I&I NETWORK NEWSLETTER

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

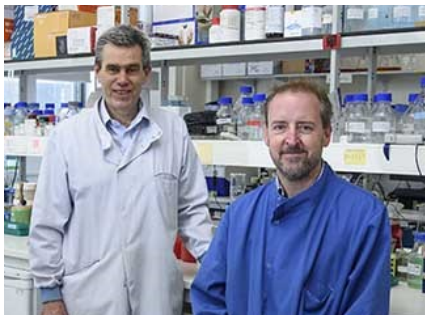
INFECTION & IMMUNITY

2021 - ISSUE 1

Consortium to study SARS-CoV-2 variants

A new national research project to study the effects of emerging mutations in SARS-CoV-2 was launched on 5 January 2021. The £2.5 million UK Research and Innovation (UKRI)-funded 'G2P-UK' National Virology Consortium will study how mutations in the virus affect key outcomes such as how transmissible it is, the severity of COVID-19 it causes, and the effectiveness of vaccines and treatments.

The Consortium, led by Prof Wendy Barclay at Imperial College London, will bring together leading virologists from ten research institutions including the University of Bristol. They will work alongside the COVID-19 Genomics UK (COG-UK) consortium, which plays a world-leading role in virus genome sequencing, and Public Health England to boost the UK's capacity to study newly identified virus variants and rapidly inform government policy. By setting up a streamlined, coordinated and openly communicated programme, that operates across the UK to study the latest virus mutations simultaneously in several labs with complimentary experimental methods, the researchers aim to produce faster, reliable results to feed into public health policy and clinical practice.



Dr Andrew Davidson (left) and Dr David Matthews (right), both from the School of Cellular and Molecular Medicine, are part of the new Consortium © Dave Pratt

UoBRISTOL EVENTS

Postgraduate Researcher's Wellbeing session
25 February 2021, 10.30 - 12.30, online

Horizon Europe webinar
25 February 2021, 10.30 - 12.00, online

Ethnicity and COVID-19: Addressing the impact of the pandemic on Black and Minority Ethnic people
25 February 2021, 11.00 - 12.00, Dr Andrea Barry (Joseph Rowntree Foundation); Dr Halima Begum (Chief Executive, Runnymede Trust); Anike Olaitan-Omole (First Love Foundation); Tony McKenzie (Joseph Rowntree Foundation), online

Getting under the skin of epidermal tissue repair and neoplasia
25 February 2021, 12.00 - 13.00, Gernot Walko (University of Bath), online

Cryo-EM of proteasomes: from fundamental studies to drug discovery
25 February 2021, 13.00 - 14.00, Paula da Fonseca (University of Glasgow), online

#covidunknowns: Vaccines
25 February 2021, 16.00 - 18.00, online

Anti-Racism Webinar Series: Racial abuse and microaggressions on campus
25 February 2021, 17.30 - 18.30, Pro Vice-Chancellor (Student Experience) Sarah Purdy and Bristol SU Union Affairs Officer, Julio Mkok, online

Introduction to PPI workshop
26 February 2021, 10.00 - 12.00, online

Infectious Disease and Epidemiology seminar
2 March 2021, 14.00 - 15.00, Dr Josephine Walker, online

Gut induced vascular plasticity drives stem cell adaptation during intestinal regeneration
4 March 2021, 13.00 - 14.00, Julia Cordero (University of Glasgow), online

Infection and Immunity Early Career Researchers' symposium 2021

Held on 13 January 2021, this morning event comprised 7 oral (hosted on Zoom) and 11 poster (hosted on Slack) ECR presentations.

We also welcomed keynote talks from two invited external speakers:

- Prof Déirdre Hollingsworth, Senior Group Leader, Big Data Institute, University of Oxford who spoke about modelling of COVID-19, and
- Prof Christopher Dye, FRS, Professor of Epidemiology, University of Oxford who presented on his work with the World Health Organisation

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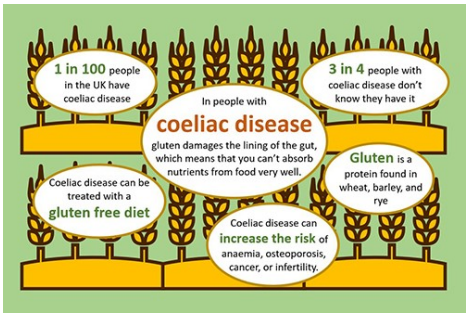
NEWS

Diagnosing coeliac disease before changing a diet

Around one in 100 people in the UK have coeliac disease, although many are not diagnosed. Untreated patients have an increased risk of anaemia, osteoporosis, cancer, or infertility. The only treatment available is a gluten-free diet. Diagnosing coeliac disease can be difficult. Some patients may be asymptomatic, while others have non-specific symptoms such as indigestion or bloating. It's thought only 30% of people with coeliac disease are actually diagnosed.

Guidelines recommend that adults and children "at high risk" of coeliac disease should be offered testing. However, it is not clear which groups are at high enough risk to justify routine testing, which symptoms should lead to testing, which tests should be offered, and whether a biopsy to confirm the diagnosis is necessary.



A survey, part of a larger project to find the best testing strategy for diagnosing whether people have coeliac disease, aims to find out how sure people want to be that they have coeliac disease before starting a gluten-free diet. The new testing strategy developed through this project has the potential to increase the number of people being diagnosed, speed up the process of diagnosis and improve patient outcomes.

Complete the survey

Genes help shape the gut microbiome

The trillions of microbes living with us are not just passengers – they actively participate in many human functions, helping us to digest food, training our immune system and even affecting our mood via the gut-brain axis. The largest and richest human microbiome inhabits the gut and contributes substantially to our health. In general, environmental factors such as diet and medication play a major role. A study by the international MIBioGen consortium highlights the common host genetic factors which also influence the composition of the human gut microbiome. They report that at least two human genes have a major impact in shaping our gut ecosystem: the lactase gene (LCT), which influences the abundance of lactose-digesting *Bifidobacteria*, and the fucosyl transferase (FUT2) gene, which determines the abundance of *Ruminococcus torques*. They also show that other human genes affecting microbiome composition are involved in important aspects of host metabolism, nutrition and immunity. Their analyses stretch as far as establishing relationships between several bacterial species and human diseases.

