in UK academic settings for bioinformatics analysis of genomic datasets derived from next-generation sequencing technologies. According to self-reported data from COG-UK, CLIMB is expected to become integral to DHSC activities, providing longer-term foundations for pathogen genomics.

**Strengthened relationships between academics, NHS, PHAs, and policymakers:** COG-UK is a consortium of 16 academic research partners, the Wellcome Sanger Institute and four PHAs (representing each of the devolved nations), other sequencing collaborators including Lighthouse Labs, and numerous NHS foundations and trusts. This consortium has fostered unprecedented collaboration across different types of stakeholders involved in public health in the interest of advancing science and informing policy. The consortium works with the GenOMICC team to link the virus to host genomes. It has also funded the Hospital Onset COVID Infection (HOCI) trial, which feeds genomic results back to NHS sites in real-time, and brought all four devolved nations together to share data. As elaborated on in Box 4, the consortium also invested heavily in strengthening relationships with policymakers (e.g. PHAs, DHSC and SAGE).

<sup>100</sup> COG-UK self-reported data.

<sup>101</sup> COG-UK self-reported data.



COG-UK has also helped improve the efficiency of genomic sequencing by reducing costs and turnaround times for sequence reporting.

Enhancements in the genomic-sequencing workforce, physical-and-data infrastructure and networks/relationships have helped scale genomic-sequencing capacity (as mentioned in [Section 4.2](#)) and efficiency. Between April 2020 and July 2021, the cost and turnaround time for sequencing and reporting decreased. Measuring the average time from sample collection to sequencing data upload across consortium sites,<sup>102</sup> the turnaround time decreased by 70 per cent (from 20 days in April 2020 to 6 days in June 2021). Measuring the average time from sample receipt at the sequencing site to sequencing-data upload across consortium sites,<sup>103</sup> the turnaround time decreased by 50 per cent (from approximately 5 days in January 2021 to 2.5 days in June 2021).<sup>104</sup> Regarding costs, COG-UK reported that their efforts researching and developing sequencing protocols and pipelines reduced the average cost of whole genomic sequencing by approximately 30 per cent between April 2020 and July 2021 (from £56 to £40 blended per sample).<sup>105</sup>

## 4.6. Impact on the international pandemic response effort

COG-UK data, methods and protocols are readily available for the international community to use for research and pandemic preparedness efforts.

Given that COG-UK research and analyses are made publicly available worldwide, anyone wishing to use COG-UK data to inform the global pandemic response can do so [Int. 3, 5, 6, 20]. All COG-UK data are uploaded to GISAID and the ENA and available for international scientific communities to use in fundamental virology, immunology and bioinformatics research, and in the design and development of vaccines, therapeutics and diagnostics. For example, in Spring 2021, early data on the Delta variant was provided at speed, guiding not only the UK government's response but enabling the international community's research and preparedness.<sup>106</sup>

Detailed information on sequencing protocols and methods available to the global community can be found on the COG-UK website,<sup>107</sup> with multiple formats available for compatibility with different resource set-ups. The website also contains a rich resource of freely available analytic tools developed by consortium members.<sup>108</sup> The ARTIC network, the majority of whose members are part of the COG-UK consortium, provided the foundational methodology for most global SARS-CoV-2

102 Turnaround time estimations are based on the following UK centres: Birmingham, Cambridge, Exeter, Glasgow, Liverpool, London, Northumbria, Norwich, Nottingham, Oxford, PHE Colindale, Portsmouth, Sheffield.

103 As above.

104 The time from sample receipt to sequencing-data upload was not measured before January 2021.

105 COG-UK self-reported data. Sequencing costs per sample were not uniform across all labs due to differences in infrastructure, technology, equipment, methods and economies of scale. This figure is the cost of sequencing alone and does not include labour or any overheads.

106 Source: COG-UK self-reported data.

107 COG-UK (2021e).

108 COG-UK (2021f).

sequencing. According to self-reported data, COG-UK members adapted ARTIC methods for SARS-CoV-2 sequencing, publishing different versions suitable for a range of set-ups,<sup>109</sup> including a low-cost environment with reduced amounts of reagents. They also reported global use of the analysis tools<sup>110</sup> and websites developed by COG-UK.

The consortium was for a long time a primary contributor of SARS-CoV-2 genome sequences to GISAID [Int. 15, 11], alongside contributions from other international efforts, e.g. in Canada, Denmark, South Africa, Brazil and localised initiatives in the USA, as some examples [Int. 15]. According to some interviewees, COG-UK sequencing data and software tools are used in various countries, with national SARS-CoV-2 genome-sequencing efforts drawing on COG-UK-developed analysis pipelines and software tools [Int. 5, 6]. COG-UK is also assisting vaccine-development efforts, the results of which have implications of global relevance [Int. 6].

In addition, the PANGO lineage nomenclature<sup>111</sup> developed by COG-UK members has become the standard naming criteria for SARS-CoV-2 viral lineages worldwide.<sup>112</sup> Having a standard nomenclature enables researchers worldwide to better understand the patterns and determinants driving the local, regional and global spread of SARS-CoV2 and to track new variants as they emerge.

### **COG-UK has shown global leadership in SARS-CoV-2 genomics and advised other nations on their sequencing processes and data-sharing policies.**

COG-UK has led the way in advancing SARS-CoV-2 genomics regarding the speed and agility of response and scale of operations. According to self-reported data from the consortium, several other countries have emulated COG-UK's working model and requested advice at both the national and institute levels. For example, COG-UK has advised the Canadian Genomics Network (CanCOGeN) on setting up their national sequencing network,<sup>113</sup> helped the French National Centre for Scientific Research (CNRS) with data-sharing and publication management policies, and responded to detailed sequencing questions from the Israeli Ministry of Health.<sup>114</sup> An interviewed member of the COG-UK leadership team also mentioned this point, highlighting that several countries did not have a pathogen-genomics capacity before the COVID-19 pandemic (or at least not as sophisticated as they do now). However, such countries have since learnt from COG-UK's example and developed and/or strengthened their own. Examples include the USA, Canada and France [Int. 1].

109 COG-UK (2021e).

110 COG-UK (2021f).

111 Cov-Lineages.org (2022).

112 COG-UK self-reported data.

113 COG-UK (2020e).

114 COG-UK self-reported data.

However, despite signs of impact on international efforts, further research would be needed to understand how international users of COG-UK data have acted on COG-UK's insights in their own national efforts, what has worked well and where country-specific circumstances required adaptations to the COG-UK approach or needed different approaches.

**Consortium members actively engaged with the international community in diverse ways to advance knowledge about SARS-CoV-2 and help build capacity and skills for SARS-CoV-2 sequencing in other nations, particularly in low-and-middle-income countries.**

In addition to making their data and methods globally available, COG-UK has engaged in diverse ways with the international community to advance scientific knowledge about SARS-CoV-2 and support efforts to build capacity and skills for SARS-CoV-2 genomic sequencing in other nations, especially low-and-middle-income countries. These engagement activities include providing advice and collaborating with international researchers to support sequencing activities and associated research, disseminating learning gained, facilitating training, participating in meetings and working groups and providing informal advice. See Box 8 for illustrations of COG-UK's engagement with the international community.

### **Box 8. Outputs and impact in action: Examples of the diverse ways COG-UK engages with the international community.**

#### **Sharing of resources and participation in sequencing and research collaborations:**

- Anyone wishing to use COG-UK data to inform the global pandemic response can do so. All COG-UK data are uploaded to GISAID, and the ENA databases and academic publications are made freely available on the COG-UK website. Methodological protocols and sequencing-and-analysis tools are also freely available on the COG-UK website.
- COG-UK members have provided advice and expertise and have been collaborating with researchers in 28 countries (including 17 low-and-middle-income countries) to support sequencing efforts.<sup>115</sup>

#### **Dissemination of learning:**

- COG-UK has made more than six hours of video presentations freely available online,<sup>116</sup> featuring consortium-wide speakers from all four nations in the UK. Presentations cover various topics, including discussions of sequencing-and-analysis techniques, variant introduction, tracking and analysis, and genomic-informed research from hospitals, care homes and university settings. Live participation included attendees from over 50 countries, and recordings have had over 60,000 views.<sup>117</sup>

#### **Facilitation of training:**

- In June 2021, the University of Cambridge and Wellcome Connecting Science each received just under £0.5 million for a joint project,<sup>118</sup> 'Leveraging COG-UK expertise to support the global dissemination of SARS-CoV2 genomic sequencing'. This endeavour, known as COG-Train, is intended to support the development of a global learning community centred around online training resources in SARS-CoV-2 sequencing and analysis and share lessons learnt from the rapid establishment of a national sequencing network. This project will help support capacity-building so that other nations, particularly in low-and-middle-income countries, can benefit from COG-UK's scientific, public health, operational and policy experience.

