Developing a Wellcome funded GW4-CAT PhD in the time of COVID-19 – Challenges, Opportunities, Collaborations

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During the COVID-19 pandemic, there have been significant challenges for clinical academics, particularly those on time-limited contracts and those pulled back to clinical services but it has provided opportunities to think outside their field and try and rapidly solve evolving clinical and policy issues – in a much more responsive way than 'normal' research.

I am one of the GW4-CAT clinical academic trainees in Infectious Disease and Medical Microbiology supervised by Peter Ghazal, Nic Timpson, and Ruth Mitchell . My original plan was to look at the haem-iron metabolism axis in infection, a fascinating (if you are into bugs) area of battle over iron, the management of iron, haem, and metabolism in hosts. [1–4]

As I was running into start my PhD in October 2020, however, COVID happened. Like many clinicians, academic time was limited and the clinical service prioritised. However, we recognised the dire need for acute COVID-19 research, particularly focussed on triaging patients, and I rapidly set up the DISCOVER study, a platform for observational COVID-19 research in Bristol, alongside an NIHR Doctoral Research Follow, David Arnold. [5]

At the time, we knew little about COVID and we were worried about being overwhelmed, so rapid triage was critical. We rushed off to our research department, proposed the idea, then rushed off to the hospital charity, cap in hand. Because of the extraordinary flexibility shown by university and hospital staff, we were able to get seed funding and full ethical approval within a month, allowing us to recruit patients with COVID-19 to assess what blood tests would predict outcome rapidly.

This rapid pivot was only possible due to the flexibility of the GW4-CAT Wellcome scheme, with quick discussions with supervisors both within the hospital and the university. The scheme focuses on answering the key questions, and developing a trainee focussed project, with trainees spending a year working with supervisors to develop a project, rather than picking one off the shelf. Because of this, I felt much more comfortable in shifting gear to this novel project, and knew I would have the support of the scheme and supervisors. I initially kept this work separate from the PhD, but realised that this cohort may well answer the questions around whether haem is critical in response to viral infections.

We rapidly set up the study and wrote up the first UK cohort of COVID-19.[6] During this study, we collected samples, producing research on how to triage patients with COVID-19,[7] kinetics of the antibody response,[8] pharmacokinetics of therapeutics,[9] and longer term outcomes in patients with COVID-19, which achieved front-page reports in the national press, and is cited in the NICE guidance on prolonged COVID symptoms.[10]

This work was only possible due the infrastructure available in Bristol and the support of the GW4 programme, rapid funding from Southmead Hospital Charity and the Elizabeth Blackwell Institute, and connections across the university hospital sphere, led by Adam Finn and his UNCOVER group. Because of these links, fostered by the GW4 programme, we have ongoing

collaborations with multiple colleagues across the University looking at platelet function, neutrophil (dys!)function, serological responses, and immune responses to COVID-19.

Importantly, we have also had discussions with Yale University about autoantibodies in patients with COVID, and are entering into a collaboration with them looking at the role of autoantibodies in severe disease.

At this point, I had further conversations with my supervisors, and realising both the challenges and opportunities of working on a novel disease, agreed to switch some of my work onto COVID-19 formally, with a focus on looking at gene expression work in acute and convalescent samples. This was a difficult decision, especially with the uncertainty about laboratory time, relevance of samples, and the difficulties inherent with planning a 3 year PhD programme on a pandemic that is inherently unpredictable. However, we agreed that focussing the molecular work on COVID-19 was the right idea.

At the same time, I started talking to another GW4-CAT trainee, Mark Gormley, a dentist, about aerosolised spread of COVID-19, a major concern impacting both dentistry and clinical medicine. Luckily, we host a world-class aerosol institute, the Bristol Aerosol Research Centre (BARC)!

We both wondered about whether we could use the expertise available in BARC to answer the questions about whether aerosol is generated by medical or dental procedures such as drilling, and also about the survival of viruses in aerosol. Over a month, we connected with BARC and set up a potential project – AERATOR – aimed to study both those questions, with leadership from Jonathan Reid at BARC and Nick Maskell as a clinician but importantly linking up with multiple clinical experts from the region such as Prof Tony Pickering , who joined us on the project.

We applied for rapid funding from UKRI and were lucky to achieve rapid COVID funding of around £450,000 and Urgent Public Health status from the NIHR.

This project is ongoing right now, with early data (prior to funding) finding intubation is not aerosol generating,[11] a change with immediate policy implications. Work published in the last week has shown continuous positive airway pressure (CPAP) and high flow nasal oxygen (HFNO), both of which are used at the moment for critically ill hospital patients, do not produce aerosols of clinical significance.[12] This has relevant PPE and policy implications and has been fed back to the NIHR and the PHE Aerosol Generating Procedures committee. Further studies are ongoing, with results expected in weeks on endoscopy and lung function testing. This is truly translational work, with me in theatre yesterday with an anaesthetist, a dentist, an aerosol

researcher, and about £20,000 worth of complex aerosol measuring kit, arguing about the size of particles and the significance to clinicians!

This funding also supports translational work at the veterinary school, where colleagues are levitating (yes, you heard that) aerosols with SARS-CoV-2 under different conditions of humidity and temperature, in order to model survival and risk to others.

Finally, I have also maintained close contacts with my clinical colleagues, helping with work on SARS-CoV-2 prevalence in healthcare settings.[13] Interestingly, this work showed that the highest risk was in nurses and medical staff on the wards, not in critical care staff, suggesting that current guidance for increased aerosol protection for critical care staff only is perhaps misguided. This research is currently being used to update our own internal guidance around mask choice in North Bristol NHS trust, showing the rapid turnaround from research to policy and decision making.

Again, the flexibility and support of the GW4 scheme allowed me to take these opportunities to change and shift my proposal, while maintain a clear focus on ensuring I achieved excellent doctoral training with clear outputs in terms of a PhD. I have been able to work with world class colleagues in performing critical research, while ensuring that my doctoral training remains a priority.

Finally, a recent paper from colleagues at Cambridge strongly implicates haem as critical in COVID-19,[14] so it turns out I am doing the same PhD after all!

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