Wade K *et al*. (2021). Large-scale association analyses identify host factors influencing human gut microbiome composition. *Nature Genetics*.

Whooping cough vaccines for pregnant women

Whooping cough is widespread, highly contagious and serious for new-born babies. However, 30% of pregnant women in the UK do not receive the whooping cough vaccine, leading to avoidable illness and death; the COVID-19 pandemic appears to be having a negative impact on these numbers. A research project, *MAternal Vaccination In the NHS (MAVIS) Study: A mixed methods approach to improving antenatal immunisation rates, focusing on pertussis*, aims to understand why pregnant women are not being vaccinated against whooping cough and how to improve delivery by maternity services and mothers' uptake of vaccines.

Pregnant women are vaccinated against whooping cough to protect babies from birth until they are old enough for their own vaccination. The pregnancy vaccine is safe and effective, estimated to prevent at least six deaths and 165 hospitalisations in babies, as well as preventing 2,050 mothers becoming ill with whooping cough each year. The vaccine is now offered at the same time as the 20-week ultrasound scan to make it more accessible for women. Unfortunately, vaccination rates are highly variable across the country and women from ethnic minority backgrounds are less likely to be vaccinated. However, the reasons for these inequalities are unknown. The project started in January 2021. Read more

Public engagement

Dr Isabel Murillo Cabeza (Cellular and Molecular Medicine) submitted a short story for children to the University of Liverpool's Literature and Science Hub "Science me a Story" competition 2020. Entitled *The tiny little virus who got lost*, the story received a notable mention.
Read it online

Our COVID-19 experts are being regularly interviewed by the press. A few examples follow; for a more exhaustive list, see the University of Bristol's SARS-CoV-2 media coverage pages:

- **Prof Adam Finn** (Cellular and Molecular Medicine and Bristol Medical School), paediatrician and member of the UK government's Joint Committee on Vaccination and Immunisation (JCVI) has appeared on Sky News (10 Jan 21), Bristol 24/7 (15 Jan 21), BBC Radio 4 Today (9 Feb 21), The Guardian (8 Feb 21), The Observer (24 Jan 21) & BBC Points West Evening News (15 Feb 21)
- Virologist **Dr David Matthews** (Cellular and Molecular Medicine) featured in The Irish Examiner (12 Feb 21), BBC Radio Bristol (10 Feb 21), BBC Science Focus magazine (6 Feb 21), ITV News (6 Jan 21) & BBC News (11 Feb)
- Virologist **Dr Andrew Davidson** (Cellular and Molecular Medicine) in Bristol Live (11 Feb 21), BBC Radio Bristol Breakfast (3 Feb 21), Chemistry World (27 Jan 21)
- **Gabriel Scally** (Bristol Medical School) is an Honorary Professor of Public Health who has been interviewed by Sky News (15 Feb 21), ITV's Good Morning Britain (15 Feb 21), The Guardian (8 Feb 21), International Business Times (7 Feb 21) & RTÉ Radio 1 Drivetime (5 Feb 21)
- Paediatric rheumatologist **Prof Athimalaipet Ramanan** (Bristol Medical School) spoke about an arthritis drug found to cut deaths in severe cases in New Scientist, Blomberg News & Financial Times (12 Feb 21)

Funding successes: Part 1

To Prof Andrew Dick (Bristol Medical School: Translational Health Sciences), £717,198 from **Janssen Pharmaceutica** for *Characterization of the IL-23 pathway in the eye including in uveitis*.

Prof Paul Race (Biochemistry) has been awarded a £26,000 **Medical Research Foundation Dorothy Temple Cross TB International Collaboration** grant with the Kenya Medical Research Institute. The funds will help kickstart *Assessment of novel natural product drug combinations for the treatment of multidrug-resistant and extensively drug-resistant TB*.

An award of £30,000 from **Cavalier Matters** has gone to Dr Melanie Hezzell (Bristol Veterinary School) for *Remodelling in Myxomatous Mitral Valve Disease: The Relationship between Inflammation and the Development of Fibrosis* starting May '21 for 5 years.

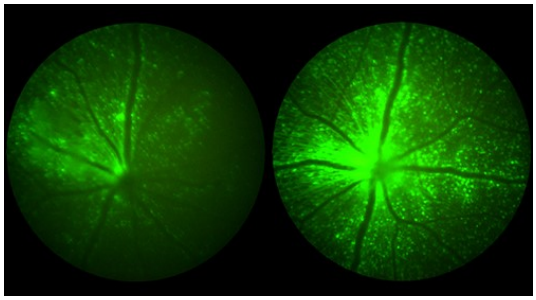
Dr Helen Weavers (Biochemistry) was awarded a £90k 3-year PhD studentship from the **National Centre for the Replacement, Refinement and Reduction of Animals in Research** for *A new* in vivo Drosophila *model of chronic inflammatory lung disease.*

The **British Heart Foundation** awarded £55,393 to Prof Paolo Madeddu (Bristol Medical School: Translational Health Sciences) for *Targeting the SARS-CoV-2 S-protein binding to the ACE2 receptor to preserve human cardiac pericytes function in COVID-19*, starting Feb '21 for one year.