#### **Participation in international workshops and meetings:**

- Consortium members have participated in WHO working groups (e.g. providing advice on naming conventions of SARS-CoV-2 variants) and the Global Early Warning System Action Collaborative Advisory Council, an initiative of the Milken Institute and a collaboration between the Rockefeller Institute and FasterCures.<sup>119</sup> In June 2021, COG-UK members also contributed to several Rockefeller Institute workshops on standards architecture for genomic surveillance.<sup>120</sup> Consortium members also participated in international collaborative meetings to exchange knowledge and ideas, e.g. a Nordic-Baltic roundtable on genome sequencing held on 8 March 2021.<sup>121</sup>

#### **Provision of informal advice:**

- COG-UK has worked closely with the UK's Foreign Commonwealth and Development Office, responding to requests for input and advice, including the provision of a factsheet on COGUK sequencing efforts (dated October 2020).<sup>122</sup>
- During the surge in cases in India caused by the Delta variant, COG-UK members provided advice to India's scientific advisory group for emergencies on SARS-CoV-2 genomic sequencing.<sup>123</sup>

115 COG-UK self-reported data.

116 COG-UK (2020).

117 COG-UK self-reported data.

118 COG-UK self-reported data.

119 COG-UK self-reported data.

120 COG-UK self-reported data.

121 COG-UK self-reported data.

122 COG-UK (2020f).

123 COG-UK self-reported data.

**COG-UK has actively shared its research, data and expertise internationally but the extent to which the COG-UK approach can be replicated in other countries remains to be seen. There may also be scope for COG-UK to incorporate learning and evidence from other contexts and sequencing initiatives into its strategies for the future.**

While COG-UK efforts to engage with international initiatives are notable, COG-UK's sequencing activity and research have predominantly been UK-focused over the evaluation timeframe. According to one interviewee, some other centres engaging with COVID-19 sequencing have sequenced samples from multiple countries [Int. 15]. The importance of public health systems (as opposed to COG-UK, strictly speaking) contributing to international efforts in this way merits attention in the future. The global push for genomics initiatives in public health, coupled with significant variation in individual countries' available resources, risks global imbalance. COG-UK has shown what is possible with sustainable funding, but many countries' public health systems do not benefit from the same financial resources. According to two experts, there is a risk in encouraging the global implementation of a very expensive tool in parts of the world where the simplest diagnostics are not even available.<sup>124</sup>

In this context, it will be important to consider how PHAs can deploy the legacy and learning from COG-UK in a way that contributes to global capacity. As noted by one expert commenting on the COG-UK model:

***'It doesn't mean it's the only model, it doesn't mean that it will work in other places, but it at least is a model of something that worked.'*** [Int. 19]

It will also be important to balance investments in sequencing with investments in other public health capacity-building priorities. While the gradual incorporation of genomics into public health and clinical practice is likely to be the appropriate path for most settings, the push to deliver more sequencing following COVID-19 has led to some capabilities being outsourced to commercial entities. If continued, this development could risk weakening the public health systems that most need strengthening [Int. 15].

According to COG-UK's self-reported data, much of what has been learnt through COG-UK's experience may be directly applicable to future pandemics or public health threats in the UK and potentially globally. Examples include the need to use genomics early on for rapid response; the importance of early access to methodological and analysis tools for genome sequencing and to linked datasets; the importance of highly effective logistics, operations, and communication; the value of distributed models of delivery to leverage complementary skills and resources and capacity; and the need to be agile and adapt to ongoing changes in the health system.

Furthermore, the self-reported data mentioned that COG-UK has in some ways provided a blueprint for rapid action in an emergency public health situation, engaging in what was described as 'bold and rapid' action in March 2020 by accepting imperfections and prioritising the speed of response. They were guided by several overarching principles: four-nations working, global data sharing and open access to methods and tools. They demonstrated the importance of a distributed network to provide sequencing to more than 100 NHS labs.<sup>125</sup> Lastly, the inclusion of the four national PHAs allowed for the sharing of genomics data across the UK for the first time.

124 Interviewee references withheld to preserve anonymity.

125 COG-UK self-reported data.

However, COG-UK's global impact has been somewhat limited by its heavily UK-centric design and funding during the period this evaluation covers. The UK's dominance in this space meant that researchers and decision makers learnt disproportionately more about what was going on in the UK, some (but not all) of which is likely to be transferable and

adaptable knowledge to other contexts [Int. 19]. The consortium's primary focus on UK-based data means that there may be limits to its internationally applicable insights. Further research is warranted to understand what may be adaptable to other contexts (and what is less adaptable) and what the UK could learn from international experiences.





## CHAPTER 5

# **Influences on COG-UK's activities**

The COG-UK consortium evolved in a rapidly changing landscape of virus evolution and in the context of evolving policies and relationships. Within this changing environment, the consortium is also a complex intervention bringing together diverse stakeholders across the four UK nations. As such, it offers fertile ground for learning about how pathogen-genomics networks function and evolve in times of pandemic shocks to public health systems and what influences the evolution and impact of responses.

The contents below elaborate on the diverse factors that influenced the consortium's efforts over time. Key influences are summarised in Table 7, Table 8 and Table 9 below and explored in subsequent sections. At the highest level, these influences relate to securing the motivation, means and agility needed to deliver on consortium activities, and more specifically:

- **The ability to mobilise and sustain individual and institutional commitment to consortium activities, including a commitment to rapid delivery and**

**responsiveness to increasing demand for sequencing activities.** In large part, this depended on:

- Individual and institutional goodwill-rooted in altruism and scientific intrigue, including a desire to use science to help with the pandemic response;
  - Leadership, governance and management support; and
  - Nurturing productive relationships and interactions between diverse COG-UK members.
- **The resource environment, including:**
    - Financial resources
    - Physical and data infrastructure, and
    - Human resources.
  - **The ability to navigate external forces, particularly related to the speed and unpredictability with which the COVID-19 pandemic unfolded.**

**Table 7. An overview of enablers and challenges related to COG-UK ability to mobilise and sustain member commitment to consortium activity**

<b>INFLUENCE: THE ABILITY TO MOBILISE AND SUSTAIN INDIVIDUAL AND INSTITUTIONAL COMMITMENT TO CONSORTIUM ACTIVITIES</b>	
<b>Key Enablers</b>	<b>Key Challenges</b>
<p><b>Individual and institutional goodwill:</b></p> <ul style="list-style-type: none"> <li>Individual and institutional goodwill enabled COG-UK to deliver on its aims and helped manage challenges related to capacity constraints over time. Altruism and scientific intrigue underpinned individual and institutional engagement and facilitated a connected network of expertise. Institutions often provided in-kind support, e.g. access to facilities and infrastructure.</li> <li>The ability of individuals to work flexibly and adapt to changing circumstances supported the scale and pace of delivery.</li> </ul> <p><b>Supportive leadership, governance, and management:</b></p> <ul style="list-style-type: none"> <li>Dedicated central and member-site leadership, governance and management – supported by operational and logistics functions – have been key to enabling COG-UK's activities. The representation of different stakeholders and geographies in governance groups supported a four-nations approach, alongside regular meetings of the COG-UK network. Designated management, operational and logistics support helped minimise administrative demands on research staff.</li> <li>Tools and processes to support the entire consortium while minimising bureaucracy (e.g. weekly reports on the percentage of samples sequenced from each nation and weekly turnaround-time reports to inform decisions about network activities) were helpful in managing the network.</li> <li>Policies to promote inclusiveness, accountability and transparency, such as an authorship policy listing anyone contributing to producing COG-UK data as an author on outputs, helped compensate people for time spent away from other research.</li> </ul> <p><b>Overall productive relationships and interactions in the COG-UK network:</b></p> <ul style="list-style-type: none"> <li>The commitment of individuals and institutions from diverse academic, NHS, and public health organisations across the four nations of the UK was a critical enabler.</li> <li>Mobilising and deepening pre-existing relationships and building new ones around a shared vision helped nurture benevolence and trust between many COG-UK collaborators and supported rapid delivery on tasks and adaptability.</li> <li>Investing time and effort into relationship-building addressed early scepticism about the value of pathogen sequencing for the pandemic response and helped bring policymakers on board with COG-UK's vision.</li> <li>Communications infrastructure, i.e. IT platforms, supported interactions between members of a distributed network.</li> </ul>	<p><b>Challenges in matching individual and institutional capacity to demand:</b></p> <ul style="list-style-type: none"> <li>Time demands placed on individuals working at an unprecedented pace, often without direct COG-UK funding, were a significant challenge.</li> <li>Human resource capacity constraints, e.g. the numbers and types of staff available early on, were challenging to manage given rapidly increasing demands for COG-UK sequencing and analytics.</li> </ul> <p><b>Governance and management challenges:</b></p> <ul style="list-style-type: none"> <li>Implementing the consortium's governance and management arrangements was not straightforward, since COG-UK had to navigate institutions' diverse pre-existing rules and operating systems.</li> <li>Early obstacles to recruiting sufficient administrative, operational and logistics support staff led to delays in implementing some contractual arrangements and policies. These obstacles were exacerbated by COG-UK not being a legal entity.</li> </ul> <p><b>Relational challenges in an inherently complex and diverse network:</b></p> <ul style="list-style-type: none"> <li>Although rare, perceptions that power imbalances between individual PHAs occasionally influenced decision making about which samples to sequence sometimes presented a relational challenge. Some network members had different views on whether sequencing should be done centrally or locally. COG-UK developed and revised its sampling strategy over time and sought to create opportunities for partners to discuss and voice their views through various discussion forums.</li> <li>It took time to establish effective communications between researchers and PHAs to support the uptake of COG-UK insights in informing decision making; relations significantly strengthened as COG-UK evolved.</li> <li>There were some communication challenges related to the decision to move towards the gradual transition of routine sequencing from academic institutions to PHAs.</li> </ul> <p><b>Wider political developments:</b></p> <ul style="list-style-type: none"> <li>Plans and decisions related to the public health system's evolving structure and organisation introduced an additional layer of complexity to pursuing a four-nations approach that central to COG-UK strategy</li> </ul>

