Written Evidence Submitted by

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Southampton University and the University Hospital Southampton NHS Foundation Trust are justifiably proud of their flexibility and impact in responding to COVID-19. As institutions, they have worked well together and levered significant results from their health, clinical and research communities. These communities responded with significant degrees of self-sacrifice, benefiting our frontline researchers, our local communities, and the citizens of the UK and wider afield. This report presents the views of several researchers and administrators keenly involved in the response to the pandemic from the University, the NHS Trust and the Wessex AHSN. Included are examples of how both University and NHS Trust responded to the COVID-19 pandemic.

Call for evidence

1. **The contribution of research and development in understanding, modelling and predicting the nature and spread of the virus;**

Basic and applied clinical research have played a fundamental role in advancing our understanding of SARS-CoV-**2.** A knowledge of the structure and function of the virus, revealing similarities to other viruses, has directed the search for potential therapeutics, as well as vaccines. Many research programmes pivoted very effectively from ongoing and unrelated research to focus on viral characteristics: A basic science example in Southampton would be the analysis of the spike glycoprotein, the structural element that allows viral entry to a cell (Crispin Lab, Biological Sciences[1]). Clinical and therapeutic examples are given below.

Data analytics and modelling at the local level are another outstanding product of the pandemic. Although planned as a strategic initiative between the University of Southampton (UoS) and the University Hospital Southampton Foundation Trust (UHS) prior to January, the pandemic, and close working relationship between these institutions, delivered analytics at pace. Existing clinical data activities, such as the Clinical Informatics Research Unit, were early responders but rapidly followed by new working groups, accelerated through collective action, of geographers, mathematicians, computer scientists and UHS data users and custodians. Analytics then played a guiding role in operational considerations around the management of the General Hospital. The importance of sound data collection and recruiting professional analytical and visualisation experts carries on through new COVID related initiatives, such as ENACT and local city-wide testing (below).

Southampton specific examples of data teams:

One team, nucleated around Electronics and Computer Sciences (Lead Prof. M. Boniface), formed in March from disciplines across the University (health sciences, statistics, data science and systems engineering), delivered tools and reports for decision makers in UHS (Business Intelligence, Chief Operating Officer, Medical Director) and more widely to the Hampshire and Isle of Wight region regarding localised insight and forecasting scenario analysis. Key results included modelling disease dynamics and hospital processes sufficiently to forecast hospitalisation, bed occupancy and deaths in response to questions regarding the time/size of peaks, impact of government social distancing policies, and in comparison with other modelling sources at regional and national level. Advanced modelling techniques are now embedded into hospital decision processes, laying the foundation

[1] Watanabe, Y et al. (2020) https://science.sciencemag.org/content/369/6501/330

for sustainable and efficient ways to manage capacity and demand for future waves. Continuous learning approaches have allowed for new sources of data (e.g. infection rates, death rates, mobility, 111 calls, etc.) to be incorporated into models as they come available, understanding of COVID-19 has increased, and modelling requirements changed (i.e shift from hospital to community impacts). The work has been disseminated widely across the Wessex region and nationally to maximise learning in advanced modelling techniques and how interdisciplinary data science teams can work with the NHS to solve challenging problems at times of crisis.

Another UoS Team, centred in Geography (lead Prof A. Tatem) mobilised to include modelling of intervention effects[2]; modelling of intervention coordination[3]; analysis and modelling of international spread, global mobility effects, transmission during train travel (in review); collaborative work with the Office of National Statistics on UK population mobility patterns and trends[4]; collaborative work with the UN on demographics mapping[5]; and support to various governments in sub-Saharan Africa on mapping[6].

The NIHR Biomedical Research Centre (Lead Prof R. Read) Data Science Cross-cutting team designed and set up a system to support the University Hospital Southampton Foundation Trust on the local Dashboard plan for daily pandemic monitoring. Working closely with other theme leads, the team supports COVID-19 studies extracting and integrating clinical and research data locally and collaborating with other NIHR infrastructures. Professor Anneke Luccassen is assessing the ethics and information governance to enable new approaches to clinical treatments. Work by the team has delivered an integrated data systems approach to SARS-CoV-2 testing and rapid communication of results to participants and the PHE SGSS system, making it an important exemplar for NHS Test-and-Trace. This has been recognised at the highest levels of government.

Integrated within the BRC Data Science cross cutting theme, the UoS Clinical Informatics Research Unit (CIRU: Lead Prof. Batchelor) hosts a number of groups which have been working effectively in response to the COVID-19 outbreak. Currently CIRU is working on 24 projects that range from Data Management Service and Research in Public Health, Clinical Informatics and the use of Artificial Intelligence and ML.