Immunomodulation delivered via gene therapy

A collaboration of researchers in gene therapy and vision science have developed an adeno-associated virus (AAV) genome-coupled immunomodulation strategy that helps cloak the AAV virus from unwanted immune responses and offers important insights into ocular inflammation. AAV is recognised as the leading vehicle for *in vivo* delivery of therapeutic genes because it is non-pathogenic and efficiently targets many different cell and tissue types. A key challenge of *in vivo* gene therapies is their potential to cause immune reactions and inflammation, which can affect how well the therapies work or last. The international team developed a "coupled immunomodulation" strategy in which short TLR9-inhibitory sequences are incorporated directly into the much longer AAV genome containing therapeutic DNA sequences. The approach showed broad anti-immunogenic potential and also highlighted that pathways other than TLR9 activation likely contribute to inflammation in the highly immunogenic model of intravitreal AAV injections.

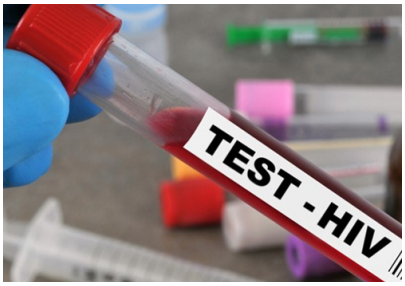
Chan YK *et al*. (2021). Engineering adeno-associated viral vectors to evade innate immune and inflammatory responses. *Science Translational Medicine*



AAVs with TLR9-inhibitory sequences incorporated into their genomes allowed significantly higher expression of a linked fluorescent reporter gene in the mouse retina (right) than AAVs that were lacking the sequences (left) following intravitreal administration
© David Copland

HIV prevention and treatment in South Africa

The unmet HIV prevention and treatment needs of female sex workers and especially their male clients could contribute substantially to ongoing HIV transmission in South Africa. Researchers used mathematical modelling to look at the contribution of commercial sex, sex between men, and other heterosexual partnerships to HIV transmission in South Africa. They found that, over a ten-year period (2010-19), sex between female sex workers and their paying clients contributed 6.9% of new HIV infections, while sex between clients with their non-paying partners contributed 41.9%. Sex between men contributed 5.3% and sex between men who have sex with men and their female partners contributed 3.7%.



Increasing treatment among female sex workers, their paying clients and men who have sex with men would be up to five times more efficient for reducing HIV transmission than increasing treatment among the general population.

Stone S *et al*. (2021). Estimating the contribution of key populations towards HIV transmission in South Africa. *Journal of the International AIDS Society*.

Diabetic eye disease clinical trials

A new approach to treating one of the leading causes of blindness among patients with diabetes is being tested in clinical trials which began in February 2021. The trial involves 48 patient volunteers with diabetic macular oedema (DMO), a disease where blood vessels leak fluid into the retina. It is the most common cause of vision loss among people with diabetic retinopathy, affecting approximately 21 million people worldwide. As part of a randomised multicentre trial, the patients, who are in treatment at retinal centres in Australia, will be given either a placebo or a dose of EXN 407, the lead chemical compound in the drops, created by Exonate, an mRNA therapy company focused on retinal diseases.

The clinical trial is the culmination of an extensive period of research, which involved academics from the University of Bristol in its early stages. This first phase of trials will involve escalating the dosages given to the 48 patient volunteers. That will be followed by an expansion phase with a larger cohort of patient volunteers and a longer drug dosing period.

The study aims to demonstrate safety and tolerability of EXN 407 by examining its effects in reducing the retinal thickness that is caused by DMO. Current treatments for DMO require intravitreal injections directly into the eye, whereas EXN 407 has been designed with sufficient ocular permeability to be given topically as eye drops.

Funding success: Part 2

Dr Polly Duncan (Bristol Medical School: Population Health Sciences) received £18,186 from **Research England** for *Primary Care Evaluation of COVID Infection Surveillance in Our Network (PRECISION),* starting Dec '20 for 4 months.

The **National Institute for Health Research (NIHR)** awarded Dr Vikki Wylde (Bristol Medical School: Translational Health Sciences) £5,557 for Management of Infected Knee Replacements – Obtaining Best Evidence (MIKROBE). A feasibility study for a randomised controlled trial of one-stage or two-stage surgery for prosthetic knee infection.

The **NIHR** also awarded Dr Sarah Denford (Bristol Medical School: Population Health Sciences) £25,306 for *Development of a novel family focused intervention to promote physical activity among young people with cystic fibrosis and their families*, starting Jan '21 for 18 months.

Dr Rachel Denholm (Bristol Medical School: Population Health Sciences) received £189,500 from **Health Data Research UK** for *Enhancing the Utilisation of COVID-19 Testing in Schools Studies: the Joint Analysis of the ONS COVID-19 School Infection Survey and COVID-19 Mapping and Mitigation in Schools (CoMMinS) Study*.

Dr David Matthews (Cellular and Molecular Medicine) was awarded £115,681 from the **Biotechnology and Biological Sciences Research Council** for *Evolution of SARS-CoV2*.

To Dr Colin Chu (Bristol Medical School: Translational Health Sciences), £1,222,367 from **MeiraGTx** for *MeiraGTx Gene Therapy for Glaucoma*.

Effective, remote hypertension management

At-home blood pressure monitoring using a web-based system offering personalised support and linked to a remote healthcare professional can result in better hypertension management than face-to-face consultations, finds a study led by the Universities of Oxford, Bristol and Southampton. In the UK over 30% of adults have hypertension, a major risk factor for cardiovascular disease. With GP surgeries currently requesting that many patients opt for virtual consultations to avoid exposure to coronavirus infection, the clinical monitoring of hypertensive patients using face-to-face consultation is a challenge for primary care. The Home and Online Management and Evaluation of Blood Pressure (HOME BP) randomised controlled trial evaluated the combination of regular self-monitoring at home with a web-based tool that offered reminders, predetermined drug changes, lifestyle advice and motivational support. Results showed that for participants managing their blood pressure at home, mean systolic blood pressure was significantly lower after 12 months compared with those managed exclusively in the clinic.

