

ODAP Report 2022-23



Table of contents

1	Summary	1
2	Funding	2
3	Key Achievements	2
4	Problems	2
4.1	Recommendations	3
5	Outputs	3

1 Summary

The ODAP has created a globally-unique research capability combining clinical data, deep phenotyping, host genome sequence, viral sequence data and clinical trial data across the four nations of the UK. ODAP-delivered research has changed the global course of the Covid-19 pandemic, and the outbreak of unexplained hepatitis in children. ODAP combines the security of an accredited trusted research environment with flexible software tools and high-performance compute power, including state-of-the-art GPU compute for machine learning and artificial intelligence applications.

The key innovation in the ODAP is the overarching ISARIC Clinical Characterisation Protocol (CCP), which enables a single set of legal agreements and regulatory approvals to apply across multiple studies, vastly decreasing the complexity of data linkage. This is known as the [ISARIC Spine](#). The Spine offers investigators access to a range of other academic and clinical data sources, creating a significant incentive for researchers to contribute data to the platform.

Access to data is at the discretion of data controllers. ODAP offers to share data controllership with any data contributor who wishes to take advantage of this service, in order to lower the barrier for access. At present, data from the [ISARIC4C](#) and [GenOMICC](#) studies is openly accessible.

2 Funding

The ODAP is funded by the Baillie Gifford Pandemic Science Hub (PSH) at the University of Edinburgh, and the University of Edinburgh City Deal for Data Driven Innovation. The set up and design was funded by UKRI (MC_PC_19025, MC_PC_19059). Funding from the National Core Studies Data and Connectivity Programme (MC_PC_20029, administered by HDR UK) supported the programme from Sept 2021 to March 2023.

3 Key Achievements

- Data ingress and linkage
- 102 Publications
- 140 users from 12 institutions (Edinburgh, UCL, Cambridge, Sheffield, Liverpool, Glasgow, Imperial, Oxford, Newcastle, Dusseldorf, Leeds, Utrecht, Harvard, MRC, Leicester, Cardiff, UK Health Security Agency and Public Health Scotland)
- Support for research to answer key public health questions
- Support for NCS and UKRI-funded research studies
 - (CI: Kamlesh Khunti)
 - SLICK. Studying Long-term Impact of COVID on Kids. A consortium involving investigators from Edinburgh, Oxford and Liverpool using data from ISARIC4C and GP records to ask, “Do children and young people need extra follow up care after having SARS-CoV-2 infection?” Funded by Health Data Research UK and the Alan Turing Institute. (CI: Dr Olivia Swann, University of Edinburgh)
 - 4C Readmission. Investigating using artificial intelligence as an aid to predict the risk of hospital readmission in patients with COVID-19. Funded by Health Data Research UK and the Alan Turing Institute. (CI Prof Ewen Harrison, University of Edinburgh)
 - GenOMICC GPU Compute. Providing GWAS-on-the-fly using GPU compute architecture through a web browser, to provide effortless data access to the raw genotype and whole genome sequence data generated by the GenOMICC study (CI: K Baillie)
 - Cancer COVID (CI Prof Carlo Palmieri)

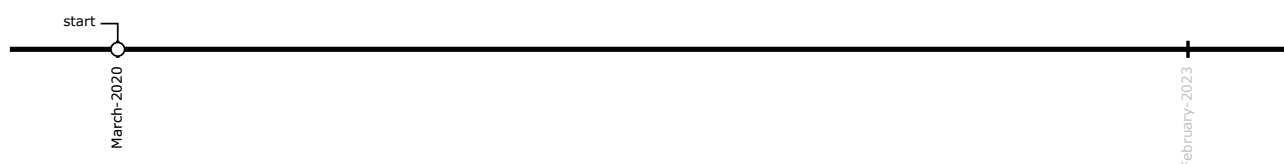


Figure 1: Timeline of data transfer and access activity

4 Problems

Fundamentally, data linkage on this scale is difficult, and the achievements of ODAP are globally unique. However there have been several key challenges in operational delivery of the ODAP. Specifically, the five-safes data access processes are not yet active. This is behind schedule.

