A National Health Data Research Capability to Support COVID-19 Research Questions

SAGE Reporting: 28 April 2020

Executive Summary:

HDR UK has teamed up with NHS Digital, the UK Health Data Research Alliance, NHS national data custodians in Scotland, Wales and Northern Ireland, and national providers of specialist data to:

- Streamline and prioritise the most important health data research questions relevant to SAGE, policy makers and the NHS
- Enable a scalable approach to linked data across the four nations
- Provide rapid access to secure analytical environments for researchers to answer these questions to improve understanding and treatment of coronavirus.

The first report was presented to SAGE on 21 April.

Update 28 April:

A. New Research Insights (Pre-peer Reviewed Findings):

- **Cancer:** HDR UK London team members at University College London and DATA-CAN (HDR UK's National Health Data Research Hub for Cancer) researchers have investigated the potential increase in excess cancer deaths both directly and indirectly related to the COVID-19 crisis. As a result of the emergency, they estimate at least 6,270 additional deaths in newly diagnosed cancer patients alone. Over 78% of excess deaths occur in cancer patients with ≥1 comorbidity, highlighting a particularly vulnerable group of patients. The researchers analysed recent weekly data from major cancer centres in the UK and found a 76% decrease in urgent referrals from GPs for people with suspected cancers and a 60% decrease in chemotherapy appointments compared to pre-COVID-19 levels. Further details and pre-print can be found here.
- **Ethnicity:** Multiple research teams are developing insights associated with ethnicity, including:
  - ISARIC CCP-UK & CO-CIN study led by Calum Semple, commissioned by SAGE, paper reviewed at SAGE on 28 April 2020.
  - Universities Hospitals Birmingham: Clinical data from >2,200 patients with confirmed SARS-CoV-2 infection plus demographics, ethnicity, baseline co-morbidities, social deprivation index and outcome (death within the census date) were included in a preliminary observational analysis. Current evidence suggests those of South Asian ethnicity may be at risk of worse COVID019 outcomes (these patients were more likely to be younger (median age 61 years vs.77 years), have no co-morbidities (27.8% vs. 16.6%) but a higher prevalence of diabetes mellitus (48.1% vs 28.2%) than White patients), but further studies are needed to understand this. Potential to replicate this with DECOVID partners in London Foundation Trusts. Further details can be found here.

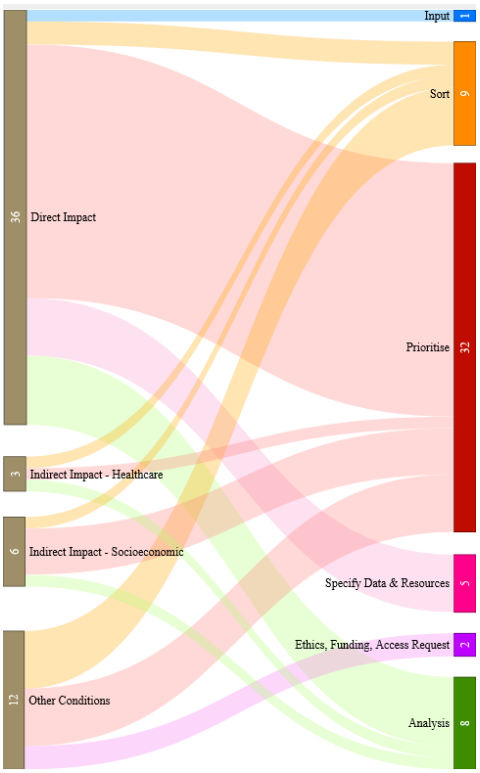
- Initial ethnicity analyses in England, by Public Health England, NHS Digital and The University of Liverpool, being made available for SAGE members.

- **Cardiovascular**: This week, the initial cardiovascular analysis (focusing on time trends in acute coronary syndromes based on hospital admissions data) led by Prof Colin Baigent (Oxford), as part of the NICOR/NHS England analysis approach, will be available for SAGE members. A broader set of analyses informing on the direct and indirect impact of COVID-19 on a wide range of cardiovascular diseases (including heart failure, stroke and others) and on the impact of cardiovascular disease on COVID-19 across all four UK nations is being coordinated by the BHF Data Science Centre.