**Table 8. An overview of enablers and challenges related to COG-UK resources**

<b>INFLUENCE: RESOURCES- FUNDING, PHYSICAL AND DATA INFRASTRUCTURE, HUMAN RESOURCES</b>	
<b>Key Enablers</b>	<b>Key Challenges</b>
<p><b>Financial resource support:</b></p> <ul style="list-style-type: none"> <li>• Timely access to substantial funding from the NIHR, MRC/UKRI and Wellcome Sanger Institute enabled COG-UK to rapidly set up operations at scale across the UK.</li> <li>• Support from the Chief Scientific Advisor helped convey the need for funding a pathogen genomics network to key national-level decision makers and ensure COG-UK's timely establishment.</li> </ul> <p><b>Physical and data infrastructure:</b></p> <ul style="list-style-type: none"> <li>• Pre-existing facilities and equipment helped support genome sequencing and research, while additionally purchased equipment helped bolster capacity across sequencing sites.</li> <li>• CLIMB's pre-existing data infrastructure, skills and goodwill bolstered its capacity to host sequencing data from diverse and distributed sites.</li> <li>• COG-UK's operational policies made it mandatory to upload sequencing data to the CLIMB data repository before payment could be authorised.</li> </ul> <p><b>Human resources:</b></p> <ul style="list-style-type: none"> <li>• Diverse research, technical, administrative, management and leadership staff were fundamental to COG-UK's ability to deliver on its aims.</li> </ul>	<p><b>Financial resource challenges:</b></p> <ul style="list-style-type: none"> <li>• Initial scepticism from some individuals with influence related to the value of pathogen genomics sequencing needed to be overcome. Although securing initial funding happened very promptly, overcoming some initial scepticism was relevant in relation to prioritising and targeting the utilisation of funds over time secure initial and subsequent funding. (Awareness-raising, support by influential individual champions and demonstrating early signs of value for policymakers helped in this regard).</li> <li>• Challenges related to the gradual transition of sequencing activity and associated funding from academic institutions to PHAs impacted those individuals who had paused their careers to focus on COG-UK and were dependent on its financial support.</li> </ul> <p><b>Physical and data infrastructure challenges:</b></p> <ul style="list-style-type: none"> <li>• Challenges with onboarding sites, securing ethical clearances and arranging for the transport of samples to respond to the surge in sequencing demand were experienced in the consortium's early stages.</li> <li>• Global shortages early in COG-UK's experience hindered access to the consumables needed for sequencing.</li> <li>• Efforts to optimise data sharing, flow and linkage faced some obstacles due to the lack of an integrated data platform and fragmented data systems, rules and governance across organisations in the four nations.</li> <li>• Limited time and capacity to translate data into user-friendly formats to feed back to the NHS hospital sites providing samples were also experienced.</li> </ul> <p><b>Human resource challenges:</b></p> <ul style="list-style-type: none"> <li>• Capacity challenges due to the scale of demand and the speed and pace at which the consortium needed to carry out sequencing, research and analyses occurred. These were primarily tackled by mobilising individual and institutional goodwill to deliver in unprecedented circumstances.</li> </ul>



**Table 9. An overview of enablers and challenges related to COG-UK ability to adapt to unpredictable conditions associated with the COVID-19 pandemic**

INFLUENCE: THE ABILITY TO RESPOND TO THE URGENT AND UNPREDICTABLE NATURE OF THE PANDEMIC	
Key Enablers	Key Challenges
<ul style="list-style-type: none"> <li>• COG-UK members' readiness to adapt the extent of their focus on research versus routine sequencing activity was vital to COG-UK's role in informing public health decision making and policy.</li> <li>• Though not without challenges, the financial resources, leadership and management ability that allowed COG-UK to rapidly bolster human-resource capacity and onboard sequencing sites underpinned COG-UK's timeliness, relevance and impact in a rapidly changing public health landscape.</li> <li>• The urgency of the pandemic challenge focused attention on the most pressing short-term needs and mobilised support, goodwill and trust with minimal bureaucracy.</li> <li>• The novelty and experimental nature of COG-UK was conducive to agility and adaptiveness, allowing for a degree of innovation and experimentation related to governance and management approaches, and minimising bureaucracy</li> </ul>	<ul style="list-style-type: none"> <li>• The consortium's constant flux as new people joined required a consistent focus on onboarding but also presented occasional challenges to maintaining effective communication and added to time demands on key staff.</li> <li>• COG-UK's fire-fighting mode of operating was taxing on staff and unlikely to be sustainable for the longer term. This is an important consideration for COG-UK's future and longer-term resourcing.</li> </ul>

## 5.1. Mobilising and sustaining commitment to consortium activities

### 5.1.1. Influences related to individual and institutional goodwill

Individual and institutional goodwill and flexibility have played a key role in COG-UK's capacity to deliver on its aims and helped manage challenges related to capacity constraints over time.

Individual commitment to COG-UK efforts was often rooted in goodwill and altruistic motivations. Three individuals engaged with the consortium reported wanting to do what they could to help respond to the pandemic and to contribute to shaping the global response [Int. 5, 6, 9]. As illustrated by one consulted expert:

*'I think it's basically people dedicated to wanting to help. It was never about money – nobody made any money from*

*this... It was about wanting to help, and I feel that is what's kept us going and kept PIs going with lack of sleep. And their staff – reminding them that they were part of something greater that has shaped the global response.'* [Int. 6]

This goodwill applies to diverse COG-UK members, including researchers in academic institutions, staff at NHS sites and PHAs. For example, one expert flagged that staff at NHS sites voluntarily sent samples during a period in which they were overworked, understaffed, and often exhausted [Int. 6]. Similarly, commenting on the goodwill and can-do attitude at a sequencing and research site, another expert noted:

*'People putting themselves at personal risk by coming onto campus, making sure that COVID-19 sequencing during lockdowns continued. Just across the board... The staff working in all weathers.'* [Int. 20]

Staff contributing to COG-UK efforts also demonstrated a strong ability to 'adapt as they go', working flexibly to support the fast turnaround times for sequencing SARS-CoV-2 samples and rapid response to the changing scale of demand for COG-UK support by public health decision-makers [Int 3]. According to one interviewee:

***'Everything was done at pace by people willing to help for the greater good.'*** [Int. 3]

COG-UK members' commitment to working together and mentoring the future generation of public health genomics leaders supported efforts to directly respond to the pandemic and ambitions to contribute to longer-term capacity-building in the public health system [Int. 2]. Many COG-UK participants – both senior and early-career staff – put their existing projects and careers on hold, took ownership of COG-UK-related tasks and worked tirelessly to fill gaps in the capacity required to respond to the pandemic through sequencing, research and analysis activities [Int. 8, 13].

Scientific intrigue also helped to mobilise participation and buy-in for COG-UK activities. Some participants saw contributions to COVID-19 research as a unique opportunity to apply their skills to something that could make a crucial difference to society [Int. 1, 5, 6]. As illustrated by one interviewed expert:

***'It was a once in a lifetime research question for them to answer... It really sparked that science interest... people really wanted to be part of the team; they didn't want to be out of it.'*** [Int. 6]

For some researchers working in the consortium, COG-UK participation has been of professional benefit to their research profile, career development [Int. 6] and individual fulfilment. As one expert commented:

***'It's been one of the highlights of my professional life, being involved in COG-UK. It's been a great privilege to be involved in it and I'm really grateful to have had the opportunity.'*** [Int. 5]

### **Matching the available individual and institutional capacity to the scale of demand for COG-UK activities was not straightforward**

Many people who contributed to COG-UK's work were only able to do so thanks to the support provided at risk by their institutions. In addition to the individual commitment discussed above, institutional support has mattered greatly [Int. 1, 8]. Some academic institutions received little or no funding from COG-UK but shouldered some costs themselves [Int. 1]. Similarly, relatively few participating individuals (e.g. academics or other researchers) were funded directly by COG-UK's award – which was mostly spent on the cost of sequencing – and so researcher salaries were primarily paid by universities and research grants [Int. 3, 10]. Academic institutions also funded the electricity requirements of the buildings and machines used for COG-UK's work [Int. 6, 10]. In commenting on the importance of institutional support, one expert noted:

***'They were keeping the lights on.'*** [Int. 10]

According to one interviewee, this in-kind institutional support is significant but not always recognised to the degree that it should be and can fall under the radar in terms of the difference it has made to the ability of COG-UK to deliver on its aims [Int. 10].

Despite strong commitment from individuals and institutions, the consortium faced challenges ensuring sufficient human-resource capacity, including research, technical,



management and administrative support over time [Int. 1, 4, 10]. Additional research and administrative staff earlier in COG-UK's existence could have helped reduce the time demands and physical and emotional toll it took to establish the processes and infrastructure supporting COG-UK's existence and function as a connected network [Int. 4].

### 5.1.2. Influences related to leadership, governance, and management

**Dedicated leadership, governance and management have been key to enabling COG-UK's activities.**

Supportive leadership was critical for COG-UK to deliver on its ambitions at pace and scale. The expertise of the central consortium leadership (e.g. Steering Committee) and leadership at individual COG-UK sites, and their unwavering dedication to COG-UK's aims, was widely acknowledged [Int. 1, 4, 7, 8, 9, 16]. In commenting on leadership as a critical ingredient in COG-UK's evolution, one interviewee highlighted:

*'The leadership of the team, led by Sharon Peacock and her team, in coordinating and talking to people and bringing the communities together was really, really critical for this.'* [Int. 4]

Diverse governance and management arrangements enabled leaders across stakeholder groups and geographies to come together and collaborate on decisions affecting the consortium more widely, helping support individual and institutional engagement in consortium activities. Examples include:

- **Representation of different stakeholders in governance groups:** As discussed in [Section 3](#), COG-UK's steering committee comprises a diverse group of people to

ensure that multiple perspectives are included when making strategic decisions, e.g. how to spend the funding award [Int. 6]. It includes people from across the four nations and with different professional backgrounds, such as clinicians, epidemiologists, statisticians and PHA representatives. Representation from each of the four nations was integral to COG-UK efforts to ensure that all nations' needs were incorporated into the consortium's ongoing strategy [Int. 6].