2. The capacity and capability of the UK research base in providing a response to the outbreak, in terms of:

Advice to government, public bodies and others on managing the outbreak

UoS and UHS have worked closely together and fed significant planning information into bodies such as the National Institute for Health Research and NHS Research and Development. These bodies have been decisive in their actions and collectively have influenced local, regional and national actions. At a wider and more central level, it seems from this vantage point that government itself could have done better in listening to and responding to, needs and alternative views outside of 'Golden Triangle' Universities.

Overall the UK responded to the COVID-19 pandemic slowly.[7] There is a very significant gap between the ambitions and efforts of the wider research community and the implementation of research outcomes. Even expedited, it may not be feasible to move from research to full-scale use at speed during a national crisis. One suggestion is that research efforts, to develop projected solutions, should therefore be focused during 'peace-time'. During a crisis the focus has to be away from long term research and on selecting and implementing existing or rapid turnaround solutions, some of which are ready to use here and now. The task of selection and implementation at scale is significant but arguably not one for the UK research base as exemplified by the urgent public

[2] https://www.nature.com/articles/s41586-020-2293-x
[3] https://www.medrxiv.org/content/10.1101/2020.06.16.20132688v1
[4] https://www.worldpop.org/covid19/uk_population_mobility/
[5] https://www.portal.worldpop.org/demographics/; https://unfpapdp.maps.arcgis.com/apps/MapSeries/index.html?appid=0f2d99e43fa94db68f5347d349433d45
[6] https://grid3.org/news/zambia-partners-with-grid3-to-produce-pop-estimates
[7] https://www.theguardian.com/world/2020/jul/24/lack-of-coronavirus-testing-and-ppe-among-uks-key-mistakes-mps-told

health (UPH) initiative that operated during COVID-19. That being said, crises also highlight weaknesses in the research base and in the systems and process for translating research into impact. It is also true, however, that central planning of research efforts seldom delivers and impedes the creativity that an advancing health system requires. There are also clear knock-on effects from adapting an ongoing research portfolio regarding 'business as usual' medical research (see below).

The development of testing, diagnostic methods and technologies

Engineering, physical sciences and chemistry offer tremendous potential for developing or enhancing testing, diagnostics and wellbeing. At the industrial level, as recognized in the Government Life Sciences Industrial Strategy, much of the commercial innovation is generated in the SME community; a fertile ground for university spinouts and building local economies. However, like the situation pre-pandemic the regulatory and approval apparatus, plus the procurement and administrative complexity, in getting any new medtech into application is appalling. Clearly, there is a need for regulation but there was no sign, from the Southampton experience, that central processes for streamlining were put in place and accelerated access made possible. This is in sharp contrast to the therapeutic and vaccine regulatory activity, which responded rapidly, decisively and effectively (see below).

Despite the above, the infrastructure built up through a long collaborative relationship between the University of Southampton and University Hospital Southampton permitted a very rapid response to the need for innovative PPE when the first patient was diagnosed at the Southampton General (the PeRSo project: H Morgan Electronics and Computer Sciences and P Elkington Medicine[8]). Other notable examples are, MisSO (producing supplies of vital solutions used to ensure facemasks for healthcare workers are fitted safely: D Boche, Medicine and S. Mahajan, Chemistry), and a molecular point of care testing device for Covid-19 (T Clark Medicine). Many other testing and diagnostic projects, as well as app development and patient, public and frontline support activities, have also taken place. See for a selection https://www.southampton.ac.uk/life-sciences/about/index.page

The development and testing of vaccines and therapeutics

Urgent Public Health procedures were very good at bringing a national and focused response. Individuals, universities and trusts, which were overseen by a flexible NIHR, performed admirably[9]. As a result, In terms of clinical trials and vaccines, the UK has been globally leading through the publishing of protocols and the running of clinical trials aiming to answer important questions. It needs to be noted that significant activity and impact took place out with the 'Golden Triangle', where resources and researchers are more distributed and focussed investment less. From Southampton, a good example is the Recovery Protocol – the trial that has given the world the three most important results in treatment trials so far: the use of Dexamethasone and Remdesivir, the uselessness of lopinavir-ritonavir, and harm of hydroxychloroquine. The Protocol generated a global impact as it influenced change in international guidelines three times within a month. While preparing this report to the Committee the University of Southampton and drug-development-company Synairgen Research Ltd have announced positive results from clinical trials of a drug (SNG001 - inhaled formulation of interferon beta) that may prevent worsening of COVID-19 in those most at risk. The odds of developing severe disease (e.g. requiring ventilation or resulting in death) during the treatment period (day 1 to day 16) were significantly reduced by 79 per cent for patients receiving SNG001, compared to patients who received placebo. A further example of pivoting to meet the pandemic challenge.