B. New Research Questions:

- The Research Funnel[1] has received **60 questions** to date, prioritised **16 new questions** submitted in the week to 24 April, of which **eight were prioritised against four SAGE priority areas** (direct impact, indirect due to health care pressures, indirect due to socio-economic factors and other) - See Appendix
- Many of these questions directly relate to SAGE unanswered scientific questions, particularly those falling in to epidemiology, serology and immunology, clinical healthcare management and data science and engineering. - See Appendix
- Working with UKRI and NIHR to agree streamlined approach to commissioning SAGE research questions related to health data and big data estimated "go live" 5 May
- Questions from CRUK associated with presentation, diagnosis, management, prognosis and susceptibility have been identified and fed into prioritisation process for 30 April 2020

The following figure shows the questions by SAGE area[2], and by stage in the funnel:



[1] Health Data Research Question funnel – process description provided in Appendix 1 21 April SAGE paper

[2] 57 questions have been prioritised by the Urgent COVID Review Group and a further 3 have been prioritised by NIHR

C. Linked NHS data in English, Scottish, Welsh & Northern Irish Trusted Research Environments (TRE)

England TRE: NHS Digital Update

- **Coded GP data:** Significant progress on GP data in England for COVID-19 related research with agreement reached with the BMA/RCGP on 23 April to make a national coded dataset available in 4-6 weeks, for approved research, via the NHS Digital Data Access Request Service/Independent Group Advising on the Release of Data (IGARD) process *(Data Collection*).
- **ICNARC data:** The Intensive Care National Audit & Research Centre (ICNARC) dataset landed within NHS Digital on 24 April, to complement the CHESS, SGSS, and NICOR datasets, and enabling linked analysis and data access *(Data Collection*)
- **SUS+**: the 'raw and more timely form' of Hospital Episode Statistics provided by c.60 providers on a weekly basis is now being used for cardiovascular analysis, joined with CHESS and SGSS data for a range of analytical purposes. (*Analysis*)
- **Predicting ventilator and ICU demand**: Rollout started for predictive demand modelling for ventilators and bed capacity for individual providers (developed in partnership with Cambridge University) *(Data Analysis and Access*)
- **Trusted Research Environment**: Focus is on linkage and use of data, while the Data Processing Services (DPS) is rapidly matured, with additional analytical tools (e.g. Stata) being loaded. (*Infrastructure*)

Wales & NI TRE:

The Secure Anonymised Information Linkage (SAIL) databank - https://saildatabank.com/ provides remote access to linked datasets on the Welsh population and also acts as the TRE for the BREATHE health data research hub for respiratory disease. Data from SAIL are being used to support the Welsh Government COVID 19 Technical Advisory Cell, which feeds into SAGE. Multiple data sources are being brought together with a team of analysts and experts from academia, Welsh Government, Public Health Wales, NHS Wales Informatics Service and the All Wales Critical Care network to answer urgent questions relating to minimising four categories of harm from COVID19:

- **Direct harm to individuals** – monitor the spread of disease and its impact in individuals in communities, households, care home, school populations and vulnerable populations (shielding list, other clinical groups (high BMI), Black Asian and Minority Ethnic (BAME) groups; identify and characterise other potential risk groups; evaluate effectiveness of shielded group interventions and inform design of further shielding interventions and identify drug treatments that may have an unexpected beneficial or harmful use
- **Direct harm to NHS resilience** - contribute to development of models to ensure NHS resources are optimised to meet requirements
- **Indirect harm through suspension of routine health services** - monitor impact from suspension or delay of screening, planned surgery and other services and of individuals not presenting with urgent conditions.
- **Indirect harm through consequences of control measures** - monitor secondary impacts on other aspects of society, e.g. education and the economy, and unintended changes in health behaviours and their impact of mental and physical health and injuries.