- **Regular meetings involving diverse COG-UK representatives:** A weekly operations meeting involving every principal investigator alongside representatives from the four nations – plus a second weekly meeting with just one representative from each of Northern Ireland, Scotland, England, Wales, the Wellcome Sanger Institute and COG-UK's core management – have helped to embed collective leadership into practice. During this additional weekly meeting, the different nations are invited to raise any issues to pass on to the Steering Committee. There is also a four-nations data meeting that focuses on improving and addressing concerns related to data sharing [Int. 6].
- **Management support, particularly operational and logistics support.** This was widely seen as a key enabler of a distributed network [Int. 2, 4, 5, 6, 7, 8, 9, 10, 17]. Operational and logistics teams and staff have helped protect researcher time for sequencing, research, and analysis activities, with support teams and functions in COG-UK taking care of logistical issues like research ethics and contracting [Int. 3]. Logistics support has also been central to responding to changes in the wider organisation of the

public health response. As reflected on by one interviewee, all the diagnostic testing was run through PHAs but quickly moved to lighthouse labs at the beginning of the pandemic. This presented a significant challenge for COG-UK; the logistic issues alone were challenging to deal with, e.g. ensuring appropriately sealed samples and dealing with different couriers. The consortium also needed to adapt to new protocols for extracting samples while trying to implement improvements to drive down individual test costs [Int. 1].

- **Functions, tools and processes to support the entire consortium with minimal bureaucracy.** For example, the core leadership team supports the entire consortium, the central communications team covers all COG-UK sites and members, and processes such as the publications policy apply to everyone [Int. 8]. An exception to this is additional and self-funded support teams and a steering committee within the Wellcome Sanger Institute (in part related to the institute effectively operating as a self-funded member of COG-UK) [Int. 8]. Operational policies and different working groups' regular meetings were designed to support effective communications across the network and limit unnecessary bureaucracy [Int. 8]. Tools such as a weekly coverage report on the percentage of samples sequenced from each nation and region and a weekly turnaround time report were seen as valuable aids for making decisions on consortium activities. The use of these tools also demonstrated commitment to activities across different sites across the four nations. For example, the weekly sequencing coverage tool helped flag areas of low sample-sequencing coverage to

understand the reasons behind this and share findings with PHAs, allowing them to follow up with individual sites and decide how to prioritise samples [Int. 6]. The weekly turnaround-time report was used internally to assess and understand delays in sequencing and identify sites that might need support [Int. 6].

- **Policies to promote inclusiveness.** An example is the COG-UK publication policy, which specifies that anyone who has worked in any capacity to produce COG-UK's data can be added to the authorship list for COG-UK outputs. This policy helps compensate people for their time away from other research [Int. 8]. One interviewee also praised the consortium for promoting women in COG-UK [Int. 17].

**Creating novel governance arrangements for a complex consortium that are compatible with pre-existing institutional systems was challenging. The consortium's novelty and the diversity of organisations it involved meant delays to implementing some contractual arrangements and policies were experienced.**

Despite a strong commitment to supportive consortium governance and management, there were some challenges over time. These related to the novelty and complexity of the COG-UK consortium model in terms of the diversity and size of the network, the pre-existing rules and operating systems across the four nations, and early obstacles to recruiting sufficient administrative, operational and logistics support.

To set up and run its work, COG-UK had to establish multiple layers of governance – including, but not limited to, a legal framework, consortium agreement, data-sharing

agreements and publication policies. It also had to develop a governance framework allowing diverse operations [Int. 10]. One interviewee highlighted that it is difficult to overstate the amount of energy required to connect people and establish a consortium that functioned coherently, emphasising the demands placed on the staff establishing governance and management arrangements [Int. 4].

***‘The amount of energy it took to really bring people together and make this work coherently cannot be underestimated.’***  
[Int. 4]

However, the team responsible for operations and logistics was relatively modest in size and therefore over-stretched throughout the consortium’s life, especially in COG-UK’s early phases [Int. 1, 10]. At times, these capacity constraints challenged efforts to maintain regular communication and cohesiveness across the consortium [Int. 10].

Although efforts to create an operational and logistics support structure to ensure efficient consortium operations were widely appreciated and acknowledged by interviewees [Int. 2, 4, 5, 6, 7, 8, 9, 10, 17], some delays may have been mitigated had the consortium had the time and resources to bolster management and administrative capacity earlier on.

In the early phases of the consortium’s existence, limited administrative and operational-support capacity delayed finalising certain contractual arrangements and policies guiding COG-UK’s activity. For example, the consortium agreement took approximately six months to finalise [Int. 11]. However, the consortium’s complexity and novelty, given the diverse organisations and stakeholders involved and the speed that the delivery

of research activities unfolded, meant the COG-UK model was novel in many ways and the contractual arrangements required ‘real-time’ experimentation and learning. Finally, one interviewee raised concern about delays in updating authorship lists according to the publication policy, suggesting this should have been prioritised to acknowledge people putting in considerable time and effort throughout COG-UK’s work [Int. 13].

Ensuring that people working in different ways across diverse sites could come together and agree on operational protocols took some time. This challenge was accentuated by the diversity of systems and rules existing across organisations across the four devolved nations. For example, each nation has a different set of rules regarding how personal healthcare data can be shared for research, even though regulations are all based on the same UK General Data Protection Regulation (GDPR) principles [Int. 12]. As one interviewee commented:

***‘To design a system that gets you through four gates is that much harder than a system that gets you through one gate.’***  
[Int. 12]

Sorting out data-flows was highly challenging; because different stakeholders built ad-hoc systems that were not part of COG-UK, the data systems were not linked up and centralised. The CLIMB database has been central in ensuring data linkage, serving as a central data repository from which many agencies can access data [Int. 3].

Reflecting on the learning to date, one interviewee also commented that creating more opportunities for interaction between third-party senior scientists and the steering committee and between the steering

committee and Governance and Advisory group may have been beneficial [Int. 1].

It should not be assumed that governance arrangements and ways of working that were effective during a time of crisis would work under more ordinary circumstances. Now that the urgent firefighting mode has somewhat diminished, one interviewee said there would be a need to stabilise COG-UK's operational, governance and management arrangements [Int. 7]. Doing so would require recognising, on the one hand, the varying interests of the four nations [Int. 2], and the differing interests of the academic and public health communities on the other hand [Int. 1]. There would also be a need to manage these arrangements differently in the future:

*'We've focused on what do we need to do today, this second, and that means you miss the ability to have any kind of strategy that extends beyond a week.'* [Int. 12]

### 5.1.3. Influences related to relationships and interactions in the COG-UK network

Collaborative relationships generally supported progress at pace and scale across a distributed network working in a pandemic context, although occasional relational challenges arose.

#### *Mobilising pre-existing relationships and establishing new ones:*

Creating and nurturing a network of expertise by bringing together individuals from diverse academic, NHS and PHA institutions in the COG-UK consortium was widely perceived to be a key enabler of COG-UK activity and impact [Int. 1- 3, 5-10]. As one interviewee commented:

*'In response to the most significant public health crisis that the world has had to deal with in this lifetime, COG-UK have managed to pull together an*

*incredibly well-connected network of experts from academia, the NHS, and public health authorities that has had a massive impact on our understanding of the disease'* [Int. 3].

The pre-existing expertise within academic laboratories and teams before COG-UK was strengthened, and new relationships were built over time. These benefits supported delivery on sequencing demands at an unprecedented pace and scale. According to some, this was achieved more readily than would have been the case in NHS or public health virology laboratory settings alone [Int. 5]. The country's scientific excellence was rapidly mobilised to help respond to the pandemic [Int. 7]. As one interviewee commented:

*'We're lucky to have very good scientists in the UK; perhaps some of the best in the world.'* [Int. 7]

Leading academic experts worked closely with PHAs, which was key to enabling research and data analysis to inform policy and public health decision making [Int. 6].

#### *A shared commitment to responding to urgent needs:*

Relationships between COG-UK's diverse stakeholders have been heavily reliant on benevolence and trust. This was partly facilitated by mobilising and deepening pre-existing relationships and partly by attracting new collaborators into the shared overarching ambition of using public health genomics research and expertise to assist with the pandemic response [Int. 4]. While funding was available for some staff, many worked as volunteers and committed significant time and organisational resources to the endeavour [Int. 5]. According to self-reported data from COG-UK, the consortium funded approximately 27 full-time research and technical staff and 17 administrative and management staff between

March 2020 and July 2021.<sup>126</sup> The consortium also benefited from the engagement of more than 800 volunteers during this period.<sup>127</sup> Overall, constructive engagement between COG-UK's partners was crucial for the consortium's impact [Int. 1].

Overall, interviewees frequently reported high levels of support and positive interactions across the consortium - between researchers, PHAs, testing sites and lighthouse labs, and especially once the need for public health genomics research and sequencing became more recognised in the public health and policy landscape (Int. 1-3, 5, 10-12, 16). As a complex consortium involving diverse personalities and stakeholders, differences in views did occur but were generally resolved through discussion and by focusing on 'getting things done' [Int. 1]. As one interviewee commented:

*'We always got by thanks to interactions with the networks....In the face of shortage in consumables and resources, other research labs as well as hospital sites were always happy to help. When a site did not have capacity for a high number of samples, they would contact other sites across the UK and distribute the excess samples across those with capacity.'* [Int. 3]

The pandemic's urgency also facilitated this highly networked and collaborative approach. One interviewee felt that the same result would have taken years to establish in the absence of the pandemic's urgency [Int. 3], especially given early scepticism amongst some decision makers about the value of pathogen sequencing for the pandemic response. As illustrated by an interviewee:

*'There were a huge number of naysayers that, for whatever reason, just didn't think that this would be of any utility whatsoever.'* [Int. 20]

#### **Efforts to ensure inclusiveness:**

Early on in the pandemic, COG-UK was viewed mainly as a research organisation, and it was, therefore, difficult to get NHS sites that were focused on conducting diagnostic tests to send samples for sequencing [Int 6]. In addition, samples could not be processed without the corresponding metadata, which labs needed to send through. This contributed to a significant problem accessing the required data at early phases of COG-UK existence [Int 1, 6]. However, the sharing of samples and metadata significantly improved as the value of pathogen genomic sequencing became more apparent to government and NHS decision makers, i.e. as mutation data was used to identify new variants, understand transmissibility, spread and symptom severity, and inform public health decision making [Int. 6].