Research and development made an enormous contribution. In the space of four months, clinical research queried 4 possible drug treatments, ruled out 2 and brought the other 2 to application. A collaboration between

[8] Elkington et al. (2020) https://engrxiv.org/rvcs3/; Elkington & Morgan (2020) https://www.sciencedirect.com/science/article/pii/S016344532030236X?via%3Dihub

[9] https://www.theguardian.com/commentisfree/2020/jul/21/vaccine-treatements-interferon-beta-1a-therapy

the University of Southampton and the University of Oxford on the vaccine trial allowed the project to develop from Phase 1 to 2 in 4 months. This incredible achievement moved at a phenomenal pace.

At the same time, it is important to highlight the scale, range and depth of cross-cutting research undertaken by the National Institute for Health Research [NIHR] Southampton Biomedical Research Centre [BRC] during this pandemic, advancing the disease understanding and underpinning the clinical application. Flexibility in response is key. Highlights of the research undertaken are:

- **The Respiratory and Critical Care** team which has 25 projects and has recruited 1,856 participants. Specific to Southampton, this team ran a number of COVID-19 trials including a) trials to determine the safety and efficacy of inhaled SNG001 (IFN-□1a for nebulisation) for the treatment of patients with confirmed SARS-CoV-2 infection, b) a clinical trial of Bovactant (Alveofact®) for the treatment of moderate to severe COVID-19, c) the Safefit trial assessing virtual clinics to deliver universal interventions to maintain and improve mental and physical health in people with cancer who are following social distancing guidance, d) evaluating the clinical impact of routine molecular point-of-care testing for COVID-19 in adults presenting to hospital, e) COVID-19 infections in people with Primary Ciliary Dyskinesia and f) examining T cell responses in virus infection (ExCel).

- **The Nutrition Research** team ran 8 projects and recruited 10,323 participants. Studies have included surveying mothers and adolescent children to ask about their COVID-19 related experience from the Southampton Women's survey; assessment of Pregnancy and Neonatal Outcomes in COVID-19 (UPH); evaluation of risk of severe illness from COVID-19 in patients with metabolic dysfunction associated fatty liver disease and increased fibrosis scores; and a study to assess whether obesity is a risk factor for greater COVID-19 severity. On-going work continues with citywide saliva-based testing in Southampton, which will inform the Cabinet Office regarding lockdown release efficacy.
- **The Microbial Science** team has 15 projects and has recruited 1,649 participants. Studies include a repurposed MRC programme to develop a genetically modified bacterial vector vaccine expressing COVID antigens, an observational study of coronavirus infection in primary or secondary immunosuppressed children, and, assessing a patented, non-toxic disinfectant with long-term residual activity to safely decontaminate surfaces of SARS-CoV-2.
- **Vaccine Trials:** By combining resources, COVID-19 vaccine trials are currently being delivered including a phase I/II study to determine efficacy, safety and immunogenicity of the candidate d) vaccine ChAdOx1 nCoV-19 in UK healthy adult volunteers (OPEN) and a phase 2/3 study to determine the efficacy, safety and immunogenicity of the same candidate vaccine

The brilliance of this Southampton response does not come without a cost that should inform future practice. Despite the benefits of having regulatory and governance pooled, which enable the progress in vaccines and therapeutics outlined above to take place in weeks not years, this is not a sustainable process outside of the pandemic. For example, research, particularly academic, would be constrained. In order to focus on COVID-19, 30 studies were set up in days rather than months, with people working round the clock. The trade-off was clear as 600 ongoing and 200 planned clinical studies were paused. Further, the costs of COVID trials were not covered with thirty studies costing approximately £120 million out of a total Clinical Research Network fund of £250 million. The NIHR has picked up the costs for accelerated progress but other funders should be contributing. Now the system faces an impossible task; maintaining COVID research, sustaining treatment and restarting normal and research activities. The system will not cope. The Government needs to seek **broad national input** from the NIHR networks and the NHS Trusts' R&D and operational offices to develop a workable and proactive plan, for the present as well as for future crises.

Another tangential issue was the UoS approach to dealing with legal risks and decisions to furlough some of its staff, which limited, in some areas, its capability as a research institution to tackle the challenges posed by the pandemic. For example, researchers in psychology and in business, with all their potential transferable skills were not adequately utilised because of furlough rules.

3. The flexibility and agility of institutions, Government departments and public bodies, and processes to respond appropriately during the crisis including:

The availability and responsiveness of funding

Funding itself has not been a limiting factor in the research during the recent crisis. Rapid response mechanisms worked well (but see the section above on the gap in clinical trial costs). However, funding for SMEs to develop novel solutions was woefully inadequate. This was worsened by the fact that the UK does not have the breadth of skills in industry to rapidly develop diagnostic solutions, unlike the experience of South Korea in the early days of the pandemic.