BREATHE:

The Health Data Research Hub for Respiratory Diseases (BREATHE) is managing national access to the COVID-19 Symptoms Tracker Dataset developed by ZOE Global and KCL. Welsh and Scottish Governments have endorsed the app and have publicly promoted use of the app to aid with research in symptom spread in the community and tracking potential cases outside of direct healthcare locations. BREATHE analysts across the UK sites are feeding back directly to the Welsh, Scottish, and Northern Irish emergency COVID committees, and are working closely with organisations in England to set up similar pipelines and support mechanisms for localised and national tracker statistics.

Scotland TRE:

Prof Cathie Sudlow contributes to the Scottish Government's COVID-19 Data Task Force. Multiple healthcare and other data sources (e.g. census and education data) are being provided and linked within the Scottish National Data Safe Haven to enable a range of priority COVID-19 questions to be addressed and to support priority COVID-19-related research, approved by Scotland's Public Benefits and Privacy Panel.

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Appendix - List of Priority Questions

The questions are being prioritised by the HDR Urgent COVID Review Group[3] and categorised by SAGE priorities: Direct Impact (DI), Indirect Impact – Healthcare Pressures (I-HP), Indirect Impact – Socio-Economic (I-SE), and Other Conditions (OC). Questions of direct relevance to the SAGE unanswered science question list, (as shared on 24 April) are shown in **bold**. The top prioritised questions (prioritised 8 out of 10 and above) and their status is provided below. Questions that had already prioritised via NIHR are shaded in green, questions related to Cardiovascular Disease are shaded in orange and cancer in blue. We will also provide a short overview of the emerging insight for each of the priority questions where applicable. The full list of 60 active questions is available in our Matchmaker Tool. Questions that have been removed from our priority list are also included in the attached footnote[4].

MM Ref.	SAGE Category /SAGE Question	Date of input	Question	Prioritisation Score (Median)	Time since input (days)	Moved stage? ↑/–/↓	Current funnel stage	(Expected) data requested	Question posed by	Support to answer question	Emerging Insight[5]
RQ18	DI **Treatments & Preventative Measures (SQ26)**	02/04/2020	RECOVERY Can Lopinavir-Ritonavir vs Interferon β vs low dose corticosteroids be effective in treating COVID 19 test +ve hospitalised patients?	Auto prioritised	27	–	7	Complete	Peter Horby, Professor of Emerging Infectious Diseases and Global Health, University of Oxford,	NHS Digitrials (Martin Landray)	>7,000 patients recruited. Initial results expected in June. The key issue at present is obtaining data on the number of cases admitted per hospital per day so that recruitment can be benchmarked and remedial actions targeted. The mortality data should be flowing this week.
RQ05	DI, OC	02/04/2020	ISARIC-CCP What are the clinical characteristics of COVID-19 positive patients; what are the determinants (genetic, other omic, prior medical history, other) of good and poor outcome; and how can knowledge of this help to target clinical and public health strategies?	Auto prioritised	27	–	7	England, Scotland population/ demo-graphic datasets	Cathie Sudlow, HDR UK Scotland, Edinburgh; and BHF Data Science Centre,	Cathie Sudlow	Ongoing support with linkage in Scotland

[3] Urgent COVID Review Group Membership - provided in Appendix 3 21 April SAGE paper

[4] Removed question: *Is the rubella vaccination (or prior exposure to German measles) protective against COVID-19 due to shared capsid sequence homology between SARS-CoV2 and Rubella?*
Rationale for removal: Following analysis of international, publicly available data, the data support team concluded that there is insufficient ecological evidence to either strongly support or refute the hypothesis:

- We do not think that further health data analysis for age groups >40 would add value because of the lack of vaccination data and the unknown exposure to wild rubella
- The numbers of COVID-19 deaths of people <40 within UK is too small to provide meaningful insight if we do any correction for co-morbidities
- It would require a significant amount of work to collect and analyse the data on exposure and less severe outcomes for people <40 within the UK
- Therefore, weighing up the benefits / costs we don't think its sufficiently helpful to test this hypothesis further using health data

Our conclusions around the further use of health data do not mean that this is not a credible hypothesis, they purely mean that further health data analysis wouldn't add sufficient value. The analysis and responses from PHE are available here and here.

