# I&I NETWORK NEWSLETTER

University of BRISTOL
Elizabeth Blackwell Institute for Health Research

INFECTION & IMMUNITY

2023 - ISSUE 4

## Global research on HIV prevention

Researchers from seven international institutions hope to transform traditional strategies used to tackle global HIV prevention for key populations particularly affected by the virus, thanks to a new £5 million Wellcome Discovery award to Prof Peter Vickerman (Bristol Medical School).

Despite efforts to eliminate HIV, levels remain high among key populations, with UNAIDS estimating that globally men who have sex with men, people who inject drugs and female sex workers have three to 11 times higher burden of HIV infection and contribute to the majority of new HIV infections. The award will fund an eight-year study to improve current prevention strategies for these key populations. While existing HIV prevention interventions work for key populations, "structural factors", such as unemployment, homelessness, stigma, violence and criminalisation, may severely limit their impact. These factors are pervasive in key populations globally and can increase the vulnerability of key populations to HIV through reducing access to health services, retention to HIV treatment, and increasing HIV risk behaviours.

Although largely overlooked in the past, initiatives to reduce structural factors and their effects are a focus of recent global HIV elimination strategies, but there is limited evidence to show why it is essential to bring these to the forefront of HIV prevention efforts and how this could be achieved.

The project will include systematic reviews, epidemiological analyses, mathematical modelling and cost-effectiveness analyses, to quantify and cost the contribution of structural factors to driving the HIV epidemic, and the impact of interventions that address them.

Read the full University of Bristol news item

## Inside this issue:

# EVENTS

**An Introduction to Co-produced Research**
10 January 2024, 12.00 - 16.00, Room G.16, Victoria Rooms, 88 Queens Road, Bristol, Bs8 1SA

**Elizabeth Blackwell Institute Annual Public Lecture 2023: Facts, fakes, society and health**
22 January 2024, 18.30 - 20.00, Patricia Kingori (Professor of Global Health Ethics, Nuffield Department of Population Health, Wellcome Senior Investigator, and Senior Research Fellow at Somerville College, University of Oxford), Conference Hall, City Hall, College Green, Bristol BS1 5TR

**Marie Curie Improving End of Life for All Research Conference 2024**
5 - 9 February 2024, online

**Infection and Immunity Early Career Researchers' Symposium**
**19 January 2024, Life Sciences Building, 10.00 - 15.00**
**ALL WELCOME**

**Keynotes**

- **Charlotte Summers**, Director of the Victor Phillip Dahdaleh Heart and Lung Research Institute, and Professor of Intensive Care Medicine University of Cambridge
- **Michelle Buckner**, Assistant Professor of Antimicrobial Resistance at the Institute of Microbiology and Infection / Impact and Engagement Lead, University of Birmingham

**More information and to register**
*Programme to be finalised soon!*

**Post ISTH & ASH Headlines 2024**
6 February 2024, 9.00 - 17.00, Austin Court, IET Birmingham, 80 Cambridge Street, B1 2NP

**The British Society for Oral and Dental Research Early Career Researcher Meeting: Big Data in HealthCare Research**
7 February 2024, 8.30 - 20.30, Bristol Dental School, University of Bristol, 1 Trinity Quay, Avon Street, Bristol, BS2 0PT

**Microbiome Interactions in Health and Disease**
14 - 16 February 2024, Wellcome Genome Campus, UK and Virtual

**Health Data Research UK conference 2024: The Grand Challenges in Health Data**
5 - 6 March 2024, Andrew Morris (Director, HDR UK) & Cathie Sudlow (Chief Scientist, Deputy Director of HDR UK), Royal Armouries Museum, Leeds and online

**Antimicrobial Resistance – Genomes, Big Data and Emerging Technologies**
13 - 15 March 2024, Wellcome Genome Campus, UK and Virtual

**VIEW THE FULL LIST OF I&I EVENTS ON OUR WEBSITE**

# NEWS

## New Discovery Science co-Leads for the I&I Network

Bristol's Infection and Immunity Research Network is delighted to announce that Drs Borko Amulic and Iart Luca Shytaj, both based in the School of Cellular and Molecular Medicine at the University of Bristol, have taken over from Angela Nobbs as discovery science co-Leads for the Network.

Borko's research focuses on cell biology and immunology of neutrophils. He and the members of his lab study how cell cycle and DNA repair proteins regulate neutrophil effector functions. Their work also aims to elucidate the function of cell cycle factors in post-mitotic cells with a goal of proposing targets for therapies in inflammatory diseases (including malaria, autoimmunity and cancer), as well as to discover ways to boost neutrophil microbicidal activity in settings such as immunodeficiency and antimicrobial resistance.

A Lecturer in Virology, Luca's main research question is finding druggable markers of HIV latency. He has studied antioxidant defences (and in particular the NADPH signalling axis) as therapeutic targets to induce a functional cure of the disease. He and his team combine transcriptomic, proteomic, and metabolomic analyses, for example to show that transition to latent HIV-1 infection downregulates glycolysis, while viral reactivation by conventional stimuli reverts this effect. He is a Chess Grand Master in his spare time.

## Amitriptyline helps relieve IBS symptoms

Amitriptyline, which is commonly used at low doses for a range of health concerns, has been found to improve irritable bowel syndrome (IBS) symptoms too, according to the results of the ATLANTIS trial.

Led by researchers at the Universities of Leeds, Bristol and Southampton, and funded by the National Institute for Health and Care Research, the study was conducted in primary care. GPs prescribed the drug and patients managed their own dose based on the severity of their symptoms, using an adjustment document designed for the trial. Most people with IBS are seen and managed in primary care by their GP, which means that the results of this trial are likely to be applicable to many people with the condition. The results showed that patients taking amitriptyline were almost twice as likely to report an overall improvement in symptoms as those taking a placebo. Now the trial team is recommending that GPs support their patients with IBS to use amitriptyline to manage their symptoms – and has made the dose adjustment document available for clinicians and patients.

Ford AC *et al*. (2023). Amitriptyline at low-dose and titrated for irritable bowel syndrome as second-line treatment in primary care (ATLANTIS): a randomised, double-blind, placebocontrolled, phase 3 trial. *The Lancet*.