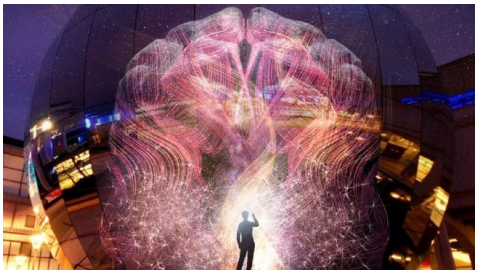
McManus RJ *et al*. (2021). Home and online management and evaluation of blood pressure (HOME BP) using a digital intervention in poorly controlled hypertension: randomised controlled trial. *British Medical Journal*.

Jean Golding Institute Seed Corn funding

The Jean Golding Institute is a central hub for data science and data-intensive research at the University of Bristol. Their areas of focus include data driven solutions to societal changes; data visualisation and materiality; data governance and reproducibility; and data science and AI fundamental research.

They have an annual funding call which fosters interdisciplinary research in data science (including AI) and data-intensive research. This year's awardees included:

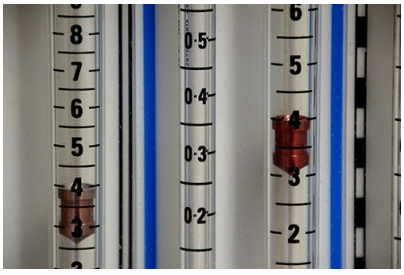
- Dr Cheryl McQuire (Bristol Medical School), Dr Luisa Zuccolo (Bristol Medical School), Dr Christopher Woods (Chemistry) and Dr Mike Jones (Biochemistry) with *Pandemics and 'infodemics': the nature, extent and reach of public health misinformation on social media during the COVID-19 pandemic*



- Dr Kevon Parmesar (Bristol Medical School): *Evaluating fairness, bias and equality in Artificial Intelligence for skin disease*
- Dr Xin Fei and Prof Xiaojun Wang (Management) with *The effective deployment strategy of COVID-19 vaccines with various efficacies to mitigate the impacts of pandemic in the UK*

Aerosol emissions in respiratory support

In 2020 the AERosolisation And Transmission Of SARS-CoV-2 in Healthcare Settings (AERATOR) was awarded funding to study a range of potential aerosol generating procedures (AGP's) commonly performed across the NHS. Currently policies around these procedures mean the use of full (FFP3) PPE and often lengthy waits between procedures to allow for cleaning and room airflow changes, resulting in increased waiting times and the cancellation of some NHS services. Risk of generating aerosols from SARS-CoV-2 directly informs an organisation about acute healthcare and PPE guidance. Continuous positive airway pressure (CPAP) and high-flow nasal oxygen (HFNO) are widely used for oxygen delivery and respiratory support for patients with severe COVID-19, and both are considered high-risk aerosol generating procedures. The team looked at whether oxygen delivery systems, CPAP and HFNO, used routinely on medical wards and intensive care units, generate aerosols. They recruited both healthy and hospitalised patients. They found in healthy volunteers, CPAP is associated with less aerosol emission than breathing, speaking or coughing. Aerosol emission from the respiratory tract does not appear to be increased by HFNO. Although direct comparisons are complex, coughing appears to generate significant aerosols in a size range compatible with airborne transmission of SARS-CoV-2. As a result, the risk of SARS-CoV-2 aerosolisation is likely to be high in all areas with COVID-19 patients.



Hamilton F *et al*. (preprint). Aerosol emission from the respiratory tract: an analysis of relative risks from oxygen delivery systems. *medRxiv*.

Funding successes: Part 3

Dr Sarah Denford (Bristol Medical School: Population Health Sciences) was awarded £25,306 from the **National Institute for Health Research (NIHR)** for *Development of a novel family focused intervention to promote physical activity among young people with cystic fibrosis and their families*, starting Jan '21 for 18 months.

Prof Jonathan Sterne (Bristol Medical School: Population Health Sciences) received £75,188 from the **University of Bern** to pursue the *Dolutegravir resistance project*, starting Jan '21 for one year.

The **Southmead Hospital Charity** awarded £12,532 to Dr Jenny Ingram (Bristol Medical School: Population Health Sciences) for *COVID-19 clinicians cohort (CoCCo) study: treatment preferences and needs*.

The **NIHR** also awarded Dr Jennifer Bailey (Bristol Veterinary School) £6,500 for Determination of cytokine profiles in inflammatory bowel disease patients demonstrating primary and secondary non-response to biologic drugs.

To Prof Moin Saleem (Bristol Medical School: Translational Health Sciences), £23,920 from the **David Telling Charitable Trust** for *Understanding DNA methylation in children with nephrotic syndrome*.

The **Medical Research Council (MRC)** awarded Prof Nicholas Timpson (Bristol Medical School: Population Health Sciences) £52,265 for *CO-CONNECT: COVID - Curated and Open aNalysis aNd rEsearCh platform*.

Also from the **MRC**, £585,249 was awarded to Prof Ash Toye (Biochemistry) for *Dissecting the role of host receptor context and cytoskeletal disruption in malaria parasite invasion.*

Bringing COVID-19 under control

An editorial co-authored by Prof Sir Jeremy Farrar, Scientific Advisory Group for Emergencies (SAGE) and Director of the Wellcome Trust, and Prof Tim Cook, Consultant in Anaesthesia and Intensive Care Medicine and Honorary Professor at the Bristol Medical School, was published in December 2020. The article states that in order for the global COVID-19 vaccination programme to be successful, the available vaccines must be able to do all three of: prevent infection becoming established in an individual, prevent disease progression and prevent onward transmission.

Vaccination is a global rather than a national necessity. The WHO ACT-accelerator and COVAX initiatives both emphasise the importance of vaccines reaching the most vulnerable and healthcare workers in all countries at a similar time. Widespread vaccination of one or a few countries without addressing this need globally is in no one's interests and will not provide the protection we all need.

If 80% of the UK population were to be successfully vaccinated there would finally be the prospect of a degree of (herd) immunity, which would reduce virus transmission in the community to very low levels and protect both those who are vaccinated and those who are not.