- **Resources.** The core team were very under-resourced from the outset due to a combination of recruitment failures and prolonged sickness absence.
- **Project management.** In the current labour market, the very short-term contracts available in ODAP have not been attractive, so we were unable to recruit effective project management. The consequence has been poor coordination across the multiple delivery teams in three different branches (administration in

PSH, infrastructure in Edinburgh Parallel Compute Centre (EPCC), linkage and information governance in Public Health Scotland (PHS)). This problem was identified in Sept 2021 and led to the appointment of Ewan Harrison as ODAP Director, which ended in June 2022. Subsequent attempts to provide project management support from HDR UK on two occasions in Sept 2022 and Nov 2022 were not successful.

- **Legal complexity.** The requirement for data processing agreements for each data contributor with two legal entities (UofE and PHS) led to confusion, because the core team at UofE did not have oversight of legal agreements signed by PHS with data contributors.
- **Optimism.** The development of information governance and data access processes consumed more resource than anyone expected, to the exclusion of key events such as data ingress. Competing priorities between the CI (focused on data ingress and linkage) and one funder (focussed on data access processes) led to confusion and misdirection of the admin team.
- **Information governance expertise.** The core project team are lacking in data governance expertise, leading to an excessive dependence on overstretched institutional legal teams in UofE and PHS.

4.1 Recommendations

- **Project management & information governance (IG).** Appoint a dedicated director for the project, with high-level expertise in information governance and the capability to think creatively about solutions to IG challenges. This has not been possible due to the absence of sufficient long-term resource.
- Provide long term resource for employment of skilled staff.
- Control of funding should go with responsibility for delivery.

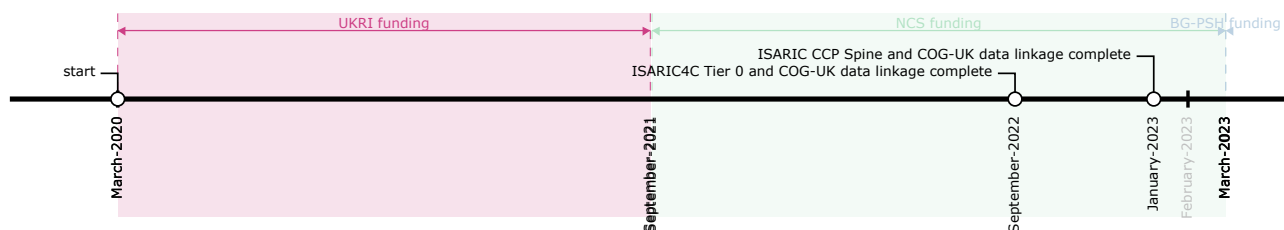


Figure 2: Timeline of data transfer and access activity

Plans:

[ppie2] startdate:nov22 enddate:jan23 [dagc2] dependency: ppie2

5 Outputs

ODAP has supported 102 papers with an average altmetric score of 611.

- Co-Infection with influenza virus is associated with worse outcomes in hospitalised Covid patients [[https://doi.org/10.1016/S0140-6736\(22\)00383-X](https://doi.org/10.1016/S0140-6736(22)00383-X)]
- Whole-genome sequencing reveals host factors underlying critical COVID-19 [<https://doi.org/10.1038/s41586-022-04576-6>]
- Risk prediction: the 4C Mortality Score [<https://doi.org/10.1136/bmj.m3339>]
- Characterisation of hospitalised cases of COVID-19 [<https://doi.org/10.1136/bmj.m1985>]
- Genetic mechanisms of severe Covid-19 [<https://doi.org/10.1038/s41586-020-03065-y>]
- Clinical characterisation of Covid-19 in children [<https://doi.org/10.1136/bmj.m3249>]
- Characterisation of in-hospital complications associated with COVID-19 [[https://doi.org/10.1016/S0140-6736\(21\)00799-6](https://doi.org/10.1016/S0140-6736(21)00799-6)]
- Treating COVID-19 patients with dexamethasone and remdesivir prevents neurological complications [<https://doi.org/10.1002/ana.26536>]
- Circulating histones play a central role in COVID-19-associated coagulopathy and mortality [<https://doi.org/10.3324/haematol.2021.278492>]
- Tissue proteomic analysis identifies mechanisms and stages of immunopathology in fatal COVID-19 [<https://doi.org/10.1165/rcmb.2021-0358OC>]