Investing in communication platforms facilitated joint working across a distributed network and helped relationship-building efforts. For example, shared Slack communications platform channels allowed teams without a deep experience of high-throughput viral genome sequencing to engage with teams who already had this expertise [Int. 5]. One interviewee suggested that for their team, Slack channels were a key enabler of quick and effective communication with individuals across the COG-UK network [Int. 5]. This communication has been essential, enabling the rapid flow of information required to share learning across the UK [Int. 5].

126 This figure represents the headcount over the evaluation timeframe and not the FTE (based on self-reported information). Note that the Wellcome Sanger Institute manages its budget separately, so these counts do not include Sanger Institute staff.

127 COG-UK self-reported data.



This was further reinforced by COG-UK's four-nation focus. Although not without its challenges, a four-nation consortium focus on governance-and-management arrangements helped embed the principle of inclusiveness into practice [Int. 6]. As illustrated by one interviewee's reflection:

*'Every Monday morning there is an operations call with every PI and the four nations, plus an additional call with just a representative from Northern Ireland, Scotland, England, Wales, the Sanger and core management where the different nations can raise any issue, which then gets fed up to the Steering Committee... The steering committee is where decisions are made in terms of strategy, how to spend the money, and how well they are doing. It is made up of people from different backgrounds (clinical, data people, PHAs), which bring different perspectives. The steering committee has the four nations represented, which has been integral to COG UK as it meant that the four nations have been involved in the strategy of the consortium.'* [Int. 6]

According to another expert:

*'An important thing.... has been the great effort put into maintaining this as a UK-wide, four nations effort, even when the levels of expertise in the backgrounds of each nation differed greatly.'* [Int. 7 - text redacted to preserve anonymity].

While relationships in COG-UK's network were generally seen as positive overall, some relational challenges were also flagged, albeit by a minority of interviewees.

Relational challenges had to do with a variety of issues. Examples include perceived power imbalances between different PHAs (and perceptions that this can influence the prioritisation of sequencing activities), occasional communication-related challenges between PHAs and researchers about take-up and use of data, differing views about where sequencing should be conducted and wider political developments [Int. 9, 11].

For example, one interviewee commented on an imbalance in the relative power and influence of PHE versus the devolved nations' PHAs<sup>128</sup>. Communication between a specific PHA and academic researchers was also seen as somewhat challenging,<sup>129</sup> in terms of not knowing the extent to which the agency was taking on board information communicated by researchers about Variants Under Investigation (VUIs) [Int. 3].

Some divergence in views related to where sequencing should be undertaken (e.g. locally or centrally at the Wellcome Sanger Institute) [Int. 9] and transparency in decision making about which activities to pursue and how to prioritise the use of funds [Int. 13] also arose within the network. For example, according to one interviewee, the way decisions about the transition of funding for sequencing activity from academic institutions to the PHAs were made created some relational challenges [Int. 13].

While the need to transition genomic sequencing services to PHAs was generally recognised across the consortium, one interviewee felt that greater involvement of distributed partner sites in central decision making related to the transition was needed.<sup>130</sup>

128 Interviewee reference withheld to preserve anonymity.

129 Interviewee reference withheld to preserve anonymity.

130 Interviewee reference withheld to preserve anonymity.



The financial and workload related implications of the transition of sequencing activity to PHAs also had significant implications for partner sites. According to this interviewee, they would have benefited from more direct engagement.

The transition of genomic sequencing services to the PHAs began in the spring of 2021. COG-UK was formed primarily as a research consortium. However, demand for COG-UK's support for routine SARS-CoV-2 sample sequencing over time required it to divert some research resources (e.g. personnel and equipment) to provide pathogen-genome data to public health and policy decision makers. After 13 months as a key SARS-CoV-2 genome sequencing network, COG-UK began enacting a plan to transition sequencing activity in England to PHE. Sequencing sites in Scotland, Wales and Northern Ireland also began transitioning NHS samples from testing in the community to their PHAs.<sup>131</sup> In this evolving public health landscape, NHS Test & Trace was given the mandate to make decisions about sampling strategy (i.e. where to sample and how to use and prioritise existing sequencing). Some COG-UK sequencing sites in English research institutions have remained a safety net should additional capacity be needed to meet surges in sequencing demand in the future.

The shift in sequencing activity meant that staff involved with COG-UK across the devolved nations had to carve out time from conducting and publishing research to focus on managerial aspects related to the transition [Int. 7]. Contracts needed redrafting, and the core management team had to adapt to reporting to COG-UK governance **and** PHA governance [Int. 8]. The core management team also had to discuss the transition with each consortium stakeholder, as part of an effort to give different stakeholders the opportunity to share their

concerns about the new approach, many of which related to contractual matters [Int. 6]. The sequencing network the consortium developed alongside methodological and analysis tools has created opportunities for COG-UK to return to its core identity as a research, data-linkage and training network. It has also provided opportunities to advance relevant practical knowledge on how pathogen genomics relates to issues such as disease severity or vaccine efficacy and patient care.

According to another interviewee, external factors such as Brexit-related politics also introduced some relational complexities, requiring the consortium to find creative ways of pursuing a four-nations approach:

*'Relationships within the COG consortium have always been good and strong. Any messiness came from the wider political context. With Brexit, the UK Parliament want to develop a UK wide public health body, whereas the devolved nations want to retain their devolved PHAs. People were given PHE honorary contracts so that they could access data, join calls, etc.'* [Int reference withheld to preserve anonymity]

Despite some challenges to collaborative working, COG-UK's generally strong and productive relationships played a key role in allowing the consortium to respond creatively to challenging circumstances – particularly in increasing demands for sample sequencing at unprecedented turnaround times and with limited staff and financial resources [Int. 4, 7]. In the face of resource shortages, research labs and hospital sites often showed a willingness to help each other (e.g. by distributing sequencing demand loads to other sites when any single site ran out of capacity) [Int. 3]. The generally supportive and productive

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131 COG-UK (2021d).

relationships between researchers and the NHS have also enabled NHS capacity-building for sequencing as individuals and institutions released staff time and enabled facility-and-equipment use for this effort [Int. 3]. COG-UK members' general willingness to ensure important work was conducted as swiftly as possible mitigated funding and capacity limitations at any single institution, with multiple parties accepting financial risk to meet the programme's goals [Int. 5].

Relationships will need to continue evolving if gains are to be sustained. COG-UK has introduced an opportunity to grow a shared sense of purpose across sequencing, public health genomics, research and innovation [Int. 16]. COG-UK's activities have established potentially valuable networks and relationships across the UK and internationally [Int. 13, 19]. However, there was a perceived risk that much of this infrastructure would not be maintained if the case for continued funding is unsuccessful [Int. 17, 19]. One expert also flagged that further investment in this space should not crowd out other global public health priorities [Int. 15]. A key future focus may reside in supporting a new pathogen surveillance system (i.e. supporting research and not pathogen-sequencing capacity) [Int. 3, 14]. Examples include developing bioinformatic tools for public health virology [Int. 5], computing infrastructure [Int. 3] and a 'genome epidemiology intelligence consortium' to help develop tools and approaches to upscale the service [Int. 16].

## **5.2. The resource environment: funding, physical and data infrastructure and human resources**

### **5.2.1. Influences related to funding**

Financial support was essential to COG-

### **UK's delivery of its aims.**

The funding COG-UK has received and the pace at which it was approved was central to allowing the consortium to come to life and to deliver on its aims. We noted in the previous section the importance of goodwill and an orientation towards the public good. However, considerable financial support was required for this altruism to be expressed. COG-UK came into existence very rapidly: COG-UK's Executive Director sent out emails and calls to colleagues and contacts regarding developing COG-UK at the beginning of March 2020, when there were still very few cases in the UK.

As mentioned earlier, COG-UK received £14,490,000 from the NIHR and MRC/UKRI and an additional £6,300,000 from the Wellcome Sanger Institute (total funding: £20,790,000) in April 2020 to support the creation of a large-scale SARS-CoV-2 sequencing capacity and academic research, including the provision of data and metadata to the COG-UK database. In January 2021, COG-UK received additional funding from the Testing Innovation Fund to further support sequencing capacity and equipment (£11,600,000). In April 2021, they received additional funding from DHSC Test and Trace for transition support and sequencing capacity (£4,999,000). The subsequent funding was awarded to COG-UK given the increased demand for its activities and specifically to bolster large-scale SARS-CoV-2 sequencing capacity and equipment and to enable the transition of routine sequencing activities to PHAs (a process that began in the Spring of 2021). One interviewee voiced a concern that the proposal was light on details and expected funders to take on a lot of trust [Int. 17].

Early scepticism about the value of pathogen genomics sequencing and research from some individuals with influence in the public health landscape,

**and subsequent rapid changes in perceptions of value, coupled with increasing demand for COG-UK work, have been challenging to manage and necessitated rapid adaptation.**

Timely access to funding and support from the government's Chief Scientific Advisor were key to establishing COG-UK at a time when, according to some interviewed experts, some government advisors did not see COG-UK's value [Int. 4, 9, 10].

When first established, COG-UK identified itself as a research network whose mission was to investigate whether they could demonstrate genomic sequencing's benefit for public health. As the pandemic progressed, COG-UK became the major service provider for sequencing, particularly after it became clear that sequencing was needed to explore variants of SARS-CoV-2 [Int. 4, 10], and financial resources were largely channelled into sequencing activity. Over time, the consortium also invested significant effort into realising efficiencies in the costs of sequencing activity [Int. 1], partly achieved through economies of scale and by introducing improvements in NHS diagnostic testing processes and protocols for extracting samples [Int. 1].