Cook & Farrar (2020). COVID-19 vaccines: one step towards the beginning of the end of the global impact of the pandemic. *Anaesthesia*.

Research and innovation awards

PhD student Dr Zoe Parr-Cortes' (Bristol Veterinary School) three-minute presentation at the Biotechnology and Biological Sciences Research Council South West Biosciences Doctoral Training Partnership annual student conference on *Medical Alert Assistance Dogs - What do they do and how can we measure it?* was voted choice winner. The event is an opportunity for all BBSRC SWBio students across the Doctoral Training Partnerships (Cardiff, Bristol, Exeter) to present their research.

Dr Aisling Kane (Computer Science) who has won the Collaborate to Innovate Medical and Healthcare Award 2020 for her work with Quinn Technology to develop an app which is allowing thousands to manage diabetes more effectively. The app allows users to input both insulin dosage and food consumption, as well as providing reminders for when regular insulin injections are due. Additional sensor data from smartphones such as activity, sleep and menstrual cycle can also be linked. Over time, the platform's algorithms learn from individual inputs and outcomes and help users adjust their insulin dosage based on what has worked for them in the past. The work originated in an Innovate UK project "Machine Learning for Enhanced Diabetes Care".

Read the full article

National study to understand long COVID

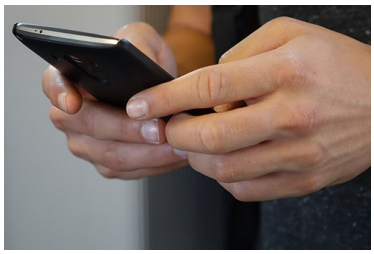
What is long COVID and how can diagnosis be improved? Using data from electronic health records and Bristol's Children of the 90s cohort study, these and other questions will be tackled by a nationwide long COVID study led by University College London (UCL). The project, *Characterisation, determinants, mechanisms and consequences of the long-term effects of COVID-19: providing the evidence base for health care services*, will explore why a meaningful number of people report persistent and disabling physical and mental health symptoms - post-COVID-19 syndrome, known as 'long COVID'. Current projections estimate 1 in 20 people with a COVID-19 infection will still have symptoms beyond 2 months, meaning a substantial healthcare investment is needed to treat and support those with the condition.

By linking together cohort studies' detailed pre-pandemic health data and using national anonymised, linked GP electronic health records, this study will seek to understand the nature of long COVID, risk factors and its impact. Findings from the study will be shared with bodies involved in developing guidelines (NICE, who are also part of this project), with government (via the Chief Scientific Advisor), with the public via social media and other outputs, and the scientific community via research publications. The study is funded by a £9.6 million National Institute for Health Research - UK Research and Innovation grant.

Read more

Cell phone data to quantify behavioural changes

Being prepared for a pandemic, like COVID-19, depends on the ability to predict the course of the pandemic and the human behaviour that drives spread in the event of an outbreak. Cell phone metadata that is routinely collected by telecommunications providers can reveal changes of behavior in people who are diagnosed with a flu-like illness. A research study, led by Emory University and devised by the University of Bristol, is based on data drawn from a 2009 outbreak of H1N1 influenza in Iceland.



The team collaborated with a major cell phone service provider and public health officials on the island to analyse metadata for over 90,000 encrypted cell phone numbers. They were able to link the encrypted data to 1,400 anonymous individuals who received a clinical diagnosis of a flu-like illness during the H1N1 outbreak. The results showed that, on average, those who received a flu-like diagnosis changed their cell phone usage behaviour a day before their diagnosis and the two-to-four days afterwards, making fewer calls from fewer unique locations. On average, they also spent a longer time than usual on the calls that they made on the day following their diagnosis. The findings represent a first step for the possible broader use of the method, specifically, if an emerging disease displays a sufficiently distinct signature of behavioural changes, the methodology could prove useful to augment monitoring efforts.

Vigfusson Y *et al*. (2021). Cell-phone traces reveal infection-associated behavioral change. *Proceedings of the National Academy of Sciences.*

Funding successes: Part 4

Prof Paul Martin (Biochemistry) received £819,299 from the **Medical Research Council** for *Screening for novel immune cell extravasation genes in* Drosophila, *mice and man*, starting Jun '21 for 5 years.

UK Research and Innovation awarded £425,455 to Prof Jonathan Reid (Chemistry) for *The Investigation of Particulate Respiratory Matter to Inform Guidance for the Safe Distancing of Performers in a COVID-19 Pandemic.*

To Prof Ian Collinson (Biochemistry), £487,585 from the **Biotechnology and Biological Sciences Research Council** for *Hijacking the Sec machinery to kill bacteria*, starting Dec '20 for three years.

Dr Ellen Brooks Pollock (Bristol Veterinary School, pictured) was awarded £253,540 from the **Medical Research Council** to set up a *COVID-19 modelling consortium*.

Southmead Hospital Charity awarded Dr Andrew Moore (Bristol Medical School: Translational Health Sciences) for *Exploring the long term impact of COVID19 on patients and their families*.

COVID vaccination programme reducing daily deaths

The UK's vaccination programme aims to have vaccinated close to 15 million people in the first four priority groups by 15 February 2021. The first four priority groups include residents and staff in care homes for the elderly (group 1), people aged 80 years and over and frontline health and social care workers (group 2), people aged 75-79 years (group 3) and people aged 70-74 years and clinically extremely vulnerable adults (group 4).

The reason why vaccination will affect deaths, hospital admissions and ICU admissions at different rates is due to the different age ranges for each: the average age of patients dying with COVID-19 is 83 years; the average age of those hospitalised is 73 years, those admitted to intensive care is 61 years. Around three quarters of COVID-19 deaths recorded in the UK have been in people aged 75 years and over. Thus, since vaccination is initially targeting mostly people aged 70 years and over, the first phase of vaccination will have a proportionally greater effect on deaths. The model predicts that with most of groups 1- 4 vaccinated, daily deaths will reduce by 88% by the end of March.