- Hospital acquired COVID-19 in England during the first wave of the pandemic [<https://doi.org/10.1186/s12879-022-07490-4>]
- Long Covid in adults discharged from UK hospitals after Covid-19 [<https://doi.org/10.1101/2021.03.18.21253888>]
- UK Paediatric COVID-19 cases in the first and second pandemic wave [<https://doi.org/10.1038/s41390-022-02052-5>]
- Vitamin D insufficiency in COVID-19 and influenza A [<http://dx.doi.org/10.1136/bmjopen-2021-055435>]
- Using a double binding antigen assay to detect and measure SARS-CoV-2 antibodies [<https://doi.org/10.1016/j.jviromet.2022.05.033>]
- Detecting SARS-CoV-2 by non-invasive means [<https://doi.org/10.1016/j.jinf.2022.05.033>]
- Understanding the Omicron variant and how it responds to vaccination [<https://doi.org/10.1016/j.cell.2022.06.005>]
- Evaluation of effectiveness of remdesivir in treating severe COVID-19 [<https://doi.org/10.1101/2021.06.18.21259072>]
- WHO guidelines on the use of chest imaging in COVID-19 [<https://apps.who.int/iris/handle/10665/361833>]
- Distinct clinical symptom patterns in patients hospitalised with COVID-19 [<https://doi.org/10.1038/s41598-022-08032-3>]
- Non-steroidal anti-inflammatory drug use and outcomes of COVID-19 [[https://doi.org/10.1016/S2665-9913\(21\)00104-1](https://doi.org/10.1016/S2665-9913(21)00104-1)]
- Role of blood cytokines IL-6 and GM-CSF in severe COVID-19 [<https://doi.org/10.1126/sciimmunol.abg9873>]
- T cells target many different parts of the virus [<https://doi.org/10.1038/s41590-020-0782-6>]
- Viral spike variants evading antibody-mediated immunity [<https://doi.org/10.1016/j.cell.2021.01.037>]
- Adeno-associated virus 2 infection in children with non-A-E hepatitis [<https://doi.org/10.1101/2022.07.19.22277425>]
- SARS-CoV-2 surface and air contamination in a healthcare setting [<https://doi.org/10.1093/cid/ciaa905>]
- Impact of ethnicity [<http://dx.doi.org/10.2139/ssrn.3618215>]
- Supporting vaccine development [[https://doi.org/10.1016/S0140-6736\(20\)31604-4](https://doi.org/10.1016/S0140-6736(20)31604-4)]
- ICECAP autopsy study [<https://doi.org/10.1164/rccm.202008-3265OC>]
- Viral RNA found in blood is not infectious [<https://doi.org/10.12688/wellcomeopenres.16002.1>]
- Developing methods of sequencing the virus [<http://doi.org/10.3390/v12101164>]
- Nuclear magnetic resonance signals in urine [<https://doi.org/10.1021/acs.analchem.2c00466>]