## The England mpox outbreak

The rapid outbreak of mpox (formerly known as monkeypox) in 2022 likely resulted from high levels of sexual mixing among some gay, bisexual and other men who have sex with men (GBMSM), with the initial downturn in cases probably due to a reduction in sexual contacts among these men. A research team led by the National Institute for Health and Care Research (NIHR) Health Protection Research Unit (HPRU) in Behavioural Science and Evaluation, a partnership between the University of Bristol and the UK Health Security Agency, also found that the scale-up in vaccination did not contribute much to the initial downturn in cases, although the very small number of cases in 2023 is likely due to sufficiently high vaccination coverage to prevent a widespread resurgence in cases. The project describes the results of mathematical modelling, funded by the NIHR, to understand the epidemiological characteristics of the mpox outbreak in England, and what contributed to the outbreak ending, to help prevent and control future outbreaks.

Zhang X-S *et al*. (2023). Mathematical modelling of the transmission dynamics and impact of control measures in the 2022 outbreak of mpox among GBMSM in England. *The Lancet Infectious Diseases*

## Diabetes management in underserved communities

Children and young people with diabetes from families in underserved communities have higher blood sugar levels than average. Providing flexible, family-focussed support and addressing socio-cultural and emotional issues could improve how they manage their condition, according to a series of papers published as part of the Diversity in diabetes study.

To start with, researchers at the diet and physical activity theme of the Bristol Biomedical Research Centre, Applied Research Collaboration West and the University of Birmingham reviewed the range of diabetes self-management programmes available to children and young people. They did this by creating an overview of research that had been produced about this topic over the past three years.

They found that interventions should be adjusted according to the needs of families, while giving them skills to manage their children's diabetes. They found that gamification (adding game-style elements like point scoring into non-game activities) could improve how children and young people engage with programmes, while also introducing them to information about their condition. Programmes could be used to motivate families and young people to engage with diabetes services.

Litchfield I *et al*. (2023). Current evidence for designing self-management support for underserved populations: an integrative review using the example of diabetes. *International Journal for Equity in Health*.

Moore T *et al*. (2023). Views of children with diabetes from underserved communities, and their families on diabetes, glycaemic control and healthcare provision: A qualitative evidence synthesis. *Diabetic Medicine*.

## Funding successes: Part 1

Dr Darryl Hill (Cellular and Molecular Medicine) was awarded a PhD studentship from **Meningitis Now** for a project looking at *Survival and adaptation of the meningococcus in aerosol droplets*, £ 157,434, starting October 2023 for 4 years.

PhD student and Academic Clinical Fellow Dr Fergus Hamilton (Bristol Medical School) received a Health Technology Assessment award of £187.128 from the **National Institute for Health and Care Research (NIHR)** for *Dexamethasone for Cellulitis (Stage 2),* starting January 2024 for two years.

Prof Jan Frayne in the School of Biochemistry received £99,500 from the **Medical Research Council**'s Impact Acceleration Award to pursue *An innovative gamma-globin erythroid reporter line for translational application in drug discovery for beta-thalassemia*, starting December 2023 for one year.

*Transforming Outcomes for Paediatric allergy in primary care (TOPIC)* has been supported by a £2,390,398 award from **NIHR**, starting December 2023 for 5 years. The project will be led by Prof Matthew Ridd (Bristol Medical School).

Prof Jules Hancox (Physiology, Pharmacology and Neuroscience) was awarded £247,868 from the **British Heart Foundation** for *Determination of the cellular basis for cardiac repolarisation delay and arrhythmia risk with synthetic cannabinoids* , starting November 2023 for three years.

## Avoiding infection when injecting drugs

The REACT (Reducing bacterial infections) toolkit aims to help support people who inject drugs care for their veins and make changes to their injecting practices to prevent bacterial infections. A small pilot study in four settings within Bristol suggests the toolkit was viewed as acceptable to people who inject drugs and a range of service providers.

The toolkit was co-produced by people who inject drugs, service providers including Bristol Drugs Project and other key stakeholders. These included researchers from the University of Bristol and London School of Hygiene and Tropical Medicine, public health experts in the UK Health Security Agency and Bristol City Council, Exchange Supplies and Linnell Communications.

Bacterial skin and soft tissue infections such as abscesses and cellulitis are common among people who inject drugs. The main cause of these infections is poor hygiene during the injection process which is contributed to in part by the places and spaces people inject in. By involving the perspectives of people who inject drugs and key stakeholders the team ensured the toolkit focused on the priorities of people who inject drugs, including pain when injecting and maintaining vein access and care. A greater emphasis was also placed on addressing environmental obstacles to safer injecting. For example, offering wipes and hand sanitiser to support skin cleaning prior to injection.

Kesten J *et al*. (2023). Development, acceptability and feasibility of a personalised, behavioural intervention to prevent bacterial skin and soft tissue infections among people who inject drugs... *Harm Reduction Journal*.

## Clinical Research Network (CRN) West of England awards

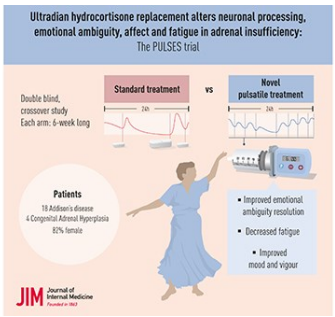
The research community from the West of England gathered to celebrate the incredible achievements of their colleagues at the Clinical Research Network (CRN) West of England's (WE) first in-person award ceremony. The event, held on 14 September 2023 at the Guildhall in Bath, recognised the work of CRN-supported staff during the last year (from 1 April 2022) across 10 categories.

Winners included:

- **CRN Local Specialty Research Lead (LSRL) of the year** – Amanda Hall, University Hospitals Bristol and Weston, LSRL Ear, Nose and Throat
- **People-centred research** – Vaccine and Testing Team, University Hospitals Bristol and Weston NHS Foundation Trust
- **Collaboration in Research** - HARMONIE Study West of England Regional Team. The study is a collaboration between Sanofi, its partner AstraZeneca, and the National Institute for Health and Care Research (NIHR) evaluating the efficacy of nirsevimab, a monoclonal antibody immunisation, in protecting against one of the leading causes of infant hospitalisation worldwide. RSV often causes only mild illnesses, like a cold. However, for some babies, it leads to more severe lung problems such as bronchiolitis and pneumonia.

## Hormone replacement treatment for adrenal conditions

A first-of-its kind hormone replacement therapy that more closely replicates the natural circadian and ultradian rhythms of our hormones has shown to improve symptoms in patients with adrenal conditions.