Cook TM & Roberts JV (2021). Impact of vaccination by priority group on UK deaths, hospital admissions and intensive care admissions from COVID-19. *Anaesthesia.*

COVID conspiracies and vaccine hesitancy

Fifteen per cent of the UK public believe that reporters, scientists, and government officials are involved in a conspiracy to cover up important information about coronavirus – but this almost triples, to 42%, among those who say they're unlikely to or definitely won't get vaccinated against the virus. A study found that this dynamic holds for belief in a number of conspiracy-related statements, and that people from BAME groups are also particularly likely to report believing such claims. The findings are based on a survey of 4,860 UK adults aged 18-75 between 21 November and 22 December 2020.

People from BAME groups (25%) are also twice as likely as white people (13%) to report believing "the only reason a coronavirus vaccine is being developed is to make money for pharmaceutical companies", and the team found that people from ethnic minorities (15%) are half as likely as those from white ethnic groups (31%) to say they would like to be vaccinated immediately.

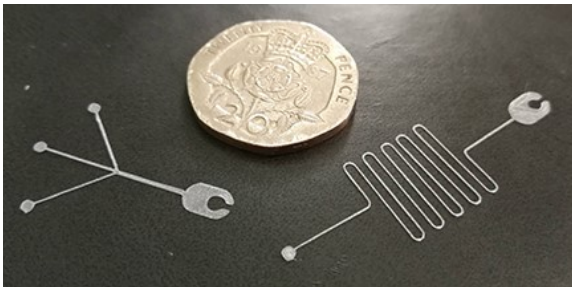
Those whose knowledge about coronavirus comes primarily from certain online sources, including social media platforms, are significantly more likely to have conspiracy suspicions about the pandemic and think various conspiracy theories are true. Relying on such sources is also associated with far greater levels of potential concern about getting vaccinated. Agreement with conspiracy suspicions relates to low trust in traditional authority sources, to the point that it constitutes a threat to public health.

Allington D *et al*. (2021). Coronavirus conspiracies and views of vaccination.

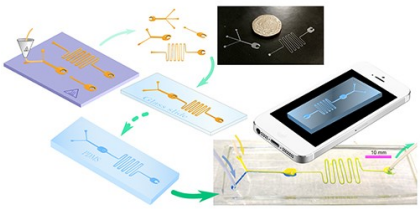
Rapid medical diagnostic tools

Microfluidic devices underpin lab-on-a-chip (LOC) technologies which are developed to provide the rapid diagnoses at that are needed at point of care (POC) for the swift and effective treatment of many diseases. Researchers at Bristol have developed a fast, reliable and cost-effective alternative for producing the soft-lithographic moulds used for fabricating microfluidic devices. This discovery means fabrication of microfluidic devices (with channel dimensions ~width of a human hair) is now both accessible and affordable using simple, low-cost 3D-printing techniques and the open-source resources developed by the team.

The technique is so simple, quick & cheap that devices can be fabricated using everyday domestic or educational appliances and at a negligible cost (~0.05% of cost of materials for a single microfluidic device). This means researchers and clinicians could use the technique and resources to help fabricate rapid medical diagnostic tools, quickly and cheaply, with minimal additional expertise or resources required.



Felton H, Hughes R & Diaz-Gaxiola A (2021). Negligible-cost microfluidic device fabrication using 3D-printed interconnecting channel scaffolds. *PLOS ONE*.



Changes in contact patterns under COVID guidance

CONQUEST (COroNavirus QUESTionnaire) is an online survey of contacts, behaviour, and potential SARS-Cov-2 symptoms for University of Bristol staff and students. The questionnaire was set-up to measure changing behaviour and contact patterns during this unprecedented time, in order to predict how COVID-19 will spread in universities settings. The survey, which went live on 23 June 2020, investigated whether there were differences in contact patterns during four different COVID-19 guidance periods: the period following the first lockdown (23 June – 3 July 2020); the relaxed guidance period (4 July – 13 September 2020); "rule-of-six" period (14 August – 4 November 2020); and the second lockdown (5 November - 24 November 2020). There was a reduction in the number of contacts during the second lockdown, returning them to the levels in the period after the first UK lockdown. The study comes at a unique time when a third national lockdown has been implemented to reduce contacts between individuals. However, the number of reported daily cases of COVID-19 is still high. The setting is important due to its uniqueness, as universities were allowed to carry on teaching throughout the lockdown, meaning that large gatherings of people were still allowed.

Trickey A *et al*. (preprint). University students and staff able to maintain low daily contact numbers during various COVID -19 guideline periods. *medRxiv*.

COVID ICU mortality

A meta-analysis of global studies has shown that intensive care morality from COVID-19 has continued to fall since the start of the pandemic, but the improvement is slowing and may have plateaued. A previous meta-analysis published in July '20 concluded that overall mortality of COVID-19 patients in intensive care units (ICUs) has fallen from almost 60% at the end of March 2020 to 42% at the end of May 2020. This new study shows that, in studies up to October 2020, ICU mortality has fallen again to 36%. So, while the situation is improving, the pace of progress has slowed. In the last few months several studies have clarified which treatments do and do not provide benefit in the ICU management of COVID-19. Steroids were shown to improve survival in patients who are oxygen-dependent or on mechanical respiratory support, while other drugs (e.g. hydroxychloroquine and remdesivir) have been shown to have no clear mortality benefit. They also note that management of COVID-19 has likely evolved over the year with changes in approaches to oxygen therapy, fluid therapy and management of blood clotting.