Increased government funding over time and adaptation in what the funding needed to be used for came with some complexities that COG-UK, as an academically led consortium, needed to adapt to and navigate [Int 8]. To elaborate, COG-UK has experienced somewhat of a shift of funding from academic institutions to PHAs in light of the previously described drive to transition routine sequencing into the PHAs [Int. 6, 7]. According to one interviewee, most members of COG-UK saw this as a move in the right direction, believing it was appropriate for PHAs to take responsibility for sequencing as a service [Int. 10]. However, the change in funding arrangements proved a difficult transition for some individuals in

academic institutions who had paused their careers to contribute to COG-UK [Int. 7, 13]. As illustrated by one interviewee:

*'It felt like the ship that we were sailing in was torpedoed, and we had to build another one.'* [Int. 7]

### 5.2.2. Influences related to physical and data infrastructure

**The equipment, facilities and data infrastructure that COG-UK has been able to tap into have been fundamental to its impact.**

The UK had an established pathogen genomics research landscape and physical infrastructure (laboratories, equipment) to conduct large volumes of genome sequencing prior to the COVID-19 pandemic. This foundation provided a strong base that could be rapidly mobilised and built on to establish COG-UK and respond to the pandemic [Int. 4, 9, 13]. The Wellcome Sanger Institute, for example, had pre-existing capacity for sequencing at an 'industrial' scale [Int. 1]. However, it took time and effort to set up a system by which Wellcome could receive samples from the Lighthouse laboratories and conduct sequencing and analysis.

Multiple interviewees also pointed to the pre-pandemic existence of the CLIMB data infrastructure and the expertise of its team members as critical to COG-UK's early impact [Int. 1, 3, 10, 13]. Developed over the last decade, CLIMB's skills in data management, data pipelines and developing integrated data systems meant that the consortium could quickly be set up as 'a virtual machine within the system' into which all sequencing data could be collated [Int. 1]. As one interviewee commented:

*'If it wasn't for CLIMB, we wouldn't have been able to get off the ground as quickly as we did.'* [Int. 10]

CLIMB-COVID (Cloud Infrastructure for Microbial Bioinformatics) is now set up as a central data repository that includes a core dataset in the public domain,<sup>132</sup> enabling data sharing and linkage with viral genome data [Int. 3]. Such data linkage was difficult to implement before COG-UK but is key to understanding how the virus impacts transmission, symptom severity as well as health outcomes from interventions such as vaccines. According to one expert, information on public health data was tricky to access and link to other data sources before COG-UK. COG-UK has set up a system enabling secure data sharing and links between health data and viral genome data [Int. 3]. However, the sustainability of the established pathogen-genomic data and physical/technical infrastructure will require a coherent strategy for public health genomics in the UK to enable the application of COG-UK's achievements to future infectious disease threats. Operational policies also supported the emerging data infrastructure and resources. For example, sites are not paid for their sequencing unless they upload their data onto CLIMB, and this has facilitated the public and global availability of all valuable data [Int. 1].

**Timely access to requisite infrastructure was an early challenge. The consortium's experience also suggests a need to build on achievements made in linking pathogen genomics and metadata and to further bolster data flow and linkage infrastructure for future pathogen genomics and pandemic response efforts.**

Despite pre-existing infrastructure and capacity-strengthening of the public health system during the pandemic, COG-UK has had to deal with early challenges related to ensuring sufficient facilities and equipment early on, accessing consumables, and establishing

dataflow and linkage. These challenges were exacerbated by the increasing demand for sequencing activities over time and the consortium's need to balance sequencing with its original research remit [Int. 3, 7, 9, 10, 11].

Had the scale of demand for sequencing activity been clear from the outset, more investment in bolstering and advancing rapid sequencing infrastructure would have been likely [Int. 11]. There were also some challenges related to onboarding different sequencing sites, getting ethics clearance and arranging for the transport of samples to sequencing sites [Int. 3].

Accessing consumables was also a challenge for COG-UK at the start of the pandemic due to a worldwide shortage of gloves and pipette tips [Int. 3]. There was also a shortage of reagents [Int. 9]. The low supply of consumables presented a key challenge to sites trying to scale-up their processes [Int. 3], although the government sought to provide national support mechanisms to help ease these procurement issues [Int. 7].

There were also challenges in optimising data sharing, data flows and data linkage [Int. 1, 5, 6, 7, 9, 10, 14]. More specifically:

- **COG-UK links with each of the large community Lighthouse laboratories and NHS hospital-testing laboratories, but no single platform links all the required data.**

Each genome sequenced in a laboratory has to be linked with a unique sample identifying number, a date, a location and an anonymised patient identifier to be useful for decision makers. Genome data cannot be uploaded to CLIMB until linked with this minimum dataset. However, the absence of an end-to-end system managing this process created

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Public data: Central Sample ID, Date of Sample (collected), Date of Sample (received), UK nation.

considerable challenges in producing linked datasets for much of COG-UK's existence [Int. 10]. Considerable work had to be done to get data onto CLIMB so that researchers could access it, including developing data-security and protection toolkits and sign-off from NHS Digital that enabled CLIMB to hold more sensitive information [Int. 11]. Although COG-UK has been aware of data connectivity issues throughout, the solution did not lie within the consortium. For example, COG-UK could not solve an NHS data-feed issue. Therefore, COG-UK worked with others in the healthcare system to gradually improve data flows [Int. 10]. There have also been some challenges funding COG-UK's time and space on the CLIMB system [Int. 13].

- **Fragmented data systems and different rules around information governance have also presented challenges to data linkage and sharing between the four nations. It took considerable effort to work with existing data-protection regulation and develop toolkits to link patient and genomic data stored in different places** [Int. 1, 5, 6]. The UK's highly compartmentalised system exacerbated this challenge, with COG-UK needing to tap into the Department of Health & Social Care, the Joint Biosecurity Centre, and the PHAs in each of the four nations with different regulations around information governance [Int. 1]. Since different hospitals used different formats for their data flows to COG-UK in some jurisdictions, collating and uploading metadata took significant time and effort [Int. 5].

These data-linkage challenges have affected the provision of sequencing data as a service to public health decision makers and COG-UK's research. Until the summer of 2021, COG-UK's priority was to link data that could inform the COVID-19 public health response. COG-UK only started to link their viral genome data to other datasets – such as Office for National Statistics (ONS) data and Real-time Assessment of Community Transmission (REACT) data, which will be critical for future research [Int. 10] – after the summer of 2021. With the transition of sequencing activity into PHAs, the consortium seeks ways to link viral-genome data with human-genome data and detailed patient information. If successful, this could help identify why and how some people experience more severe disease than others, for example, and could in the future also entail bringing in artificial intelligence to predict who is at risk of needing hospital care and/or at risk of poor outcomes.<sup>133</sup>

COG-UK was rapidly established without the luxury of developing a simple, harmonised data-flow structure from the outset. Since problems rooted in IT architecture are very challenging to resolve in the short term, the consortium has had to rely on workarounds. Sequencing volumes during the early stages of the pandemic meant that it was possible to use manual workarounds, resulting in a system reliant on heavy manual input from a small number of individuals to reformat data manually [Int. 5]. With hindsight, and knowing the level of throughput they would end up dealing with, one interviewee suggested COG-UK would have gone to greater lengths to avoid manual workarounds, obtaining metadata via less labour-intensive routes for the local teams and referring labs [Int. 5]. Ad-hoc IT solutions are now in place that have



reduced manual workload in the short term, but there are continuing efforts to harmonise data flows at a greater scale [Int 5].

Finally, there is some scope to improve communication of COG-UK data and analytics in the future, optimising the data's user-friendliness and ease of interpretation by stakeholders external to COG-UK (e.g. in the NHS). One interviewee commented on the importance of providing a mechanism to translate the COG-UK outputs into usable information at the Trust/hospital level in the future [Int. 5].

### 5.2.3. Influences related to human resources

As discussed throughout this report, diverse research, technical, administrative, management and leadership staff were fundamental to COG-UK's ability to deliver on its aims. The speed and pace at which the consortium needed to carry out sequencing, research and analysis tasks and the scale of demand for COG-UK work meant that staff capacity to respond depended on a significant degree of individual and institutional goodwill (as already discussed and elaborated on in [Section 5.1](#)). Human resource capacity challenges were primarily addressed by mobilising this goodwill and investing in training. A sustainable strategy for the future depends on the ability to secure longer-term resourcing and professional development support that can reduce dependence on goodwill and support stable career pathways requiring less 'fire-fighting' modes of work delivery.

## 5.3. Influences related to the ability to respond to the pandemic

**The pandemic's urgent and unpredictable nature caused many challenges for COG-UK, requiring plans to be adapted.**

As previously mentioned, COG-UK operates in a complex and rapidly evolving environment; adaptability to changing circumstances has been at the core of its evolution and function. As flagged by one interviewee:

*'We've had to adapt every step of the way... what we stand for repeatedly changes.'* [Int. 10]

The lack of predictability associated with the pandemic made it difficult to plan for the optimal focus of COG-UK resources and required the consortium to be 'fleet on their feet' to respond to emergence [Int 3, 10, 12]. As one interviewed expert commented:

*'It feels like we're building the wings when we're flying the plane.'* [Int. 3]

COG-UK showed adaptability in diverse ways. As previously discussed, it had to adjust the balance of research activities and sequencing services for public health decision makers and policymakers to help manage and respond to the pandemic. Doing so required adapting the focus of individuals and institutions from the consortium and sustaining their buy-in for a revised emphasis. As of November 2021, COG-UK began handing the service role over to the PHAs and transitioning back to a more research-centred focus [Int. 10]. That said, adapting to changing demands required the rapid means to bolster funding and staff capacity and mobilise relationships to support this change in focus. The consortium itself has also been in a state of constant flux as new people have joined, requiring a consistent focus on onboarding and presenting occasional challenges to maintaining effective communication [Int. 10].