The optimal functioning of regulatory and ethical processes

The regulatory and academic ethics processes have been streamlined. For example provision of an 'expedited route for CE marking for PPE'. For researchers, this allowed a more adaptive response to the COVID-19 challenge. However, there is still significant scope for improvement here. There has been a lack of clarity on the new expedited regulatory framework, a lack of transparency in how that is interpreted by the notified bodies, and a lack of clarity on what standards are needed above and beyond CE marking by the regulator in this area, the Health and Safety Executive ['HSE']. It appears that CE marking is necessary but not sufficient for PPE approval, and additional evidence above and beyond that needed for CE marking has been requested by HSE. The requirement to provide that evidence should have either been included in the CE mark, or suppliers should been made aware of the additional requirement at the start of a CE application, not at the end. As a result, a locally designed piece of PPE, with potential to have national impact, is not yet available to those who need it. We have seen many weeks of delays, in part because a public body has run a process sequentially which could have been run in parallel.

Public bodies within the national NHS structure have also provided 'open-inboxes' to suppliers and innovators. This is fast, and easy to initiate, but produces a very significant volume of unstructured information about what the offer is. Those same public bodies then lacked the expertise and capacity to triage through the large volume of offers. Whilst this situation was rectified after some weeks, valuable offers of industry support were unanswered for weeks, causing delay and frustration. The simple solution (now largely in place) is that all offers of support are made through online webforms which capture essential information and with clear processes in the back end for rapid first-line triage.

A streamlining of Information governance processes, through COPI (Control of Patient Information) Notices, has ensured that healthcare organisations, arm's length bodies and local authorities can share necessary data more easily in response to COVID-19. Easier access to the data benefits not only immediate service delivery but also research and planning for improving service delivery and individual treatment.

The availability and influence of scientific advice in all Government departments and public bodies—including by departmental Chief Scientific Advisers

This needs to be answered in a public enquiry. Currently, the impact of COVID-19 on the citizenship of the UK is one of the worst in the world.

The extent to which decisions taken drew on that advice

See above

4. The capacity to manufacture and distribute testing, diagnostics, therapeutics and vaccines: Both standing capacity and capacity able to be mobilised

The capacity and capability of the UK research MedTech base has been constrained. The issue lies in the process of regulatory approval at central government. This has been slow, poorly equipped and unable to cope. This impeded the potential of research conducted locally, and great delays have been caused to research ideas that could have had a positive national outcome. There was also lack of clarity on the applicable regulations and the

roles, and therefore capacity, of regulatory bodies. This was worsened by a necessity to simultaneously deal with multiple regulators, and by an inability to engage with key decision makers to promote solutions being advanced by research at the University. This made researchers hostages to regulations, which hinders innovation in time of need (a test that is 80% accurate is better than no test, and PPE that is 90% effective is better than no PPE). Further, the UK appears not to have the capacity and capability to assist groups/industry to develop novel technologies and to move these through the regulatory approval routes with the appropriate testing needed for deployment. It is worth remembering that 50% of the Life Sciences industrial activity is in SME led Medtech, employing more citizens than pharma (Life Sciences Industrial Strategy).

Centralising the testing for COVID was also an odd move when Universities during lockdown had capacity and staff to operate over regional areas. Mothballing space and furloughing talented staff, has had knock-on effects that would have been mitigated by better planning and use.

5. The capturing during the crisis of data of the quantity and quality needed to inform: decisions made during the crisis and to maximise the learnings afterwards

The COVID-19 crisis has starkly shown the deficiencies of a piecemeal health and care data environment that is oriented towards performance management. Inconsistencies in data collection and capture hindered the ability for commissioners to make the best-informed decisions. Moreover, the lack of infrastructure and staff to facilitate data integration, analysis and interpretation has hindered decision-making and learning. A better use of the wide academic and clinical communities would have improved the robustness of the analysis and the confidence borne out of inclusion.

6. The mechanisms for communication of scientific evidence internationally, within national governments and with the public:

See above for Geography engagement at the global level (1) and trial results influencing the international treatment of COVID-19 (2).

7. The UK's readiness for future outbreaks, including a consideration of: the National Risk Register; the UK Pandemic Influenza Strategy; and PHE's Global Health and Infectious Diseases Strategy.

Post pandemic wave 1, there is a need to continue with vaccine development and with COVID treatment and research, as well as a need to restart the paused programmes. From an NHS research perspective there is not enough capacity in the system. Clinical research is not prepared for a second wave. There is not enough staff, space, or critical facilities, such as imaging. (Pre-pandemic imaging was working at full capacity; now the machines need to be cleaned after every patient). While Clinical Research Facility staff are on vaccine trials, how can other studies take place?

A massive step change in virtual working does offer the possibility of much more streamline working across the knowledge creation/knowledge translation spectrum. It is possible to get people from diverse backgrounds and geographies in the same virtual room more readily and at vastly reduced cost. It is not a silver bullet but it is an enabler.

(July 2020)