[5] Pre-peer reviewed findings

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RQ01	DI **Virology (SQ11)**	02/04/2020	COG-UK Can study of the whole virus genome enable scientists to monitor changes at a national scale, reveal how the virus is spreading and whether different strains are emerging?	Auto prioritised	27	–	7	Population clinical datasets (e.g. HES)	Ewan Harrison, HDR UK Cambridge; HDR UK fellow	Ewan Harrison	10,567 Viral Sequences now available online https://www.cogconsortium.uk/data/ This is the largest national repository of viral genome sequences in the world. Continuing to explore linkage to clinical data in each devolved nation.
RQ34 and RQ47	DI, I-SE	06/04/2020	How can we explain the differences in COVID-19 cases and deaths by key socio-demographic factors of age, sex, socioeconomic status, geographical location and ethnicity (BME groups)? Specifically, why do BME groups appear to have increased risk of severe COVID outcomes (e.g. ventilation and mortality)? How do these vary across the UK and compare against international cases? How can this information be used for more effective stratification and strategies? Initial aim: To investigate and quantify variation in the incidence (test-positive rate) and outcome of COVID-19 on individuals from Black, Asian and Ethnic Minority (BAME) populations in the UK.	10	23	↑	8	University Hospitals Birmingham NHS Foundation Trust & DECOVID Partner Trusts	Rhoswyn Walker Chief Science Strategy Officer, HDR UK; Aligned question submitted by Prof. Melinda Mills, Leverhulme Centre for Demographic Science, University of Oxford	Elizabeth Sapey, HDR UK Pioneer Health Data Hub & University Hospitals Birmingham NHS Foundation Trust	Clinical data from >2200 patient with confirmed SARS-CoV-2 infection plus demographics, ethnicity, baseline co-morbidities, social deprivation index and outcome (death within the censor date) included in a preliminary observational analysis. Current evidence suggests those of South Asian ethnicity may be at risk of worse COVID019 outcomes (including more likely to be younger and have no co-morbidities), but further studies needed to understand this. Potential to replicate this with DECOVID partners in London Foundation Trusts. Further details can be found here.
						↑	7	NHSD and PHE datasets); CHESS, SGSS, NICOR		PHE, Jem Rashbass, NHSD	

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						↑	8	ISARIC CCP-UK study and CO-CIN data set		Calum Semple, Liverpool	ISARIC CCP-UK & CO-CIN study led by Calum Semple, commissioned by SAGE, paper reviewed at SAGE on 28 April.
						–	5	ONS, ICNARC, DECOVID, DISCOVER-NOW		Ben Humber-stone, ONS DISCOVE-NOW	
RQ03	DI **Immunology and serology (SQ4, SQ6)**	07/04/2020	How do we support the scale-up of COVID-19 testing, by making sure that the data that is provided on the confirmed state of COVID-19 diagnosis and antibody levels is robust and reliable?	9.5	22	↑	7	Tissue directory	Philip Quinlan, Head of Digital Research Service at University of Nottingham, UKCRC Tissue Directory Coordinating Centre	Philip Quinlan	Ongoing, results so far: Helping PHE to plug gap in samples from those with mild symptoms. Connection has been made with project in Barts hospital, which involves the taking of blood samples from staff members (some of whom also displayed mild symptoms). Working with SME (Tissue Solutions Ltd) who are assisting with logistics to connect collection and sending samples for research. 20 requests for samples so far.
RQ50	DI **Immunology and serology (SQ4, SQ6)**	20/04/2020	How long will immunity last following infection, and what level of protection is available against different mutant strains? NEW QUESTION	9	9	↑	3		Chris Wigley & Parker Moss, Genomics England		
RQ04	DI **Epidemiology (SQ1)**	07/04/2020	How can we accurately measure the ongoing prevalence of COVID-19 in the population following identification of a "good enough" antibody diagnostic? (This requires representative and random sampling from the whole or at risk sub-populations)	9	22	–	3		Rhoswyn Walker, Chief Science Strategy Officer,		