The pandemic itself has changed as infection, hospitalisation and death rates have varied, and understanding of the pandemic has also developed over time [Int. 10]. Even when efforts to plan ahead were made, a sudden change in the course of the pandemic could render these preparations inadequate. For example, COG-UK anticipated that a surge in sequencing capacity would be required over the winter of 2020 due to the typical seasonal variation in infection rates of viruses from the coronavirus family. The consortium began preparing for this surge capacity during the summer of 2020. However, the emergence of the Alpha (B.1.1.7) variant required an unexpectedly rapid change of pace they had not accounted for [Int. 8].

COG-UK is also intimately linked with the wider public health testing system, which has had a downstream impact on the consortium's work every time that system changed, necessitating the establishment and nurturing of new relationships and workflows [Int. 10]. As one interviewee highlighted:

*'We are a part of a bigger ecosystem, and that ecosystem is often changing – constantly changing – and we need to try and keep up with it.'* [Int. 10]

**Despite the inevitable challenges that a changing environment gives rise to, the urgency of a pandemic also helped enable rapid progress and influenced the consortium's agility and adaptiveness.**

The pandemic's urgency rapidly mobilised goodwill, fostered trust and helped remove some level of bureaucracy that would typically be a part of establishing complex consortia. For example, it incentivised people and institutions to establish arrangements such as material transfer agreements faster than under normal circumstances [Int. 3]. One interviewee highlighted that COG-UK was only established at such a pace and scale because of the pandemic, suggesting it would have likely taken

years to establish such a network within a less urgent context [Int. 3]. Another interviewed expert commented in a similar light:

*'There was a fire raging and we needed to try to put it out.'* [Int. 7]

However, a fire-fighting mode is unlikely to be sustainable for the long term. This acknowledgement was part of the reason for the transition of sequencing activity to PHAs so that academics could focus on research and analyses [Int. 7].

Alongside the skills of the people involved, the consortium's novelty and experimental nature have helped support its agility and adaptiveness. According to one interviewed expert, the ability to respond to changes in sequencing demands in a conventional public health virology network would have been very difficult [Int. 5]. The involvement of people in academic genome sequencing core labs, with backgrounds in R&D and in-service development, also supported agility:

*'COG-UK has been criticised for being an academic-led, quasi-research operation, but actually that is one of the key factors enabling them to be so agile and adaptable.'* [Int. 5]

There was a clear consensus among interviewees that COG-UK could have long-lasting beneficial consequences for the wider public health genomics landscape. Within this broad consensus, however, there were more nuanced arguments. Some suggested that COG-UK should have a more focused role in the future, e.g. training [Int. 8], while others saw an argument for keeping COG-UK as a strong network supporting UK-wide research [Int. 2, 13]. Another view was that COG-UK remains a valuable way to maintain momentum and dynamism in the field of public health genomics as a whole [Int. 1]. At least one interviewee noted its potential contribution to continued innovation [Int. 3]. At the same

time, another cited the benefits of having a 'relationship holder' between the genomics research community and the government [Int. 18]. Regarding how COG-UK might operate in the future, one interviewee noted that the way academic researchers could work together during a crisis might not be sustainable in more 'normal' times [Int. 10]. There was also

a view that delivering a beneficial legacy did not necessarily require COG-UK to continue in its current form [Int. 12, 20]; instead, the networked pathogen genomics platform COG-UK helped establish is likely to have an important role in managing future research needs in response to public health threats.



## CHAPTER 6

# **Conclusions and next steps: a sustainable and scalable legacy?**



In this final chapter, we reflect on the scalability and sustainability of COG-UK's legacy in the wider public health genomics landscape in light of the learning gained. The previous chapters show widespread agreement that COG-UK has made a significant and valuable contribution to the UK's public health genomics landscape. Second, as a response to a global pandemic, we have argued that there is much to learn from this agile, focused and (in terms of its primary aims) successful consortium. For both these reasons, it provides fertile ground for considering important questions regarding the future of sequencing and public health genomics in the UK and beyond. By understanding COG-UK, we find important lessons (but not an entirely transplantable blueprint) for future action. Given the way the consortium operated in the phase of existence covered in this evaluation – relying heavily on a firefighting mode of operations and individual and institutional goodwill – some adaptations and a long-term resourcing strategy would be needed to support the sustainability of the consortium and its ability to tackle other public health threats in the UK and coordination with international initiatives.

### **6.1. How might COG-UK's achievements be used to contribute to a sustainable and scalable legacy?**

When reflecting on the original theory of change set out by COG-UK (as introduced in [Section 3](#) of this report), the consortium's evolution demonstrated progress against all the categories of desired achievements set out in the theory of change. The absence of tightly specified targets and milestones for most activities is related mainly to the rapid emergence of COG-UK and being set up to operate, adapt and respond to a time of crisis. Therefore, it is not possible to make definitive

claims about whether the progress made was sufficient or not. However, it is clear COG-UK made significant contributions to the pathogen-genomics landscape and COVID-19 response on various fronts. We can summarise these achievements (all discussed more fully in previous chapters) as follows:

***COG-UK mobilised and energised sequencing services, research-and-analytics capacity and capabilities to contribute to the knowledge base about SARS-CoV-2 and demonstrated 'real-world' utility and impact in supporting the pandemic response:*** This included

overcoming logistical and administrative challenges and achieving testing at scale. It also included advancing the infrastructure and relationships that support data-sharing, data-linkage and open access to data analytics and methodological tools. The consortium also ensured ways to share practical know-how quickly across the country, using data, analyses and interpretation expertise to support policymaking and public health interventions and inform vaccine effectiveness evaluations. Sequencing is one area where clear targets were exceeded. COG-UK initially set out to sequence 180,000 genomes between April 2020 and September 2021. However, the consortium exceeded that target multifold, sequencing over 800,000 SARS-CoV-2 genomes across the UK between 1 April 2020 and 31 July 2021. However, this scale of sequencing influenced how much the consortium could focus on research studies.

***Public health genomics skills, expertise and infrastructure across the four nations were rapidly redirected to support the COVID-19 pandemic response, and COG-UK's resources and activities contributed to strengthening pathogen genomics capacity and capabilities across the UK.*** This effort entailed refocusing researchers, their careers and research efforts on COVID-19 public-health-and-sequencing priorities. It also involved profound

and far-reaching stakeholder engagement, up-skilling of existing talent and training the next generation of leaders. Such efforts enabled the creation of a new paradigm for thinking about the role of pathogen genomics in the UK public health system's preparedness and resilience to deal with infectious disease emergencies. This was made possible due to the pre-existing relationships and infrastructure COG-UK mobilised and the new relationships it established. Another key enabler was the leadership and commitment of individuals across academic organisations, public health agencies, NHS sites and other diagnostic settings and across England, Scotland, Wales and Northern Ireland to make a difference to the public health response and the devastating impact of the pandemic.

***Building a UK-wide fully functioning genomics consortium at an unprecedented pace and scale fundamentally depended on rapidly mobilised resources and a leadership focus on building a distributed network with central coordinating capacity. There is an opportunity ahead to ensure the sustainability of the 'community of practice' COG-UK established and its applicability to future public health threats.*** The governance, management, operational and logistics arrangements enabling this were a significant output in and of themselves, potentially offering an adaptable model to future public health genomics collaborations in the UK and internationally. However, the degree to which the COG-UK networked approach will end up being a sustainable, long-term platform able to support UK resilience and preparedness for future pandemics remains to be seen. As we elaborate on below, it will depend on continued financial investment, broader efforts to nurture and expand the progress made in requisite relationships and skills and wider

developments in the data and data-linkage infrastructure COG-UK has invested in.

***As we have shown, the consortium has also had some international influence and impact on global pathogen-genomic sequencing efforts and skills.*** However, there is untapped potential to expand on international impact through enhanced training activity. Moreover, there is an opportunity to expand the mutual exchange of insights and learning COG-UK can offer and gain from others through deeper and wider-reaching embeddedness in global networks and collaborations.

## **6.2. Looking to the future, there are a series of important considerations for decision makers to reflect on in light of learning from COG-UK's experience**

At the time of producing this report – November and early December 2021 – the UK faced a critical moment in shaping COG-UK's legacy. There is an opportunity to build on the momentum, expertise, experiences and relationships that have developed since April 2020 and build a public health genomics ecosystem with pathogen-sequencing networks at its core. This legacy could contribute to strengthening networks across the UK and encourage cross-organisational and interdisciplinary working. It could add further to the global presence of UK science. These potential benefits should be sufficient to command the interest of policymakers and research leaders. However, the benefits of investing in sustainable pathogen genomics research and sequencing capacity also need to be balanced and actioned with due recognition of wider public health system capacity building

needs and investments (beyond genomics alone) and interconnected with them.

The model through which COG-UK contributed to the COVID-19 pandemic response in the UK was not designed to be sustainable in its current form, in that the academic sites in the network were originally not envisaged as a supplier of routine sequencing services but as a research network. The consortium is transitioning back to academic institutions focusing on research and analysis to support advancement of knowledge and to provide answers to questions of public health significance. Therefore, what needs to be sustained is not necessarily the network as it operated during this evaluation's timeframe but the ecosystem built around COG-UK's work.

In this light, COG-UK's legacy will depend on the abilities of decision makers in the public health system to transition from an emergency response operation to a legacy of sustained impact. This transition will require decision makers to:

1. Deliver public health genomics capacity guided by a clear, prioritised, long-term strategic plan;
2. Maintain momentum, motivation and goodwill to support a network that can bring together diverse types of organisations across the four nations without overly relying on goodwill alone;
3. Ensure the involvement of all relevant actors;
4. Stabilise and ensure adequately funded governance, management and administrative arrangements to support networked pathogen-genomics capacity in the UK;
5. Advance data linkage in the public health landscape;

6. Ensure a sustainable division of labour between diverse stakeholders in the public health genomics landscape;
7. Revisit COG-UK's role (or of its legacy) in the global pathogen genomics landscape.