- Adverse outcomes in COVID-19 patients with underlying respiratory conditions [[https://doi.org/10.1016/s2213-2600\(21\)00013-8](https://doi.org/10.1016/s2213-2600(21)00013-8)]
- Pulmonary Microthrombosis and Vasculitis in Life-Threatening Respiratory Virus Diseases [<http://doi.org/10.1093/ofid/ofaa640>]
- Using imaging in COVID-19 – UK National COVID-19 Chest Imaging Database [<http://doi.org/10.1183/13993003.01809-2020>]
- Outcomes of hospitalised COVID-19 patients with interstitial lung disease [<https://doi.org/10.1164/rccm.202007-2794oc>]
- Outcomes of COVID-19 hospitalisation among patients with HIV [<https://doi.org/10.1093/cid/ciaa1605>]
- Co-Infections, Secondary Infections, and Antimicrobial Usage [[https://doi.org/10.1016/S2666-5247\(21\)00090-2](https://doi.org/10.1016/S2666-5247(21)00090-2)]
- Testing the tests [<https://doi.org/10.12688/wellcomeopenres.15927.1>]
- COVID-19 and Cancer [<http://doi.org/10.1136/esmoopen-2020-000825>]
- Detection of antibodies to determine population exposure [<https://doi.org/10.2807/1560-7917.ES.2020.25.42.2000685>]
- Symptom clusters [<https://doi.org/10.1101/2020.08.14.20168088>]
- New immune biomarkers for COVID-19 [<https://doi.org/10.1111/imm.13585>]
- Vulnerability of Down's syndrome (DS) patients to severe COVID-19 [<https://doi.org/10.1016/j.eclinm.2021.100769>]
- Modelling the association of tiered restrictions with COVID-19 deaths and hospital admissions [[https://doi.org/10.1016/s1473-3099\(20\)30984-1](https://doi.org/10.1016/s1473-3099(20)30984-1)]
- Multi-model forecasts to inform the response to COVID-19 in the UK [<https://doi.org/10.1101/2020.11.11.20220962>]
- Admission Blood Glucose Level and Its Association With Cardiovascular and Renal Complications in Patients Hospitalized With COVID-19. [<https://doi.org/10.2337/dc21-1709>]
- Clinical features and prognostic factors in Covid-19: A prospective cohort study. [<https://doi.org/10.1016/j.ebiom.2021.1033>]
- Device-assessed sleep and physical activity in individuals recovering from a hospital admission for COVID-19: a multicentre study. [<https://doi.org/10.1186/s12966-022-01333-w>]
- Estimating distribution of length of stay in a multi-state model conditional on the pathway, with an application to patients hospitalised with Covid-19. [<https://doi.org/10.1007/s10985-022-09586-0>]
- Obesity, chronic disease, age, and in-hospital mortality in patients with covid-19: analysis of ISARIC clinical characterisation protocol UK cohort. [<https://doi.org/10.1186/s12879-021-06466-0>]