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RQ32	DI, OC	06/04/2020	Understanding vulnerable patients: How are underlying conditions defined, and what is the impact of infection on a range of outcomes, and what are the benefits of 'shielding' and other preventive interventions?	9	23	–	4		Harry Hemingway, Professor of Clinical Epidemiology at UCL	Harry Hemingway & Spiros Denaxas	Initial understanding of underlying conditions supported by HDR UK COVID-19 Phenotype open resource. covid19-phenomics.org
RQ41	DI **Clinical Health Care Management (SQ20)**	07/04/2020	Are there any treatments which show evidence of improving outcomes for patients infected with coronavirus? Clinicians are having to make real-time decisions today, on the best possible treatment options for critically ill patients without robust evidence of harm or potential benefits of the therapeutic interventions. Better use of routine medication data could provide additional evidence to inform these decisions prior to the definitive outcomes of clinical trials.	9	22	–	3		Liz Sapey, Alastair Denniston, Tanya Pank Hurst, PIONEER & INSIGHT Hubs		
RQ59	DI, I-HP, I-SE, OC **Clinical Health Care Management (SQ23)**	21/04/2020	What are the direct and indirect effects of SARS-Cov2/COVID-19 on incidence, presentation, diagnosis, management, and prognosis of cancer patients and which patients are most susceptible to these direct and indirect effects?	8.5	8	↑	3	Linked datasets to including cancer registry, primary care and hospital records	Jonine Figueroa, Academic researcher, University of Edinburgh	Alvina G. Lai and Harry Hemingway UCL & HDR UK London Charlie Davie, Mark Lawler & the DATA-CAN Health Data research Hub team	Investigated the potential increase in excess cancer deaths both directly and indirectly related to the COVID-19 crisis. As a result of the emergency, they estimate at least 6,270 additional deaths in newly diagnosed cancer patients alone. Over 78% of excess deaths occur in cancer patients with ≥1 comorbidity, highlighting a particularly vulnerable group of patients. The researchers analysed recent weekly data from major cancer centres in the UK and found a 76% decrease in urgent referrals from GPs for people with suspected cancers and a 60% decrease in chemotherapy appointments compared to pre-COVID-19 levels. Further details and pre-print can be found here.

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RQ52	DI, OC **Immunology and serology (SQ4, SQ6)**	20/04/2020	What is the most effective approach (ease, cost and impact) for identifying people as recovered/immune so that they can come out of lockdown?	8.5	9	↑	3		Chris Wigley & Parker Moss, Genomics England		
RQ11	DI, I-HP, OC **Clinical Health Care Management (SQ16 & SQ23)**	02/04/2020	Where hospitals have EHRs is it possible to provide real time data on outcomes per COVID-19 admission by age and by co-morbidities by hospital? To understand whether there are hospitals that appear to have better outcomes for particular co-morbidity sub-groups (indicating potentially more effective interventions to learn from)?	8.5	27	↑	7		Jose Sousa, CTU Manager, School of Medicine, Dentistry and Biomedical Sciences, Queens University Belfast		
RQ29	I-HP, OC **Clinical Health Care Management (SQ16 & SQ23)**	02/04/2020	What is the influence of COVID 19 epidemic in the UK and the NHS response to this on presentation, management and prognosis of non-COVID disease, in particular cardiovascular diseases such as MI and stroke?	8.5	27	–	6-7		Cathie Sudlow, HDR UK Scotland, Edinburgh; and BHF Data Science Centre	BHF Data Science Centre	Analyses of acute coronary syndromes underway both by NHS England team and by an academic/NHSD/NHSE/ NICOR group, but emerging results have not available outside that group. Approvals being sought for broader set of analyses across all four nations and covering a broader set of cardiovascular conditions and procedures.
RQ48	DI, I-HP **Clinical Health Care Management (SQ23)**	12/04/2020	Cancer and COVID-19; how do we manage cancer optimally through a public health crisis?	8	17	↑	3		Mark Lawler, Faculty of Medicine, DATA-CAN		