Armstrong RA *et al*. (2021). Outcomes from intensive care in patients with COVID19: a systematic review and meta-analysis of observational studies. *Anaesthesia*

Global taskforce to demystify vaccine hesitancy

A European Research Council-funded pioneering project, led by the University of Bristol and involving teams in Canada, Germany, Finland, France, and Portugal, will harness the potential of health care professionals to challenge misconceptions about vaccination, reinforce confidence in vaccines, and encourage uptake of the COVID-19 vaccine, including being immunised themselves.

Vaccine hesitancy, defined as the delay or refusal of vaccination without medical guidance, has been recognised as a serious threat by the World Health Organization (WHO). Misinformation on the internet is a commonly cited cause and health care workers have been identified as trusted influencers, who can help sway vaccine decisions. Some evidence also indicates that not all health care workers are fully inclined to be vaccinated; latest figures from the Office for National Statistics (ONS) in the UK show although only 1% of those offered vaccination against COVID-19 have turned it down, there is significant variation by age. Some 5% refused in the 30 to 49-year-olds age group, 2% among 50 to 69-year-olds and less than 1% in those aged 70 or above. It is possible many of the 30 to 49-year-olds are health and social care workers, since they are among the limited other groups already eligible to receive the vaccine, besides people aged 65 and above, due to being at greater risk. The percentage of refusals among health care workers are even higher in other countries.

The £2.7 million project will systematically investigate attitudes towards vaccinations among health care workers in the participating countries. The guidance will be deployed by the WHO and the United Nations International Children's Emergency Fund (UNICIF) for worldwide benefit. Read more

ELIZABETH BLACKWELL FUNDING

Nurturing Research. Improving Health.

Elizabeth Blackwell Institute and Cabot Institute for the Environment: Joint call on Climate Change and Health

The aim of the call is to support new interdisciplinary collaborations between University of Bristol researchers in the area of Climate Change and Health that would lead to major research bids in this space. Initial areas of interest identified include: food security/quality/nutrition; mental health/wellbeing; ***infectious diseases***; health data science/data intensive research; impact on health systems; extreme weather and hydrological exposure; environment, ecological shifts and health.

Deadline for applications: 12 noon 4 March 2021

EBI Early Career Fellowship

With support from the Rosetrees Trust and Wellcome Trust Institutional Strategic Support Fund (ISSF) the Elizabeth Blackwell Institute has funding available for a researcher in the area of mental health for young people.

Stage 1 deadline: 30 March 2021

EBI Identifying Candidates for Wellcome Trust Investigator Awards

This scheme is designed to support a small number of permanent academic staff at UoB within the first five years of their appointment, who are planning to apply for an Investigator Award from the Wellcome Trust. Applications will be accepted on a rolling basis.

Heads of School are asked to nominate members of staff who can be eligible for this scheme by emailing ebi-health@bristol.ac.uk

Closing date: none

EBI Seed Fund: Public Engagement with Health Research

Seed funding is available for health researchers who would like to deliver public engagement events and activities. Applications accepted on a **rolling** basis.

EBI Workshop Support

Support interdisciplinary workshops in health research at new or emerging interface between two or more disciplines. Applications **reviewed all year**.

Returning Carers Scheme

To support academic staff across all faculties in re-establishing their independent research careers on return from extended leave (16 weeks or more) for reasons connected to caring (e.g. maternity leave, adoption leave, additional paternity leave, leave to care for a dependant).

Closing date: 30 April and 31 October each year

FUNDING OPPORTUNITIES

Would you like to receive timely, tailored funding opps information?
Do you want to know what funding opportunities come up in your research area?
Get tailored funding alerts?

Research Professional provides access to an extensive database of funding opportunities, and can send out tailored alerts based on keywords that you input, ensuring that the funding alerts you receive are the ones you want to hear about. UoB staff and students have **FREE** online access to the database from any device – once you've registered then you can view upcoming funding opportunities from home or away, not just while on the University network.

You can search for funding information by discipline, sponsor, database searches, by recent calls or by upcoming deadlines. If you register for the site and log in, you'll be able to:

- **Set up automated funding opportunity email alerts** - **tailored according to your discipline and research interests**, an easy process that will take just a few minutes to set up through the use of keywords
- **Save searches and bookmarks** - store items of interest for future reference, download and email to colleagues
- **Sign up for higher education news bulletins** – want to hear about what is going on in the broader HE environment? Latest news on the REF, setting up of UKRI etc? Sign up for the 8am playbook or the Research Fortnight news publications and stay up to date with the latest news.

For further information on Research Professional, go to the RED website.

National Cancer Institute and others
Advancing translational and clinical probiotic/prebiotic and human microbiome research (R01 clinical trial optional): AIDS-related

Closing date: 07 May 2021 Award amount: unspecified

This supports translational and clinical studies using a variety of probiotic and prebiotic carriers to generate measurable functional evidence for the safe and effective use of these carriers in maintaining health or preventing and treating diseases, as well as studies to develop new or refine known biomarkers of health and disease with respect to probiotic or prebiotic interventions. This FOA calls for interdisciplinary collaborations across scientific disciplines engaged in microbiome and probiotic or prebiotic research that address the following topics: nutritional science; microbiology; virology; microecology and microbiome; genomics; immunology; computational biology; chemistry; bioengineering; integration of omics; computational approaches in DNA technologies.

Medical Research Council
Programme grants – infections and immunity

Closing date: 12 May 2021 Award amount: unspecified

These provide large and long-term renewable funding for projects related to infections and immunity. The purpose is to help the medical science community to think bigger. A programme is defined as a coordinated and coherent group of related projects that may address an interrelated set of questions across a broad scientific area.

Coalition for Epidemic Preparedness Innovations
Complementary clinical trials – expanding access to COVID-19 vaccines and rapid response to clinical development gaps

Closing date: 28 May 2021 Award amount: USD 140 million

This supports clinical trials with the aim of rapidly expanding access to and confidence in COVID-19 vaccines by generating clinical evidence in certain vulnerable populations or age groups, or addressing clinical development gaps. Complementary clinical trials which represent amendments or extensions to ongoing trials, as well as new clinical trials, are eligible. Clinical trials which expand access and capacity in low- and middle-income countries are particularly encouraged.

