

I&I NETWORK NEWSLETTER



2021 - ISSUE 4



Vaccinating for flu and COVID together is safe

Earlier in the pandemic it was not known whether further booster doses of COVID-19 vaccines would be required to give continued protection, and how giving boosters may fit in with the seasonal flu vaccine programme. The [Combining Influenza and COVID-19 Vaccination \(ComFluCOV\)](#) study looked to establish the safety of co-administering the most widely used COVID-19 and influenza vaccines in the UK and describe the expected side effects and immune responses to the vaccines when they are given together. Two

COVID-19 and three influenza vaccines were tested, meaning six combinations in all.



The immune responses to both the influenza and COVID-19 vaccine were preserved when given together, and 97% of participants said they would be willing to have two vaccines

at the same appointment in the future.

The results of the study were presented to the Joint Committee on Vaccination and Immunisation (JCVI) for their consideration and helped policy makers in planning the future of these important vaccination programmes.

The ComFluCOV study was led by the Bristol Trials Centre (CTEU) at the University of Bristol and University Hospitals Bristol and Weston NHS Foundation Trust.

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EVENTS

One Health Data Science

15 December 2021, 13.00 - 14.00, Andrew Dowsey (Bristol Veterinary School), online

WHO guidelines for the management of symptomatic sexually transmitted infections (STIs): Evidence and recommendations

16 December 2021, 13.00 - 14.00, Dr Teodora Elvira Wi (Department of Global HIV, Hepatitis and STIs Programmes, World Health Organization), online

Research Learning Event - Impact

10 January 2022, 11.00 - 12.30, online

GW4 AMR Alliance Bid Development and Networking event

13 - 14 January 2022, central hotel (to be confirmed) in Exeter

Infection & Immunity Research Network Early Career Researchers' Symposium

16 February 2022, 17.30, Life Sciences Building

Keynotes: Alex McCarthy (Imperial) and Laura Bowater (East Anglia)

Abstract submission deadline: 5 January 2022

Cash prizes to be won for both oral and poster presentations

Attendance is FREE and includes a buffet lunch

More information: <http://www.bristol.ac.uk/infection-immunity/seminars/2022/ecrsymposium.html>

Bristol Digital Futures Institute Symposium

19 January 2022, 11.00 - 16.30, We The Curious, Anchor Road, Bristol, BS1 5DB

Research/Clinician Infection and Immunity Matchmaking Meeting

31 January 2022, 14.00 - 15.30, online

Bristol Cats Study meeting

9 February 2022, 11.00 - 12.30, online

Molecular Graphics and Modelling Society: Young Modellers' Forum

11 February 2022, 9.00 - 17.00, online

Essential Guide to Grant Applications (Research Design Service training)

15 - 17 February 2022

NHS Long Term Plan

1 March 2022, 9.25 - 17.00, The Studio, Manchester

NEWS

Fat matters more than muscle for heart health

An observational study has found that changes in body fat impact early markers of heart health more than changes in body muscle, suggesting there are greater benefits to be expected from losing fat than from gaining muscle.

More than 3,200 young people in Bristol's [Children of the 90s](#) birth cohort study were measured repeatedly for levels of body fat and lean mass using a body scanning device, at 10, 13, 18 and 25 years old. Handgrip strength was also

tested when they were aged 12 and 25 years.

Findings showed that gaining fat mass was strongly and consistently related to poorer metabolic health in young adulthood as indicated, for example, by higher levels of harmful cholesterol. These effects were much larger (often about 5-times larger) than any beneficial effect of gaining muscle. Where there were benefits of gaining muscle, these were specific to gains that had occurred in adolescence – suggesting that

this early stage of life is a key window for promoting muscle gain and reaping its benefits. They also found that improving strength (based on handgrip) has slightly greater benefits for markers of heart health than gaining muscle itself, suggesting that the frequent use of muscle, rather than the bulking up of muscle, may matter more.

Bell J *et al.* (2021). [Body muscle gain and markers of cardiovascular disease susceptibility in young adulthood: A cohort study.](#) *PLoS Medicine*.

Superbugs is back!!!