- Studying the Long-term Impact of COVID-19 in Kids (SLICK). Healthcare use and costs in children and young people following community-acquired SARS-CoV-2 infection: protocol for an observational study using linked primary and secondary routinely collected healthcare data from England, Scotland and Wales. [https://doi.org/10.1136/bmjopen-2022-063271]
- Endomembrane targeting of human OAS1 p46 augments antiviral activity. [https://doi.org/10.7554/eLife.71047]
- Clonal hematopoiesis is not significantly associated with COVID-19 disease severity. [https://doi.org/10.1182/blood.2022015]
- Potent cross-reactive antibodies following Omicron breakthrough in vaccinees. [https://doi.org/10.1016/j.cell.2022.05.014]
- Development and validation of the ISARIC 4C Deterioration model for adults hospitalised with COVID-19: a prospective cohort study. [https://doi.org/10.1016/S2213-2600(20)30559-2]
- Importance of patient bed pathways and length of stay differences in predicting COVID-19 hospital bed occupancy in England. [https://doi.org/10.1186/s12913-021-06509-x]
- Viral Coinfections in Hospitalized Coronavirus Disease 2019 Patients Recruited to the International Severe Acute Respiratory and Emerging Infections Consortium WHO Clinical Characterisation Protocol UK Study. [https://doi.org/10.1093/ofid/ofac531]
- Towards nationally curated data archives for clinical radiology image analysis at scale: Learnings from national data collection in response to a pandemic. [https://doi.org/10.1177/20552076211048654]
- Procalcitonin Is Not a Reliable Biomarker of Bacterial Coinfection in People With Coronavirus Disease 2019 Undergoing Microbiological Investigation at the Time of Hospital Admission. [https://doi.org/10.1093/ofid/ofac179]
- An international observational study to assess the impact of the Omicron variant emergence on the clinical epidemiology of COVID-19 in hospitalised patients. [https://doi.org/10.7554/eLife.80556]
- SARS-CoV-2 Omicron-B.1.1.529 leads to widespread escape from neutralizing antibody responses. [https://doi.org/10.1016/j.cell.2021.12.046]
- COVID-19 pneumothorax in the UK: a prospective observational study using the ISARIC WHO clinical characterisation protocol. [https://doi.org/10.1183/13993003.00929-2021]
- Pandemic, Epidemic, Endemic: B Cell Repertoire Analysis Reveals Unique Anti-Viral Responses to SARS-CoV-2, Ebola and Respiratory Syncytial Virus. [https://doi.org/10.3389/fimmu.2022.807104]
- Hospital-acquired SARS-CoV-2 infection in the UK's first COVID-19 pandemic wave. [https://doi.org/10.1016/S0140-6736(21)01786-4]
- A prenylated dsRNA sensor protects against severe COVID-19. [https://doi.org/10.1126/science.abj3624]
- Changes in in-hospital mortality in the first wave of COVID-19: a multicentre prospective observational cohort study using the WHO Clinical Characterisation Protocol UK. [https://doi.org/10.1016/S2213-2600(21)00175-2]
- Cycle threshold values are inversely associated with poorer outcomes in hospitalized patients with COVID-19: a prospective, observational cohort study conducted at a UK tertiary hospital. [https://doi.org/10.1016/j.ijid.2021.08.022]
- Omicron-B.1.1.529 leads to widespread escape from neutralizing antibody responses. [https://doi.org/10.1101/2021.12.03.47]
- Obesity, Ethnicity, and Risk of Critical Care, Mechanical Ventilation, and Mortality in Patients Admitted to Hospital with COVID-19: Analysis of the ISARIC CCP-UK Cohort. [https://doi.org/10.1002/oby.23178]
- Common, low-frequency, rare, and ultra-rare coding variants contribute to COVID-19 severity. [https://doi.org/10.1007/s00439-021-02397-7]
- Analysis of SARS-CoV-2 known and novel subgenomic mRNAs in cell culture, animal model, and clinical samples using LeTRS, a bioinformatic tool to identify unique sequence identifiers. [https://doi.org/10.1093/gigascience/giac045]
- Outcome of COVID-19 in hospitalised immunocompromised patients: An analysis of the WHO ISARIC CCP-UK prospective cohort study. [https://doi.org/10.1371/journal.pmed.1004086]
- Pregnancy and neonatal outcomes of COVID-19: The PAN-COVID study. [https://doi.org/10.1016/j.ejogrb.2022.07.010]
- The impact of viral mutations on recognition by SARS-CoV-2 specific T cells. [https://doi.org/10.1016/j.isci.2021.103353]
- Understanding the burden of interstitial lung disease post-COVID-19: the UK Interstitial Lung Disease-Long COVID Study (UKILD-Long COVID). [https://doi.org/10.1136/bmjresp-2021-001049]
- Ten months of temporal variation in the clinical journey of hospitalised patients with COVID-19: An observational cohort. [https://doi.org/10.7554/eLife.70970]
- Long Covid in adults discharged from UK hospitals after Covid-19: A prospective, multicentre cohort study using the ISARIC WHO Clinical Characterisation Protocol. [https://doi.org/10.1016/j.lanepe.2021.100186]
- A Hybrid Architecture (CO-CONNECT) to Facilitate Rapid Discovery and Access to Data Across the United