Royal Society
University research fellowships

Closing date: 07 September 2021 Award amount: unspecified

These enable early-career scientists who have the potential to become leaders in their field to build an independent research career in the natural sciences. This covers all fields of natural sciences, including biological research, chemistry, engineering, mathematics and physics, but excludes clinical medicine.

Royal Society
APEX awards

Closing date: 28 October 2021 Award amount: £110,000

These enable established, independent researchers with a strong track record in their respective area to pursue genuine interdisciplinary and curiosity-driven research to benefit wider society.

National Science Foundation
Ecology and evolution of infectious diseases

Closing date: 17 November 2021 Award amount: USD 2.5 million

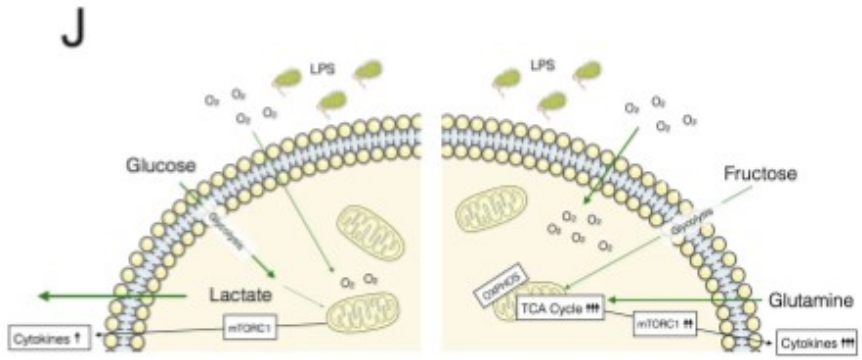
Supports collaborative research on the ecological, evolutionary and social drivers that influence the transmission dynamics of infectious diseases.

THIS ISSUE'S FEATURED ARTICLE

Fructose reprogrammes glutamine-dependent oxidative metabolism to support LPS-induced inflammation

Jones N, Blagih J, Zani F *et al*. (2021). *Nature Communications*.

Fructose intake has increased substantially throughout the developed world and is associated with obesity, type 2 diabetes and non-alcoholic fatty liver disease. Currently, our understanding of the metabolic and mechanistic implications for immune cells, such as monocytes and macrophages, exposed to elevated levels of dietary fructose is limited. Here, we show that fructose reprograms cellular metabolic pathways to favour glutaminolysis and oxidative metabolism, which are required to support increased inflammatory cytokine production in both LPS-treated human monocytes and mouse macrophages. A fructose-dependent increase in mTORC1 activity drives translation of pro-inflammatory cytokines in response to LPS. LPS-stimulated monocytes treated with fructose rely heavily on oxidative metabolism and have reduced flexibility in response to both glycolytic and mitochondrial inhibition, suggesting glycolysis and oxidative metabolism are inextricably coupled in these cells. The physiological implications of fructose exposure are demonstrated in a model of LPS-induced systemic inflammation, with mice exposed to fructose having increased levels of circulating IL-1β after LPS challenge. Taken together, our work underpins a pro-inflammatory role for dietary fructose in LPS-stimulated mononuclear phagocytes which occurs at the expense of metabolic flexibility.



Schematic outlining fructose metabolism promoting inflammation. mTORC1 mammalian target of rapamycin complex 1, OXPHOS oxidative phosphorylation, TCA tricarboxylic acid.

The study shows that fructose causes the immune system to become inflamed and that process produces more reactive molecules which are associated with inflammation. Inflammation of this kind can go on to damage cells and tissues and contribute to organs and body systems not working as they should and could lead to disease.

The research also brings a deeper understanding about how fructose could be linked to diabetes and obesity - as low- level inflammation is often associated with obesity. It also builds on the growing body of evidence available to public health policy makers about the damaging effects of consuming high levels of fructose.

CONTACTS

The Infection and Immunity Network is run by a Steering Group:

Co-Chair: Philip Bright
Clinical Immunologist

Co-Chair (interim): Katy Turner
Senior Lecturer in Veterinary Infectious Diseases

- Borko Amulic - Lecturer in Immunology
- Matthew Avison - Co-Director, Bristol AMR
- Andrew Davidson - Senior Lecturer in Virology
- Stephanie Diezmann - Senior Lecturer in Fungal Pathogens
- Adam Finn - Professor of Paediatrics
- Hannah Fraser - Research Fellow in Infectious Disease Mathematical Modelling
- Wendy Gibson - Professor of Protozoology
- Kathleen Gillespie - Reader in Molecular Medicine, Head of the Diabetes and Metabolism Research Group
- Melanie Hezzell - Senior Lecturer in Cardiology
- Peter Muir - Clinical Virology
- Angela Nobbs - Lecturer in Oral Microbiology
- Annela Seddon - Director of the Bristol Centre for Functional Nanomaterials
- Sandra Spencer - Research Development Associate & Network Facilitator
- Peter Vickerman - Professor of Infectious Disease Modelling
- Linda Woolridge - Chair in Translational Immunology
- Catherine Brown - Network Administrator and Newsletter editor

The content of this newsletter is not the intellectual property of the Network, but rather an amalgamation of information obtained through a variety of sources including our community members; research groups such as Bristol AMR and Infection, Inflammation and Immunotherapy; and University of Bristol school bulletins and press releases. Affiliations are stated wherever possible, however please note that omissions do happen and we apologise in advance for any you may come across. All information is merely for educational and informational purposes. We cannot offer medical advice and any queries regarding treatment for a specific medical condition or participation in a clinical trial should be addressed to your healthcare provider. While the information herein has been verified to the best of our abilities, we cannot guarantee that there are no mistakes or errors.

e: infection-immunity@bristol.ac.uk
w: http://www.bristol.ac.uk/infection-immunity/
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