Large scale genomic surveillance of SARS-CoV-2 in the UK: challenges and lessons learned

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Genomic Surveillance Operations Lead

28th of September 2021
Wellcome Sanger Institute

A world leader in genome research that delivers insights into human and pathogen biology that change science and medicine
Our Covid operations so far...

- **Samples handled**: +20 million
- **Weekly capacity**: 50,000
- **Variants of concern reported**: +400k

COVID-19 surveillance (as of 20 September 2021)

- **690,348**: coronavirus genomes sequenced by the Sanger Institute
- **1,024,987**: coronavirus genomes sequenced by the COVID-19 Genomics UK (COG-UK) consortium
- **300+**: Sanger staff have contributed to the 7-days-per-week operation
Believe it or not, 18 months ago, this is how we started
Completely new challenge!
We were figuring out how to work as a large team to best effect

First stand up meeting on the 17th of March 2020
Tanya Brooklyn chairing
“The teams, they didn’t have to come on site. You volunteered to come on site and everyone put their hands up. It was great!”
High throughput genomic monitoring of the SARS-CoV-2 virus in the UK, aiding public health officials in their response to the coronavirus pandemic.

Monitor the virus for genetic mutations which could have public health implications
Operational Data Flows

- Box manifest (which plates in which boxes)
- Plate Maps (which sample in which well)

Sample Metadata Flows

- Sample prioritisation for sequencing
- Samples filtered out
  - Samples with ct values >30
  - Plate maps, barcodes and box manifests
- Samples of interest

Sample Flow

- Daily deliveries from all labs
- 7 day/week
- Boxes of 96 well plates of DNA/RNA extracts
- Barcoded boxes and plates

Check Point

- If above capacity, sample storage and destruction (after 7 days)
- Selected samples are protected

Upload to CLIMB

Reporting to UK government (including variants)
Samples storage

Five temporary refrigerated containers at the car park
Each container holds 273 boxes
Each box holds 80 96-deep-well plates (~2 million samples in each container)
New labs dedicated to Covid

Robotics: 4 Beckmans and 2 Bioseros
Redundancy and resilience - global shortages

7 Illumina Novaseq - 10k samples per machine.
Average 2.5M reads per sample
The Journey

April 2020
- Samples per week: 600
- Turnaround (days): 26
- Failure Rate: 30%

September 2020
- Samples per week: 3,000
- Turnaround (days): 19
- Failure Rate: 25%

Jan 2021
- Samples per week: 7,000
- Turnaround (days): 19
- Failure Rate: 20%

September 2021
- Samples per week: 40,000
- Turnaround (days): 5
- Failure Rate: 15%
Samples sequenced per week

- Samples sequenced
- Sanger's capacity

Number of samples sequenced

Week

20/04/2020 to 06/09/2021
Close to 50,000 samples sequenced per week.
Samples received and sequenced per week
Samples received and sequenced per week

- Samples sequenced
- Sanger’s capacity
- Samples received

181,000 samples received and sequenced per week.
### Journey of Improvement

#### Weekly average performance

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Covid: New variant found ‘due to hard work of UK scientists’

By Rachel Schraer
Health reporter

22 December 2020 | Comments

Coronavirus pandemic

How the U.K. Became World Leader in Sequencing the Coronavirus Genome

U.S. is catching up but most countries are way behind; Britain alerted world to new variant

The Wall Street Journal

UK variant hunters lead global race to stay ahead of COVID

By DANICA KIRKA March 28, 2021
Delta variant

https://covid19.sanger.ac.uk
COVID-19 Genomic Surveillance

TIMELINE
29 August 2021

NATIONAL OVERVIEW
England
Explore local authorities on the map

LINEAGES
- Alpha
- Beta
- Delta

TOGGLE ALL

Map
Lineage: Delta (AY.4)
Colour by: Proportion
Colour Scale: Quadratic

Incidence

Proportion

R

Data updated 5 September 2021, 17:31

https://covid19.sanger.ac.uk
Challenges

- Global shortage of supplies
- Constantly changing landscape
- Logistics - getting samples and metadata to Sanger
- Sheer volume of samples handled
- Large team work
- External dependencies
- Timeliness of outcome
- Managing expectations - everyone wants their samples sequenced!
- Sample prioritisation - outbreaks, Eagle project and samples of interest
- Internal reporting - build a new system to track samples
- External reporting to Department of Health and Social Care - manual then fully automated
- Staff self-isolating, limited number of staff on site
- Floods, fires, sweat and tears, but also laughter
Lessons Learned

- Develop a really good relationship across all parts of the end-to-end process including external organisation
- Do not focus on targets but seek improvement and perfection
- Work really hard at creating a single view of the process through performance data
- Expect bumps in the road, bend and flow with them and seek improvement over a long period of time
- Continually invest in the science and robotics and support functions (IT, Facilities, HR)
- Recruit lab leaders that are used to high throughput labs
- Develop more capacity than you need, to cope with issues and problems
- The data QC part of the process to ensure high quality of data.
- Difficulties were with the constantly changing landscape and external dependencies as it was hard to pick apart what changes were having impact as often another part of the process would also be in flux.
More to do...

Improve, improve, improve
Increase capacity
And more!
Acknowledgements

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Dominic Kwiatkowski
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