Following a public engagement activity in Cardiff in 2019 which informed the next generations about mi-



crobes, infection and antimicrobial resistance, *Superbugs*, led by Dr [Jon Tyrell](#) in the School of Cellular and Molecular Medicine, has evolved to a bilingual (English and Welsh) online platform. The

website seeks to inspire future scientific leaders and has online and downloadable activities for school-age children to explore. The research team, together with primary and secondary school teachers from across Wales, worked together to create the resource to support the new curriculum; it launched on 18 October 2021.

Superbugs is a joint initiative run by staff from the universities of Bristol and Cardiff and

funded by the Wellcome Trust ISSF and Cardiff University Systems Immunity Research Institute.

[Watch the YouTube introduction](#)



[Go to the Superbugs website](#)

SARS-CoV-2 inhibitor drugs

Once SARS-CoV-2 invades a healthy human cell, the virus's genetic material commandeers the cell's machinery and forces it to make new copies of the virus. A vital step in this viral life cycle involves cutting a very long 'polyprotein' into its constituent viral proteins. The virus has two molecular machines called protease enzymes that act as 'molecular scissors'; one of these, called the main protease, or Mpro, chops up the

polyprotein, cutting it at 11 different places.

A group from Bristol and Oxford combined computational and experimental expertise to build an atomic level picture of the structure, dynamics and interactions of Mpro. These models allowed them to see how the viral Mpro 'scissors' work. The team then designed new peptides, which are short pieces of protein, as inhibitors, to bind tightly to Mpro and prevent it from working. Tests determined that all 11

protein cut sites and four of these designed peptides not only bound to the molecular scissors, but they outcompeted the natural protein cut sites and so inhibited Mpro. To date there are no drugs designed specifically to target COVID-19, so this is a major advance in the race for SARS-CoV-2 inhibitor drugs.

Chan HTH *et al.* (2021). [Discovery of SARS-CoV-2 Mpro peptide inhibitors from modelling substrate and ligand binding](#). *Chemical Science*.

Allergies not linked to mental health traits

Researchers from the University of Bristol wanted to find out whether allergic diseases actually cause mental health traits including anxiety, depression, bipolar disorder and schizophrenia or vice-versa.

The team sought to isolate the effects of these allergic diseases by using Mendelian Randomisation, which allowed them to identify genetic variants linked to these allergic diseases and then investigated how these variants were causally related to the presence of mental health conditions based on a sample of 12,000-344,901 individuals. Although researchers identified obser-

vatational associations between allergic disease and mental health traits, these were not replicated in the team's causal analysis. Little evidence of a



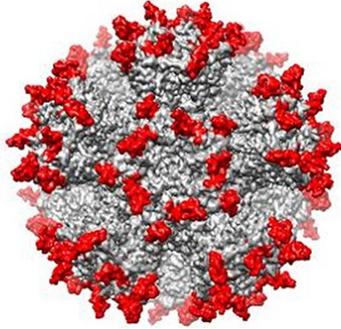
causal relationship between the onset of allergic disease and mental health was found, suggesting that the observational associations found were due to confounding or other forms of bias.

The authors conclude that intervening on the initial presentation of allergic disease is unlikely to improve mental health outcomes. Likewise, preventing the onset of mental health traits will unlikely reduce the risk of allergic disease. However, further research is required to investigate whether intervening on the progression of allergic disease after onset has any causal impact on mental health.

Budu-Aggrey A *et al.* (2021). [Investigating the causal relationship between allergic disease and mental health](#). *Clinical and Experimental Allergy*.

Investment in vaccine innovation

Faster vaccine development could be a step closer thanks to £4 million investment to Imophoron Ltd, a Bristol University biotech start-up developing a novel, next generation rapid-response vaccine platform called AD-Domer™. Imophoron will use the investment to bring AD-Domer™ vaccines to clinical stage, initially targeting three viruses, RSV (respiratory syncytial virus), COVID-19, and



mosquito-borne Chikungunya.

ADDomer™ is a new type of vaccine that can be produced and stored at warmer temperatures, removing the need for refrigeration, in a major advance in vaccine technology.