Low levels of cortisol are typically a result of conditions such as Addison's and Congenital Adrenal Hyperplasia. The hormone regulates a range of vital processes, from cognitive processes such as memory formation, metabolism and immune responses, through to blood pressure and blood sugar levels. When low, it can trigger symptoms of debilitating fatigue, nausea, muscle weakness, dangerously low blood pressure and depression. Although rare, these adrenal conditions require lifelong daily hydrocortisone replacement therapy. Although existing oral hormone replacement treatment can restore cortisol levels, it is still associated with an impaired quality of life for patients, believed to be due to not mimicking the body's normal physiological timing, missing cortisol's anticipatory rise and lacking its underlying ultradian and circadian rhythms.

The new 'Pulsatility' therapy, the culmination of ten years research by the Bristol team, is designed to deliver standard hydrocortisone replacement to patients via a pump which replicates more closely cortisol's natural rhythmic secretion pattern. The pump has revealed promising results in its first clinical trial.

Russell G *et al*. (2023). Ultradian hydrocortisone replacement alters neuronal processing, emotional ambiguity, affect and fatigue in adrenal insufficiency: The PULSES trial. *Journal of Internal Medicine.*

## Funding success: Part 2

Dr Giulia Bigotti (Bristol Medical School) was awarded £330,00 from the **British Heart Foundation** to investigate the extracellular matrix protein agrin and its potential of inducing cardiac repair. The potential of the C-terminal portion of agrin for cardiac regeneration has been known for a few years. The idea to further shorten the C-terminal part of the protein and produce a miniaturised form that only contains the region of agrin believed to be directly responsible for the cardioprotective effect. Local administration of such protein(s) to patients with a damaged heart (after open heart surgery, for example) would help 1) more potently regenerate heart muscle and contrast heart fibrosis, 2) enhance other cardioprotective effects such as suppression of the inflammatory response and improved angiogenesis, already shown in mice and pigs for the full-length agrin C-term. The funding is for three years.

Dr Rachel Denholm received £74,518 from **Health Data Research UK** for *Characterising a high-risk Type 2 Diabetes phenotype using big data – the role of comorbidity and ethnicity*, starting October 2023 for four years.

Dr Gareth Jones (Cellular and Molecular Medicine) was awarded £250,000 from **Sanofi-Aventis Deutschland GmbH** for a project entitled Targeting cellular metabolism to treat Th17-driven pathology, starting October 2023 for two years.

Dr Tristan Cogan (Bristol Veterinary School) was awarded £4,237 from the **Morris Animal Foundation** for *Assessment of a Novel Point of Care Gamma Interferon Testing Technology alongside the Evaluation of a Loop Mediated Isothermal Amplification System for the Detection of Latent and Active form of Tuberculosis in Primates in remote Settings*, starting October 2023 and completing in December 2023.

## Strep A vaccine research

University of Bristol scientists Dr Anu Goenka, Dr Alice Halliday and Dr Darryl Hill (all based in the School of Cellular and Molecular Medicine) have been supported by the Spencer Dayman Meningitis Foundation to pursue a project entitled *The AVIATOR Strep A Study (Vaccine development using a tonsil organoid system)*, which aims to develop a 'Group Strep A' vaccine. Invasive Group A streptococcus (iGAS) can cause diseases such as bacterial meningitis.

The project, which received funding in the region of

£57,000, started in October 2023 and is expected to complete in September 2024.

The funding charity was set up in 2002 in memory of Spencer who died of meningitis and sepsis at 14 months. Read the BBC news article here: https://www.bbc.co.uk/news/uk-england-bristol-66987033.

Dr Goenka, together with Dr Steve Dayman MBE (pictured here), explain the significance of this research on BBC Points West on 7 October 2023. View the except here: BBC PW 7th Oct 2023 compressed.mp4 (University of Bristol login required).

## Feeding dogs raw meat and risk of antibiotic resistance

*E. coli*, which can cause food poisoning, is also the UK's most common cause of urinary tract and bloodstream infections, which can be life-threatening. Ciprofloxacin belongs to a group of antibiotics called fluoroquinolones, which are used to treat a range of bacterial infections in humans and animals. The World Health Organisation classes these antibiotics among the highest-priority critically important antibiotics.

A study by researchers at the University of Bristol looked for ciprofloxacin-resistant *E. coli* carried in the intestines of 600 healthy pet dogs. They asked dog owners to complete a survey that provided details about their dog, its diet, environments the dog walked in and if the dog had been treated with antibiotics. The microbiology data along with the survey data enabled statistical analysis, which showed that feeding uncooked meat to dogs was the only significant risk factor associated with excretion of these resistant bacteria in the dog's faeces. This work supports other published studies demonstrating associations between dogs being fed raw meat and excreting resistant *E. coli*.

Sealey JE *et al*. (2023). One health transmission of fluoroquinolone-resistant E. coli and risk factors for their excretion by dogs... . *One Health*

## £10.5 million investment for vaccine manufacture

A new collaborative initiative between UK universities and countries worldwide to share cutting-edge vaccine technology to prevent future global outbreaks of infectious diseases has been awarded £10.5 million from the Department of Health & Social Care (DHSC) and the Engineering and Physical Sciences Research Council (EPSRC).

The funding will support the Future Vaccine Manufacturing Research Hub (FVMR Hub), set up originally in 2017 by Imperial College London with University of Bristol as a partner, to continue operations for a further five years, until 2029.

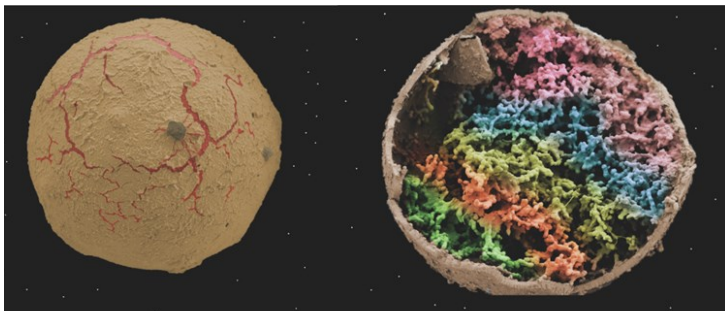
As part of this partnership, world-leading vaccine scientists at Bristol are working with one of Vietnam's major vaccine manufactuers, Vabiotech, to share their expertise in using a powerful recombinant production technology which relies on a synthetic baculovirus used as a production tool. The technology, pioneered at Bristol, is uniquely suited for producing next-generation vaccines in large quantities in insect cells that can be easily cultured at low cost in Vietnam.