- Kingdom in Response to the COVID-19 Pandemic: Development Study. [<https://doi.org/10.2196/40035>]
- Residual Lung Abnormalities Following COVID-19 Hospitalization: Interim Analysis of the UKILD Post-COVID Study. [<https://doi.org/10.1164/rccm.202203-0564OC>]
 - Two doses of SARS-CoV-2 vaccination induce robust immune responses to emerging SARS-CoV-2 variants of concern. [<https://doi.org/10.1038/s41467-021-25167-5>]
 - Analysis of SARS-CoV-2 in Nasopharyngeal Samples from Patients with COVID-19 Illustrates Population Variation and Diverse Phenotypes, Placing the Growth Properties of Variants of Concern in Context with Other Lineages. [<https://doi.org/10.1128/msphere.00913-21>]
 - Prospective validation of the 4C prognostic models for adults hospitalised with COVID-19 using the ISARIC WHO Clinical Characterisation Protocol. [<https://doi.org/10.1136/thoraxjnl-2021-217629>]
 - Clinical characteristics with inflammation profiling of long COVID and association with 1-year recovery following hospitalisation in the UK: a prospective observational study. [[https://doi.org/10.1016/S2213-2600\(22\)00127-8](https://doi.org/10.1016/S2213-2600(22)00127-8)]
 - Safety, tolerability and viral kinetics during SARS-CoV-2 human challenge in young adults. [<https://doi.org/10.1038/s41591-022-01780-9>]
 - Hospital admission for symptomatic COVID-19 and impact of vaccination: analysis of linked data from the Coronavirus Clinical Information Network and the National Immunisation Management Service. [<https://doi.org/10.1111/anae.15677>]
 - SARS-CoV-2 RNA detected in blood products from patients with COVID-19 is not associated with infectious virus. [<https://doi.org/10.12688/wellcomeopenres.16002.2>]
 - Multi-ancestry fine mapping implicates OAS1 splicing in risk of severe COVID-19. [<https://doi.org/10.1038/s41588-021-00996-8>]
 - Impact of cardiometabolic multimorbidity and ethnicity on cardiovascular/renal complications in patients with COVID-19. [<https://doi.org/10.1136/heartjnl-2021-320047>]
 - Mendelian randomisation identifies alternative splicing of the FAS death receptor as a mediator of severe COVID-19. [<https://doi.org/10.1101/2021.04.01.21254789>]
 - Acute kidney injury in patients hospitalized with COVID-19 from the ISARIC WHO CCP-UK Study: a prospective, multicentre cohort study. [<https://doi.org/10.1093/ndt/gfab303>]
 - The COVID-19 pandemic and global environmental change: Emerging research needs. [<https://doi.org/10.1016/j.envint.2020.105750>]
 - Implementation of corticosteroids in treatment of COVID-19 in the ISARIC WHO Clinical Characterisation Protocol UK: prospective, cohort study. [[https://doi.org/10.1016/S2589-7500\(22\)00018-8](https://doi.org/10.1016/S2589-7500(22)00018-8)]
 - Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study. [[https://doi.org/10.1016/S2213-2600\(21\)00383-0](https://doi.org/10.1016/S2213-2600(21)00383-0)]
 - Pan-ancestry exome-wide association analyses of COVID-19 outcomes in 586,157 individuals. [<https://doi.org/10.1016/j.ajhg.2021.05.017>]
 - Fatal COVID-19 outcomes are associated with an antibody response targeting epitopes shared with endemic coronaviruses. [<https://doi.org/10.1172/jci.insight.156372>]
 - COVID-19 symptoms at hospital admission vary with age and sex: results from the ISARIC prospective multinational observational study. [<https://doi.org/10.1007/s15010-021-01599-5>]
 - Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. [<https://doi.org/10.1002/uog.23619>]
 - Fitting to the UK COVID-19 outbreak, short-term forecasts and estimating the reproductive number. [<https://doi.org/10.1177/09622802211070257>]
 - Using trained dogs and organic semi-conducting sensors to identify asymptomatic and mild SARS-CoV-2 infections: an observational study. [<https://doi.org/10.1093/jtm/taac043>]
 - SARS-CoV-2 environmental contamination from hospitalised patients with COVID-19 receiving aerosol-generating procedures. [<https://doi.org/10.1136/thoraxjnl-2021-218035>]
 - SARS-CoV-2-specific nasal IgA wanes 9 months after hospitalisation with COVID-19 and is not induced by subsequent vaccination. [<https://doi.org/10.1016/j.ebiom.2022.104402>]