For comparison, COVID-19 vaccines by AstraZeneca, Moderna and BioNTech need to be cooled at 4°C, -20°C or even -80°C. ADDomer™, engineered using a synthetic,

thermostable protein scaffold, could revolutionise the way vaccines are designed and produced. Tests revealed that the ADDomer™ COVID-19 vaccine can be delivered by various routes, including intranasal, which would end the need for trained health-care professionals to administer the vaccine, reducing the cost and complexity of rolling out a pandemic vaccine programme.

[Watch the video](#) explaining what ADDomer™ is and how it works.

Image: ADDomer™ COVID vaccine

Fighting antimicrobial resistance with farmers

The University of Bristol has showcased the antimicrobial resistance (AMR) research impact generated by Prof [Kristen Reyher](#) (Bristol Veterinary School) and Prof [Matthew Avison](#)'s (School of Cellular and Molecular Medicine) 'One Health Selection and Transmission of Antimicrobial Resistance' (OH STAR), 'One Health Drivers of Antibacterial Resistance in Thailand' (OH DART) and 'Future-proofing Antibacterial Resistance Risk Management Surveillance and Stewardship in the Argentinian Farming Environment' (FARMS-SAFE) projects.

For example, their OH STAR study examined the commonly held view that AMR on



farms affects humans, but after sampling 4,500 *Escherichia coli* samples from 53 dairy farms monthly over 2

years, they found that virtually no sharing of AMR between farms and humans, and that resistant bacteria are spread by humans not cattle.

Overall their teams' work has promoted the responsible use of antimicrobials on farms, and has impacted farming management and policy-making both locally and globally.

[Read the full impact case study](#)

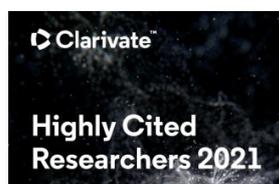
[Sign up to the Bristol AMR Newsletter](#) which provided this extract

Highly Cited Researchers 2021 List

The Highly Cited Researchers 2021 list, from Clarivate, recognises 16 University of Bristol researchers who demonstrated significant influence in their chosen field or fields through the publication of multiple highly cited papers during the last decade.

Among them are:

- Prof [Tom R. Gaunt](#)'s research interests lie in the development and application of computational methods in population health sci-



ences

- Prof [Julian P. T. Higgins](#) has wide-ranging research interests which span all areas of systematic review and meta-analysis
- Prof [Matthew Hickman](#)'s research focuses on infectious disease control and the epidemiology and public health consequences of drug use, e.g. Hep C
 - [Peter Vicker-man](#) is Professor of Infectious Disease Modelling
 - Prof [Deborah](#)

[Lawlor](#)'s research is perinatal, reproductive and cardio-metabolic health

- Prof [Jonathan Sterne](#) has interests in clinical epidemiology of HIV and AIDS in the era of antiretroviral therapy
- Prof [Kate Tilling](#) looks at the development and application of statistical methods to causal problems in epidemiology/health services research

[See the full list](#) of highly-cited researchers at Bristol

Support for research into coronary heart disease

Two members of the [Bristol Heart Institute](#) have received funding which will further research into congenital heart disease (CHD).

The Medical Research Council awarded Prof [Paolo Madeddu](#) (Bristol Medical School) funding for *Gene-inspired therapy to rescue cardiovascular disease in progeria*. Hutchinson-Gilford progeria syndrome (HGPS) is a rare disease caused by an abnormal gene and related protein. Because there is no effective cure children with HGPS will, on average, die of cardiovascular disease at around 14 years old. This project proposes a new

treatment where a gene, found in people who live a long and healthy life, is transferred to rescue the premature cardiovascular senescence typical of HGPS patients. Madeddu and his team discovered a beneficial variant of the BPIFB4 gene and preliminary studies have shown that the longevity BPIFB4 mutation can benefit some molecular mechanisms that are dysfunctional in children with HGPS.

Madeddu, Prof [Massimo Caputo](#) and Dr [Elisa Avolio](#) received funding from Heart Research UK for *Targeting pericytes for halting pulmonary*

hypertension in infants with CHD. At least 5-10% of patients with congenital heart disease develop pulmonary arterial hypertension (PAH), which can lead to heart failure. The risk of developing pulmonary hypertension is higher for children living in poor countries and areas of social deprivation, because of the limited access to specialist centres where the cardiac defect can be recognised and corrected before complications arise. Recent research indicates pericytes – multi-functional cells embedded within the walls of capillaries – could be targeted for the treatment of PAH.