To mark the announcement and to kick-off operations, University of Bristol researchers welcomed representatives from the Vietnamese Ministry of Health, the Vietnamese Embassy in the UK, the CEO and research team of Vabiotech, and leading vaccine scientists and Hub partners from Imperial College London with a reception in the Wills Memorial Building *(pictured, © Bhagesh Sachania Photography)*

Read the full story

## Biofilm Create! Competition 2023

The National Biofilms Innovation Centre, of which the University of Bristol is a member, announced the winners of their 2023 Biofilm Create! Competition. It has two categories: photography and art, and offers an opportunity for contributors to explore biofilms in their everyday environments and scientists to look at creative ways of showcasing their research. You can view all of the entries received on NBIC's Biofilm Image Gallery and Biofilm Art Gallery.



Amongst the **Photography Category Winners** were Huan Ma (PhD student, Chemistry) and Xiayi Liu (PhD student, Bristol Dental School) for *Bacterial planet* (£250 Amazon voucher).

*A long time ago, in a microbial universe far, far away…. There existed a drab planet where burning desert sands spread all over its surface, and red lava rivers roared deafeningly (left image). It appeared as though no microbes could survive on this harsh planet. However, life, even on a microscopic scale, has an uncanny ability to create miracles.* Lactococcus lactis (L. lactis) *discovered a way to thrive on this unforgiving planet. They migrated from the ground to the planet's interior and established a thriving and vibrant bacterial metropolis (right image). In this underground bacterial city, each bacterium was interconnected by a network of extracellular polymeric substances, which facilitated the sharing of information and nutrients. Together, they formed a resilient, unified front against the planet's hostile environment. The images were captured using scanning electron microscopy and false coloured. We immobilised* L. lactis cells *within polymer vesicles, allowing the bacteria to grow and form biofilms inside these vesicles. The resulting hybrid bacterial vesicles proved to be highly effective in the production of lactic acid. It offers a promising new approach to harnessing biofilms for various practical applications in our daily lives.*

## European Aerosol Conference Science Conference 2023

PhD student in the School of Cellular and Molecular Medicine Robert Alexander presented at the European Aerosol Conference Science Conference 2023 held 2 – 8 September 2023 in Málaga, Spain. His talk put forward Darryl Hill's Group findings on what are the main drivers for pathogen decay in respiratory aerosol. Rob works on the replication and modelling of infectious respiratory droplets in humans and animals.

Rob was able to attend thanks to a travel grant from the Aerosol Society.

## New climate change and health research projects

Generously funded by the University of Bristol US Foundation, this funding call supported interdisciplinary research studies aiming to understand and shape responses to the enormous challenges of climate change impacts on health.

Climate change is one of the biggest health threats facing humanity and is already affecting human health around the world. Impacts of climate change on health are not evenly distributed, but they are likely to increase.

The Climate Change and Health research programme, a joint research initiative between Elizabeth Blackwell Institute for Health Research and Cabot Institute for the Environment, is looking into the intersection between climate change and health to help us find solutions for a healthier future.

**Funded projects 2023:**

Hydro-epidemiological modelling to understand Leptospira transmission risk and interventions, Investigators: Dr Rodolfo Bezerra Nobrega, Dr Zoe Ward, Prof Guy Howard and partners at University of Bahia, Brazil

Risks for micronutrient losses due to vector-borne plant viruses affecting nutritious crops in Sub-Saharan Africa, Investigators: Dr Angeliki Papadaki, Dr Dan Bernie and Dr Nina Ockendon-Powell

UNSEEN heatwave mortality, Investigators: Dr Chin Yang Shapland, Dr Eunice Lo, Prof Dann Mitchell, Prof Kate Tilling.

Read more

## Eczema study wins Research Paper of the Year award

University of Bristol-led research comparing the effectiveness and safety of different types of moisturiser for childhood eczema has won the Royal College of General Practitioners (RCGP) Research Paper of the Year (RPY) Award 2022.

The research was led by Matthew Ridd, a GP and Professor of Primary Care at Bristol's Centre for Academic Primary Care and the award was announced at the RCGP Conference in Glasgow, 19-20 October 2023. The National Institute for Health and Care Research (NIHR)-funded 'Best Emollients for Eczema (BEE)' clinical trial compared lotions, creams, gels and ointments used to treat childhood eczema. The trial found no difference in the effectiveness or safety between the four emollient (moisturiser) types, leading the authors to conclude that "the right moisturiser for children is the one that they like to use."

The study, the first in the world to compare different types of moisturiser directly, highlighted the importance of patient education and choice when deciding which moisturiser to use for children with childhood eczema. The findings were published in The Lancet Child and Adolescent Health in May 2022.

The five-year study involved over 500 children and their parents, recruited from 77 GP practices across England. It was a partnership with the Universities of Nottingham and Southampton and with support from Bristol Trials Centre, UK Dermatology Clinical Trials Network, and Bristol, North Somerset and South Gloucestershire (BNSSG) Integrated Care Board.

## Type 2 diabetes remission diet impacts on metabolic health

People with type 2 diabetes who took part in a diet-assisted weight loss trial, showed differences across a wide range of potential biomarkers of metabolic health one year later. The study used data from the Diabetes Remission Clinical Trial (DiRECT) and represents a collaboration between the Universities of Bristol, Glasgow and Newcastle.

Weight loss is now a key intervention for patients with type 2 diabetes thanks to DiRECT, which found a primary-care deployed dietary weight loss programme, Counterweight-Plus, could put the condition into remission. The programme has been adopted by the NHS as a clinically proven intervention. However, its impact on patients' wider metabolic health was largely unknown. To determine if weight loss benefits extend to wider metabolic health, the team analysed levels of over 1,000 metabolites in blood samples before and one year after beginning the intervention. Around 14% of all metabolites measured were found to be altered; many of the changes in response to the diet had previously been reported as moving in the opposite direction prior to type 2 diabetes onset. These changes were evident many weeks after the conclusion of the weight loss phase of the intervention, suggesting sustained benefits to patient health. The findings support the growing consensus of the importance of excess weight as a contributor in the pathogenesis of type 2 diabetes and, as a treatment target.

Corbin L *et al*. (2023). The metabolomic signature of weight loss and remission in the Diabetes Remission Clinical Trial (DiRECT). *Diabetologia*

## Awards and recognition

Dr Kushala Abeysekera (Academic Clinical Lecturer in Public Health and Epidemiology: Gastroenterology, Bristol Medical School, pictured right) was awarded the Dame Sheila Sherlock Award as best hepatology young investigator in the UK.