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RQ27	I-SE, OC	13/04/2020	Can we predict the likelihood of ICU admission from COVID-19 patient demographics, pre-existing conditions, symptoms and clinical data collected on hospital admission?	8	16	↑	3	Patient-level de-identified hospital records for COVID patients	Marko Balabanovic, Medopad		
RQ57	DI, OC	20/04/2020	How can we build from existing studies (e.g. Kings and internationally) that have looked at the effect of ACE inhibitors and Angiotensin Receptor Blockers on predisposition to COVID-19, as well determining the severity of COVID, to ensure that all potential confounders are robustly addressed using larger and more diverse datasets? Particularly including older patients who are likely to be on multiple antihypertensives?	8	9	↑	4	Linked datasets (primary care, secondary care, COVID lab data, mortality data, intensive care data) across all four nations of the UK	Professor Sir Munir Pirmohamed, University of Liverpool	Cathie Sudlow BHF Data Science Centre	Small UK study (from Kings) which shows ACEI were protective against severe COVID + two studies from China which show the same. Another study from China shows a small (p=0.06) increase in risk. All of these are on preprint servers and have not been peer reviewed. Difficult to account for all confounding factors in these studies. Good to look at ACE-I and ARBs separately, as well as together.
RQ51	DI, I-SE **Immunology and serology (SQ 1 & SQ6)**	20/04/2020	Asymptomatic carriers: do they exist, and what proportion of the population fit into this category? Does this differ with age?	8	9	↑	3		Chris Wigley & Parker Moss, Genomics England		
RQ07 and RQ14	DI, I-HP **Data Science & Engineering (SQ32)**	02/04/2020	Can we use data science to support front line decision making in Intensive Care Units? E.g. at the point of peak need, if patient requirements outstrip ventilation capacity, how should hospitals stratify and prioritise patients for ventilation?	8	27	–	4		Simon Ball, Medical Director, University Hospitals Birmingham;	Hubs – Pioneer, Discover NOW	
RQ30	OC	02/04/2020	What is the influence of pre-existing cardiovascular disease on outcomes of COVID-19 infection?	8	27	↑	4-5		Cathie Sudlow, BHF Data Science Centre,	BHF Data Science Centre	

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RQ22	I-SE **Behavioural Science (SQ45)**	02/04/2020	What are the psychological, social and economic consequences of policies to limit the spread and flatten the peak of COVID 19?	8	27	–	7		David Porteous and Cathie Sudlow; HDR UK Scotland (on behalf of Generation Scotland and other UK cohorts)		
RQ23	DI, I-SE **Behavioural Science (SQ39)**	02/04/2020	Socioeconomic inequalities: Analysis by postcode IMD. What's the best way to provide targeted and tailored messages to diverse communities?	8	27	–	4		Linsey Hovard		
RQ35	DI, I-SE **Clinical and Health Care Management (SQ17)**	02/04/2020	How can we ensure that we fully understand variations in response to COVID-19 infection at the molecular, environmental, social and economic levels, by effectively coordinating the UK's longitudinal population studies to gain a much richer understanding of disease progression and outcomes?	8	27	–	3		Mary De Silva, Debbie Lawlor, Martin Tobin. John Danesh, Nic Timpson, & David Porteous; Wellcome Trust COVID-19 Longitudinal Population Study Steering Group		
RQ36	DI	02/04/2020	How can we maximise the speed and power of host genomic studies internationally to inform drug development?	8	27	–	3		Martin Tobin + (International) COVID-19 Host Genomics Initiative		
RQ39	OC	02/04/2020	Current guidelines recommend shielding is carried out for patients receiving immunosuppressants, however there is mixed evidence as to whether these patients will have poorer outcomes following coronavirus infection. Could we compare the outcomes data for patients who are receiving / not immunosuppressants and validate whether this population group are more vulnerable?	8	27	–	3		Liz Sapey, Alastair Denniston, Tanya Pank Hurst, PIONEER & INSIGHT Hubs		

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RQ40	OC	02/04/2020	Are there any concomitant treatments/ongoing prescribed medication which are making the outcomes of coronavirus infection worse for patients? This information would help clinicians to understand if there are any ongoing treatments which should be stopped as a priority when patients present with suspected COVID-19. For example, help to better understand existing theoretical associations between anti-hypertensives and NSAIDs and COVID-19 outcomes	8	27	–	3		Liz Sapey, Alastair Denniston, Tanya Pank Hurst, PIONEER & INSIGHT Hubs		