#### **6.2.1. Delivering public health genomics capacity guided by a clear, prioritised, long-term strategic plan developed in a stakeholder-inclusive way**

The immense stakeholder goodwill and resource injection towards COG-UK's establishment should not undermine the need for a clear, prioritised and implementable long-term strategic plan to nurture public health genomics research and sequencing capacity in the UK. Any such plan will likely need to reconcile potentially different public-health investment priorities among stakeholders. Clarity of purpose and leadership that can articulate a vision and work within a distributed leadership system across organisational boundaries and the four nations will be needed to support the implementation of a sustainable and scalable plan of action.

Building a new and energised shared vision with feasible, suitable and acceptable goals is critical. Such goals will need to reflect the scientific community's priorities and those of citizens and patients and align with government and public health decision makers' long-term priorities across the UK's four nations. A long-term vision should balance the 'supply' of public health genomics insights and the informed 'demand' to use them.

#### **6.2.2. Maintaining momentum, motivation and goodwill without overly relying on goodwill alone**

COG-UK has built and benefited from goodwill and a shared sense of purpose across the worlds of genomics research, public health and sequencing. The result was an appetite for



pathogen genomics research and sequencing as an essential element of the COVID-19 response. This shift changed how many decision makers view and value public health genomics. However, as COVID-19's context within public health becomes less one of crisis and more one of 'the new normal', the question for decision makers is how COG-UK's diverse multi-stakeholder community can continue to share goals and work towards the public interest. Maintaining momentum is not only about goodwill; long-term funding and sustaining committed leadership will also be key. Ensuring a workforce-development strategy that considers novel PHA career pathways to support the transition of routine sequencing from research institutions to PHAs will also determine the success of any efforts to harness and propel COG-UK's legacy.

Sustaining a vibrant and connected pathogen-genomic landscape beyond the COVID-19 response will also depend on how effectively this landscape is convened, led and coordinated. COG-UK's leadership established guiding principles that helped steer the ship in times of crisis. However, if COG-UK (or some similar entity) does not play these convening and leading roles in the future across different types of infectious-disease needs, then decision makers need to understand where such leadership might come from. For example, a single national authority such as the UK Health Security Agency has a broader remit and would have to demonstrate the technical capacity to convene the delivery of sequencing, research activity, training, methodological tool development and inter-organisational collaboration in the public health system. It would also need to secure academic and public health support across the regions and nations of the UK and balance a coordinated national approach to overseeing public health genomics activity whilst at the same time recognising and responding to

some unique local needs in the devolved nations. Should coordination and convening functions reside in a networked institutional structure (i.e. a consortium akin to COG-UK), there would be a need to identify elements of the current leadership, governance, management and coordination model and membership that apply to new infectious disease areas and where unique demands may lie.

### **6.2.3. Ensuring the involvement of all relevant actors**

COG-UK was set up at speed and built upon existing networks without the time or necessity for a stakeholder analysis to ensure all potential contributors were integrated optimally into consortium activities. For example, the private sector is an important source of innovation that can bring additional resources. Therefore, it is worth reflecting whether particular industry actors would need to be involved in a future effort building on COG-UK's legacy. Expanding pathogen-genomic sequencing-and-research capacity, bolstering data-linkage infrastructure, growing international collaboration and strengthening UK-wide governance are also likely to involve wider groupings than those currently involved in COG-UK.

Embedding the patient voice into future efforts will also be necessary as the pathogen-genomics effort moves away from fire-fighting modes of operating. Patient and public engagement and involvement informing priorities for a future pathogen-genomics research network in the UK will help ensure that research activities answer questions of relevance to the society that research advancements serve.

Our evaluation suggests a further potential to extend the role of pathogen genomics in the NHS. This endeavour would require close engagement between public health genomics researchers and NHS staff to identify the types

of analytics that would be most meaningful in informing NHS service delivery. Examples include analytics related to issues such as timely outbreak identification, infection prevention and control and understanding links between different patient profiles, disease severity, treatment options and patient outcomes.

#### **6.2.4. Stabilising and ensuring adequately funded governance, management and administrative arrangements to support networked pathogen genomics capacity in the UK**

Good governance and appropriate management-and-administrative arrangements are essential for effective working in networked models of delivery and for accountability. COG-UK was established at high speed and in response to an impending emergency. Although the governance arrangements worked in a time of crisis, they would need to be revisited and appropriately funded in any future that sustained the legacy of COG-UK. Governance arrangements would have to consolidate and expand on COG-UK's four-nations approach, as infectious disease threats know no boundaries. In the context of collaboration between diverse stakeholders, governance arrangements would also have to respect the Haldane principle<sup>134</sup> that guarantees academic researchers their independence while also supporting synergies, maintaining networks and ensuring leadership for a shared sense of purpose across research-and-sequencing services.

At the same time, governance arrangements would need to support collaborative work across diverse institutional structures. During the rapid

response to COVID-19, much bureaucracy was streamlined or worked around – enabling contractual arrangements in COG-UK to support collaboration between organisations across different stakeholders. These arrangements may not be sustainable or scalable under 'normal' conditions, given the different rules and operating procedures in various settings across the UK. However, our data suggests that attention should be given to where and how far such elements may be adaptable for future efforts. Further research would be needed to understand this important question.

#### **6.2.5. Advancing data linkage in collaboration with other key actors in the health data infrastructure**

One of the fundamental success criteria for future public health research efforts and their ability to support preparedness, resilience and response to future pandemic threats is the ability to establish and sustain an effective data infrastructure that links genomics data with patient and wider public health systems data. Linked data sets will be fundamental to understanding the relationship between infectious-disease genetics and infectious agent behaviour on the one hand and disease severity and patient outcomes on the other. It will also underpin efforts to inform the development and evaluation of medical innovations (e.g. vaccines, therapeutics and diagnostics) and efforts to understand the effectiveness of non-pharmacological public health interventions. COG-UK has, with partners and with the support of the CLIMB data and cloud computing infrastructure held by public health partners,<sup>135</sup> already made significant

134 UK Parliament (2021).

135 Funded by the MRC, CLIMB launched in 2016 as a shared computing infrastructure for the medical microbiology community. It is a collaboration between Warwick, Birmingham, Cardiff, Swansea, Bath and Leicester Universities, the MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, and the Quadram Institute in Norwich: <https://www.climb.ac.uk/>

strides in linking viral-genome data and some types of patient metadata (e.g. epidemiological data). Wider collaboration in the future will be needed on data-linkage issues if COG-UK's legacy is to be sustained and extended. With this in mind, COG-UK joined the Health Data Research Alliance in the summer of 2021 to contribute to creating an ever-more unified approach to the use of health data across the UK<sup>136</sup> as well as to work with partners on issue related to data standards and quality, and patient, practitioner and public engagement.

#### **6.2.6. Achieving a sustainable division of labour between diverse actors with a stake in the public health genomics landscape**

As routine sequencing activity transitions to PHAs in the UK, attention is needed to ensure the sustainability of the workforce necessary to service routine sequencing requirements. PHA capacity will need to be built and scaled to avoid resorting to the safety-net of university sequencing sites. PHA staff who can support public health genomic sequencing activities need to be budgeted for, employed and trained.

Similarly, COG-UK has trained researchers across the UK to support pathogen genomics research. Many early-career and established researchers paused their non-Covid-19 related research to assist with the pandemic response, including routine sequencing activities. The transition of routine-sequencing funding to PHAs has left some researchers without the support needed to continue in their roles. Trained staff represent future research leaders for public health; retaining the skills and capacity built up in the academic system will also require focus and investment from the research-funding community.

At the same time, it would be helpful to consider how workforce needs might differ if COG-UK (or its legacy) were to become a pathogen genomics sequencing research-and-analysis network for other infectious diseases (e.g. influenza or Respiratory Syncytial Virus) and other types of challenges where pathogen genomics activity could be useful (e.g. antimicrobial resistance). The expertise needed to support a broader scope is not fully known. Much of COG-UK's core infrastructure, e.g. institutional relationships, equipment and facilities, may readily apply to other conditions. However, further research will be needed to identify which skill requirements may be unique and which new relationships need to be established in the public health genomics landscape. In particular, the applied nature of much of public health genomics researchers' work participating in COG-UK may call for upskilling the workforce in interdisciplinary approaches to public health genomics research to ensure outputs that lead to actionable and practical knowledge and insights.

#### **6.2.7. Revisiting the UK's role in the global public health genomics landscape**

COG-UK has bolstered the role of UK science in the global public health genomics landscape. As discussed earlier in this report, COG-UK members' advice and expertise have impacted how other international efforts addressed the sequencing, research and analysis needs of responding to the COVID-19 pandemic. COG-UK not only focused on training UK researchers and public health experts but also staff internationally. Further potential exists to develop COG-UK as a global training resource and network for sharing expertise. This endeavour would require resourcing and collaboration with international authorities such

as WHO, the US Centre for Disease Control, the European Health Emergency Preparedness Authority and European Centre for Disease Prevention and Control as some potential examples, to help focus training efforts and facilitate the mutual exchange of international expertise.

At the same time, COG-UK is primarily built on UK data; a future legacy effort would benefit from an explicit focus on integrating

data, analyses and insights from international experiences as well. This process would help minimise the risk of the UK's public health system working in isolation from wider efforts towards preparedness and resilience to future public health threats. It would also potentially support coordinated divisions of labour globally, in terms of prioritising and answering key research question of global health significance.

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