Each year BASL (British Association for the Study of the Liver) presents the Dame Sheila Sherlock research prize, one of the highlights of its Annual Meeting. This prize is awarded annually to recognise the enormous contribution of Dame Sheila Sherlock to the development of Hepatology as a discipline in its own right. Kushala delivered the 30-minute prize lecture during the plenary session *Sustainable Hepatology- The use of technology and AI to improve outcomes in liver disease* and received the award at the BASL annual meeting on 20 September 2023.

Dr Drinalda Cela, former PhD student in Borko Amulic's Research Group in the School of Cellular and Molecular Medicine (pictured below), was awarded a prize for 'Outstanding Excellence in a doctoral dissertation' for the Faculty of Life Sciences 2022/23. Her dissertation was entitled *Molecular Regulation of Neutrophil Responses*. Drinalda is now working as a postdoctoral research at The Francis Crick Institute in London.

## Funding successes: Part 3

Dr Anu Goenka (Cellular and Molecular Medicine) has received £26,803 from the **European Society for Paediatric Infectious Diseases** Springboard Award; the scheme funds protected research time for clinician-scientists who are progressing towards academic independence (Oct 2023-Sep 2024).

Prof Ingeborg Hers (Physiology, Pharmacology and Neuroscience) was awarded £910,903 from the **Biotechnology and Biological Sciences Research Council** for *PROTACs as a novel approach to target tyrosine kinases for degradation in human platelets*, October 2023 for three years.

Prof Richard Wall (Biological Sciences) was awarded £95,390 from the **CVS Group Plc** for *Assessing the environmental risk from ectoparasite treatments in companion animals*, starting September 2023 for three years.

A £29,562 **Academy of Medical Sciences** Starter Grant for *Investigating the rise of liver disease in young adults in the UK* was awarded to Dr Kushala Abeysekera (Bristol Medical School), starting September 2023 for two years.

Prof Adam Finn (Cellular and Molecular Medicine) received £88,439 from **Pfizer Inc** for *AvonCAP GP2 - Respiratory Syncytial Virus (RSV) repeat sampling cohort (2023/24),* November 2023 for one year. The AvonCAP Study is looking at how respiratory disease may change following COVID-19, with a focus on pneumococcus and RSV.

## Being taller may protect against heart disease and stroke

Being taller during the course of a person's lifetime could protect against heart disease and stroke in later life, according to a new University of Bristol-led study. The research analysed height and genetic data on over 454,000 individuals and the genetic markers associated with five types of cardiovascular disease. These included stroke, coronary artery disease, peripheral artery disease, irregular heartbeat (atrial fibrillation), and thoracic aortic aneurysm.

From their analyses, results showed that individuals who are taller in early life typically have lower risk of coronary artery disease. However, novel evidence from this work indicates that this is likely

attributed to individuals remaining taller throughout the life course — as taller children on average grow to be taller adults — and that it is adulthood height which is largely responsible for this protective effect. In contrast, results from this study suggest that being taller in childhood may also increase later life risk of other cardiovascular disease outcomes such as thoracic aortic aneurysm and irregular heartbeat (atrial fibrillation), irrespective of adulthood height.

Richardson T *et al*. Effects of childhood and adult height on later life cardiovascular disease risk estimated through Mendelian randomization. *medRxiv (preprint that has not been through peer review)*

## University STAR Awards

The STAR Awards recognise and celebrate the outstanding contributions of staff across the institution.

CONNECTED - Community Network for Vector-Borne Plant Viruses - is building a sustainable network of international scientists and researchers to address the challenges of vector-borne plant viruses. It is led from the University of Bristol (UK) by Network Directors Prof Gary Foster, Dr Andy Bailey and Pro Neil Boonham (Newcastle University). From 1 October 2023 the CONNECTED Network, website, resources and membership, have been jointly hosted by the International Institute for Tropical Agriculture (IITA) and the International Livestock Research Institute (IRLI). IITA is an award-winning, research-for-development organization, providing solutions to hunger, poverty, and the degradation of natural resources in Africa. ILRI work across Africa and Asia to improve food security and reduce poverty through research.

CONNECTED boasts over 1670 members from 97 countries. The team have turned a roller-coaster of sudden changes to the national and international funding landscape into a series of successes.

With 685 STAR Award nominations received from across the University of Bristol, the CONNECTED team were shortlisted in the final three in the "Embracing Change" category, celebrated this success with other nominees at a celebratory dinner in the Wills Memorial Building on 14 September 2023.

## Bristol soil study unearths microbe diversity discovery

Human impacted soils tend to harbour different microbial communities to those areas less affected by human activities. A team of researchers working with Bristol school children studied the species of bacteria found in soils at two local schools, Merchants Academy and Brunel Academy, the Avon riverbank, Queens Square, Fenswood Farm and Ashton Court Deer Park.

They found that human impacted soils still showed a large diversity between sites in terms of the microbes present, and the study highlighted that other factors like the geochemical make-up of the soil and environmental factors also play a key role.

Many important biotechnologies like novel antibiotics are found in the soil. Building on this interest the multidisciplinary team from the University of Bristol investigated what the soils of Bristol contained to try and understand how discoveries in soils might be used in a fair and equitable way. It started as a curiosity-driven project about soil to help researchers connect science to the wider community; yet conversations emerged about how science and technology could be more responsible. This led the team to develop a new approach to guide research in a way that does not treat nature as a resource to be exploited.

Tarnowski MJ *et al*. (2023). Soil as a transdisciplinary research catalyst: from bioprospecting to biorespecting. *Royal Society Open Science*.

## NIHR Research Professorship award

Matthew Ridd (pictured), Professor of Primary Health Care and GP, is one of six researchers to have been awarded a National Institute for Health and Care Research (NIHR) Research Professorship.

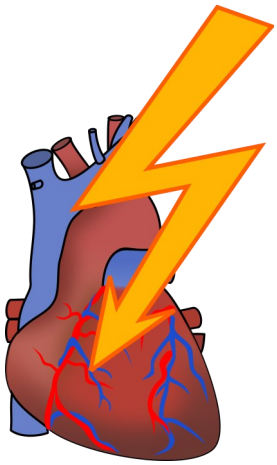
Matthew, based in Bristol's Centre for Academic Primary Care, will carry out research to treat eczema in children and identify and address children's food allergies.

The NIHR Research Professorships scheme funds and supports research leaders of the future to improve the health and wealth of the nation through research. It also aims to strengthen and benefit health, public health and care research leadership at the highest academic levels.

This year, each of the successful applicants will receive five-year awards of up to £2 million to carry out research that will positively impact the lives of people and communities across the UK. They will receive a package of extensive support, including three support posts and access to a leadership and development programme.

## Fossil fuels responsible for heart arrhythmias in mammals

One of the most common by-products of the burning of fossil fuels, phenanthrene, causes heart arrythmias in mice, proving for the first time it is toxic to mammals, new research has discovered.



The study is led by The University of Manchester in collaboration with the University of Bristol and Moscow State University, and funded by the British Heart Foundation.

Thanks to earlier work by one of the lead authors Prof Holly Shiels from Manchester in conjunction with scientists at the University of Bristol, Moscow State University, National Oceanic and Atmospheric Association (NOAA) and Stanford University, phenanthrene's toxicity to the hearts of fish and crustaceans (crayfish) has been well established. But now the team has discovered the change also occurs in healthy mouse hearts when directly exposed to phenanthrene, mimicking what happens when we breath in pollution.

Phenanthrene is a polycyclic aromatic hydrocarbon (PAH) that is present in crude oil and emitted into the air when fossil fuels are burnt; it is present in the gas phase of air pollution and also adheres to the surface of particulate matter (PM). It can be inhaled into the lung and then translocated into the bloodstream, eventually finding its way to the heart. In the study, when phenanthrene was applied to an isolated mouse heart, it caused monophasic tachycardia. The team showed that phenanthrene disrupts the contractile and electrical function of the mouse heart by blocking ion channels required for synchronous beating of the heart.

Yaar S *et al*. (2023). Global air pollutant, phenanthrene, and arrhythmic outcomes in a mouse mode. *Environmental Health Perspectives*.

## New intervention for male urinary problems

A new intervention for men with urinary problems trialled across GP practices has shown a sustained reduction in symptoms. The University of Bristol-led Treating Urinary Symptoms in Men in Primary Healthcare (TRIUMPH) study involved over 1,000 participants and 30 GP practices.

The severity and prevalence of lower urinary tract symptoms [LUTS] in men increases with age (up to 30% in men over 65 years), with greater numbers likely to be affected as the population ages. Symptoms can have a substantial impact on quality of life but can also influenced by lifestyle factors.

Bristol Medical School researchers sought to trial whether a new intervention, comprising a healthcare professional consultation and an information booklet providing conservative and lifestyle guidance, could be more effective than usual care. The findings showed a range of troublesome urinary tract symptoms improved over 12 months in a population of men with moderate symptom severity, using a standardised booklet and manualised approach to symptom management. Analyses of symptoms in each trial arm found the intervention achieved a greater reduction in symptoms than usual care, and that the difference was maintained in the longer term. Implementation of this intervention as management in primary care has the potential to improve care and reduce drug prescriptions.

Drake MJ et al. (2023). Treating male lower urinary tract symptoms in primary healthcare using conservative interventions: the TRIUMPH cluster randomised controlled trial. *BMJ*.

## Highly Cited Researchers 2023 list

A total of 20 University of Bristol academics have been named on Clarivate's Highly Cited Researchers 2023 list - up by three on last year.

The annual list acknowledges the most influential researchers in the world, who have published multiple papers frequently cited by their peers during the last decade. The full list of names has been taken from papers ranked in the top 1% of most cited works for their field and publication year in the Web of Science citation index.

The Bristol academics on the list include:

- Professor of Medical Statistics and Epidemiology Jonathan Sterne, Bristol Medical School; one of his main research interests lies in clinical epidemiology of HIV and AIDS in the era of antiretroviral therapy
- Professor in Public Health and Epidemiology Matthew Hickman, Bristol Medical School; research programme focuses on infectious disease control and the epidemiology and public health consequences of drug use
- Professor of Infectious Disease Modelling Peter Vickerman, Bristol Medical School. His research focuses on the use of mathematical modelling to help understand the transmission of different infectious diseases and impact and cost-effectiveness of prevention measures. Specific expertise focuses on the transmission of HIV, HCV and other STIs amongst different high-risk groups including female sex workers, men who have sex with men and injecting drug users.

Read more

## Newborn illness linked to 71% of child deaths up to age 10

Drawing on data from Bristol's National Child Mortality Database (NCMD), the study examined 4,829 deaths of children up to age 10 which occurred in England between April 2019 - March 2022. Researchers used statistical techniques to derive the relative risk, comparing children with, or without, neonatal illness on risk of death. The study built on earlier work by the same group which showed that 42% of all child deaths occurred within 28 days of birth; it found that perinatal events like preterm birth, perinatal brain injury and neonatal infections had an impact on child survival for many years after. Furthermore, the increased risk applied across a range of causes. Children affected by perinatal events were found to be over-represented among deaths due to infections and sudden, unexplained deaths in infancy and childhood. Overall the team found 71.6% of the child deaths were among children who had evidence of some neonatal illness. Of these, 82.7% were children who died before 1 year of age, and 33.9% were those who died over the next nine years. This new evidence suggests that improvements to perinatal health and preterm births as well as a focus on reducing brain injury around birth could improve child health in the future.

NCMD National Child Mortality Database

Luyt K *et al*. (2023). Newborn health and child mortality across England. *JAMA Network Open*.

## Improving global diversity in population health

An international collaboration is aiming to improve global health by uncovering the effects of genomic and environmental diversity on differences in disease risk observed across the global population, thanks to a new partnership of 20 research groups from around the world.

The groundbreaking five-year project, led by researchers in the University of Bristol, the MRC Unit The Gambia at London School of Hygiene & Tropical Medicine and the CSIR Centre for Cellular and Molecular Biology in India, will explore key population health questions using datasets from across African, Asian, and North and South American continents.

DIVERSE EPIGENETIC EPIDEMIOLOGY PARTNERSHIP

The Diverse Epigenetic Epidemiology Partnership (DEEP) study, funded by the Medical Research Council, will generate genomic datasets in underrepresented populations. The study will develop software and infrastructure and conduct advanced statistical analyses to build new resources. These new resources will sit alongside international health and genetics databases to look at trends in variation in DNA methylation - a process where chemical groups attach to DNA in order to help to turn genes on and off. This research will enable identification of disease-causing mechanisms that are common worldwide and those which are unique to particular groups or regions. It will help with answering questions such as whether medicines developed in one part of the world will be effective for all. Ultimately the DEEP study hopes to enable targeted interventions or treatments and reduce global health disparity and inequity.

Read the full news item

## Award for improving quality of sexual healthcare

A collaborative project working with child sexual abuse survivors to improve their experiences of sexual health services has won a British Medical Association (BMA) prize. At a ceremony on 31 October 2023, Dr Jane Meyrick, Associate Professor of Health Psychology at the University of the West of England (UWE) and Dr Michelle Cutland from The Bridge Sexual Abuse Referral Centre (SARC) were presented with the 2023 BMA MEDFASH prize. They accepted the prize on behalf of the collaboration, including The Green House, the specialist support service for young survivors of child sexual abuse and their families in Bristol, South Gloucestershire, Bath and North East Somerset, and North Somerset.


Through Bristol Health Partners Sexual Health Improvement Health Integration Team, researchers worked with service providers in partnership with survivors of child sexual abuse to identify changes that could be made to the patient pathway to improve sexual health follow-up for patients, parents, and health professionals.

The partnership work resulted in a new patient pathway for The Bridge SARC in Bristol into local sexual health services for our children and young people, designed through supported engagement with The Green House's Voice Group of young survivors. The redesigned and co-created pathway has been in use since January 2023. Improvements will be captured through a similar collaborative evaluation and will be survivor led.

Read more

## Extreme heat and disease in urban areas

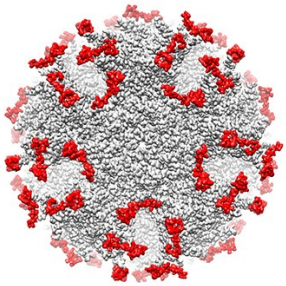
Advanced tools and more experimental studies are needed to urgently understand the impact of extreme heat events on urban health and wellbeing in the UK. A study under the TRUUD project aims to reduce non-communicable disease (NCD - such as cancers, diabetes, obesity, mental ill-health and respiratory illness) and health inequalities linked to the quality of urban planning and development.

The team looked at gaps in our knowledge between the urban environment and heatwaves, indoor heat, and non-communicable diseases and examined what we already know about the effects of extreme heat, NCDs and related risk factors to help urban planners factor health considerations in the decision-making process. Findings consistently demonstrated that higher temperatures above defined heat thresholds were significantly associated with increased mortality rates. The studies included in the review reported that for every 1°C rise above the heat threshold, mortality increased by up to 2.5%, emphasising the urgent need for mitigation strategies. Furthermore, the projected impact of temperature rise on heat-related mortality showed alarming figures, with estimates suggesting a potential 90% increase in heat-related deaths between the 2020s and 2050s under medium-emission scenario.

Ige J *et al*. (2023). A systematic review of the impacts of extreme heat on health and wellbeing in the United Kingdom. *Cities and Health*.

## ADDomer™ can tackle viral infections

New research has demonstrated the potential for the ADDomer™ platform to produce thermostable vaccines and reagents to tackle viral infections The study was led by the University of Bristol and Imophoron, a biopharmaceutical company developing thermostable nanoparticle vaccines using its ADDomer™ platform.



The research team explored the innovative technology behind the development of an ADDomer vaccine targeting severe acute respiratory syndrome COVID-19 (SARS-CoV-2). The study, using an integrated approach, combined synthetic, computational and structural methods with in vitro antibody selection and in vivo immunisation to design, produce and validate nature-inspired nanoparticle-based vaccines and reagents.

The research demonstrates the use of Imophoron's patented multivalent nanoparticle superbinder technology against SARS-CoV-2, including immune-evasive variants of concern.

Berger I *et al*. (2023). In vitro generated antibodies guide thermostable ADDomer nanoparticle design for nasal vaccination and passive immunization against SARS-CoV-2. *Antibody Therapeutics*.

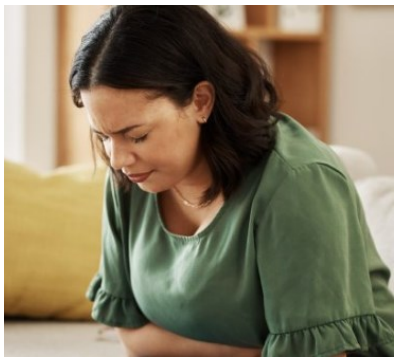
*Image shows the ADDomer™ COVID vaccine*

## Diagnostic process for coeliac disease

Patients experience uncertainty when following the traditional diagnostic pathway for coeliac disease, according to a recent study. The team from the University of Bristol and NIHR Applied Research Collaboration (ARC) West suggested that GPs could improve this by:

- Keeping coeliac disease in mind as a possible diagnosis
- Sharing information on blood tests

Researchers also discussed how the uncertainty patients experience during testing for coeliac disease needs to be addressed when considering diagnostic pathway changes, such as a move towards using only blood test results for diagnosis.



Getting diagnosed with coeliac disease can take a long time. This is because symptoms are usually non-specific and can be attributed to other conditions. This often leads to a delay between when symptoms first develop and when a patient is diagnosed.

Researchers wanted to understand the experience of someone who had undergone diagnosis. They spoke with 20 adults, many of whom had been experiencing non-specific symptoms for years before coeliac disease was confirmed. They found patients also experienced uncertainty while undergoing testing for the disease, which caused further anxiety.

Harper A *et al*. (2023). Understanding the patient experience of coeliac disease diagnosis: a qualitative interview study. *British Journal of General Practice*.

# FUNDING OPPORTUNITIES

**Research Professional** provides access to an extensive database of funding opportunities. UoB staff and students have **FREE** online access to the database – once you've registered then you can view upcoming funding opportunities from any device. 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
- Save searches and bookmarks - store items of interest for future reference, download and email to colleagues
- Sign up for higher education news bulletins

**For further information on Research Professional, go to the Division of Research, Enterprise and Innovation (DREI, formerly RED) website**

Research Professional

**National Institute for Health and Care Research**
Interventions to reduce Antimicrobial Resistance (AMR)

Closing date: 3 January 2024 Award amount: unspecified

The aim of the Health Technology Assessment (HTA) Programme is to ensure that high quality research information on the clinical effectiveness, cost-effectiveness and broader impact of healthcare treatments and tests are produced in the most efficient way for those who plan, provide or receive care from NHS and social care services. The HTA Programme is interested in receiving applications for the evaluation of health care interventions to reduce the development and spread of antimicrobial resistance and consequent morbidity.

**Medical Research Council**
Research grants - infections and immunity

Closing date: 10 January 2024 Award amount: unspecified

These fund focused research projects that may be short- or long-term in nature related to infections and immunity, as well as method development and continuation of research facilities. Projects may involve more than one research group or institution.

**Lupus Research Alliance**
Lupus Insight Prize

Closing date: 16 January 2024 Award amount: USD 100,000

Provides research funds to an outstanding investigator with a documented record of creativity, innovation, and productivity who has made a novel insight or discovery in a research area applicable to the pathogenesis or treatment of lupus. The investigator must have a high likelihood of generating further significant advances by applying the insight to lupus.

**International Waldenstrom's Macroglobulinemia Foundation**
IWMF-LLS Strategic Research Roadmap Initiative

Closing date: 17 January 2024 Award amount: USD 400,000

Pledged to promote and support basic research leading to improved understanding of the cause, diagnosis, treatment, and cure for the disease Waldenstrom's macroglobulinemia (WM).

**European Society of Clinical Microbiology and Infectious Diseases**
CAREer grants

Closing date: 17 January 2024 Award amount: unspecified

Support the career development of all those in the fields of clinical microbiology and infectious diseases who face challenges in advancing their scientific careers due to responsibilities such as childcare or unexpected situations preventing them from working full-time.

**Innovate UK**
Transforming cancer therapeutics

Closing date: 124January 2024 Award amount: £2 million

To support innovation projects that focus on advancing next-generation immunotherapies for cancer or life-changing treatment options for childhood cancers.

Your project can include: experimental evaluation at laboratory scale; use of in vitro and in vivo models to evaluate proof of concept or safety; exploration of potential production mechanisms Prototyping; product development planning; intellectual property protection; a demonstration of clinical utility and effectiveness; a demonstration of safety and efficacy including phase 1 and 2 clinical trials; regulatory planning.

Your project can focus on one or more of the following: next generation immunotherapies and immunomodulatory drugs; manipulation of the tumour microenvironment to promote immune responses against solid tumours; novel therapeutics that consider the unique characteristics of paediatric or young people's cancers; clinical decision support tools to optimise therapeutic dosing for children and young people.

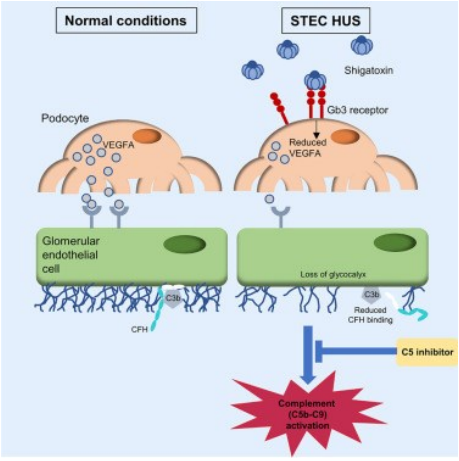
# THIS ISSUE'S FEATURED ARTICLE

## Shiga toxin targets the podocyte causing hemolytic uremic syndrome through endothelial complement activation

Bowen EE, Hurcombe JA, Barrington F… Licht C, Saleem MA & Coward RJM (2023). *Med*.

The commonest cause of kidney failure in children is due to toxin producing bacteria that enters the circulation through the gut resulting in a disease called Haemolytic Uraemic Syndrome (HUS), the most common type of which is Shiga toxin-associated haemolytic uraemic syndrome (STEC-HUS), which can be particularly devastating in young children.

STEC-HUS commonly happens after a gut infection. Exactly why the kidney is so susceptible to injury in STEC-HUS has until now, remained unclear. The research, funded by the Medical Research Council and Kidney Research UK and led by scientists from Bristol Renal, wanted to identify the mechanism underpinning the disease pathway. Using laboratory models, they found a specific cell in the kidney - the podocyte - which plays a crucial role in renal function. It is targeted by the Shiga toxin and then 'talks' to local blood vessels causing small blood clots to form. This is due to the activation of the 'complement' pathway, and can lead to an eventual loss of kidney function. Critically, the team demonstrated in both mouse models and in human kidney cells that STEC-HUS can be successfully treated by inhibiting the complement pathway early in the disease process with a drug called Eculizumab. The team has demonstrated that early use of Eculizumab can prevent Shiga-toxin driven kidney failure and the drug has therapeutic potential for this devastating disease that can result in life-long dialysis, and death, for some children.




*Background*: Shiga toxin (Stx)-producing Escherichia coli hemolytic uremic syndrome (STEC-HUS) is the leading cause of acute kidney injury in children, with an associated mortality of up to 5%. The mechanisms underlying STEC-HUS and why the glomerular microvasculature is so susceptible to injury following systemic Stx infection are unclear.

*Methods*: Transgenic mice were engineered to express the Stx receptor (Gb3) exclusively in their kidney podocytes (Pod-Gb3) and challenged with systemic Stx. Human glomerular cell models and kidney biopsies from patients with STEC-HUS were also studied.

*Findings*: Stx-challenged Pod-Gb3 mice developed STEC-HUS. This was mediated by a reduction in podocyte vascular endothelial growth factor A (VEGF-A), which led to loss of glomerular endothelial cell (GEnC) glycocalyx, a reduction in GEnC inhibitory complement factor H binding, and local activation of the complement pathway. Early therapeutic inhibition of the terminal complement pathway with a C5 inhibitor rescued this podocyte-driven, Stx-induced HUS phenotype.

*Conclusions*: This study potentially explains why systemic Stx exposure targets the glomerulus and supports the early use of terminal complement pathway inhibition in this disease.

# CONTACTS

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

Co-Chairs (discovery science): Borko Amulic - Senior Research Fellow in Immunology
Luca Shytaj - Lecturer in Virology

Co-Chairs (clinical): Julia Colston - Consultant in Infection
Ed Moran - Consultant in Infectious Diseases

- Matthew Avison - Professor of Molecular Bacteriology
- Charles Beck - Consultant Epidemiologist & Head of Team, Field Service South West, National Infection Service, UK Health Security Agency
- Sinead English - Senior Research Fellow (early life effects in ecology and evolution)
- Hannah Fraser - Research Fellow in Infectious Disease Mathematical Modelling
- Clare French - Research Fellow in Research Synthesis
- Anu Goenka - Clinical Lecturer in Paediatric Infectious Diseases and Immunology
- Melanie Hezzell - Associate Professor in Cardiology
- Rajeka Lazarus - Consultant in Infection
- Anna Long - Senior Research Associate (Diabetes UK RD Lawrence Fellow)
- Jamie Mann - Senior Lecturer in Vaccinology & Immunotherapy
- Suzanne Mills - Research Development Associate Health and Life Sciences
- Adrian Mulholland - Professor of Chemistry
- Angela Nobbs - Senior Lecturer in Oral Microbiology
- Laura Peachey - Lecturer in Veterinary Parasitology
- Annela Seddon - Professor of Physics
- Peter Vickerman - Professor of Infectious Disease Modelling
- Catherine Brown - Network Administrator



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

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