[Read the full article](#)

Welsh animal project to combat antimicrobial resistance

Arwain DGC (Defnydd Gwrthfaicrobaidd Cyfrifol) Cymru is at the forefront of the drive to prevent the spread of antimicrobial resistance (AMR). It comprises a schedule of activities and brings together experienced collaborators to deliver a wide-ranging programme addressing AMR in animals and the environment. Included are key Welsh agricultural stakeholders (Menter a Busnes, Welsh Lamb and Beef Producers Ltd and Welsh Agricultural Organisation Society), academic institutions (University of Bristol and Aberystwyth Uni-

versity School of Veterinary Science) and veterinary delivery partners (Iechyd Da and Milfeddygon Gogledd Cymru). Closely aligned to the Welsh



Government's five-year [AMR in Animals and the Environment Implementation Plan \(2019 – 2024\)](#). This project has received funding through the Welsh Government Rural Communities - Rural Develop-

ment Programme 2014-2020, which is funded by the European Agricultural Fund for Rural Development and the Welsh Government.

Furthering their global leadership on understanding associations between antimicrobial use and AMR on farms and designing an active surveillance programme for Wales are Professors [Kristen Reyher](#) and [Matthew Avison](#) and their teams, part of [Bristol AMR](#) at the University of Bristol.

[Read the full press release](#)

Veterinary surgeon Eleri Davies (right) of Farm First Vets with farmer Cath Godfrey from The Artha Farm, Tregare, Mounmouthshire

Outstanding excellence in a doctoral dissertation

Dr Fiona Kinnear (pictured), National Institute for Health Research (NIHR) Bristol Biomedical Research Centre Nutrition theme PhD student (now graduated), was awarded the prize for outstanding excellence in a doctoral dissertation for the University of Bristol's Faculty of Health Sciences in 2020/21. Fiona successfully defended her thesis at her viva in October 2020.

Each year, the University's Research Degrees Examination Board presents a prize for a doctoral candidate in each Faculty. The award re-

flects the very high standard of Fiona's work, and demonstrates the effort and commitment she brought to her research.

Fiona's thesis was entitled *Nutrition and physical activity intervention for families with Familial Hypercholesterolaemia*. Familial Hypercholesterolaemia (FH) is an inherited condition which causes very high levels of blood cholesterol and requires lifelong pharmacological treatment. The aim of Fiona's PhD was to explore the influence of diet and physical activity up-

on blood cholesterol in children and their parents with FH.

Fiona's co-supervisors were Professor Julian Hamilton-Shield, Dr Fiona Lithander, Dr Aidan Searle and Professor David Stensel, Loughborough University.



Presentation to the US Food and Drug Administration

Professor Jonathan Sterne (pictured), Deputy Director of the National Institute for Health Research Bristol Biomedical Research Centre (NIHR Bristol BRC), presented evidence to the US Food and Drug Administration (FDA) on COVID-19 vaccination boosters on 17 September 2021. The presentation was part of the FDA's advisory committee meeting to discuss Pfizer-BioNTech's application for a COVID-19 booster in the US. [The meeting can be](#)



[publicly viewed online.](#)

His presentation, entitled *Real world effectiveness of COVID-19 vaccines*, followed on from a recently published [Lancet Viewpoint opinion piece](#) by a group of authors including Prof Sterne. In the piece, the authors summarised current evidence on vaccine efficacy, which does not appear to show a need for boosting in the general population, because efficacy of the existing vaccines

against severe disease remains high. The authors argued that even if humoral immunity, measured by neutralising antibody titres, appears to wane, this does not necessarily predict reductions in vaccine efficacy over time. Additionally, reductions in vaccine efficacy against mild disease do not necessarily predict reductions in the (typically higher) efficacy against severe disease. The presentation took place before the omicron variant was known to be circulating.

Who should be offered testing for coeliac disease?

A team of researchers, based at the NIHR Applied Research Collaboration (ARC) West, the University of Bristol, University of Southampton, the Royal Hospital for Sick Children, University College London and York Teaching Hospital NHS Foundation Trust, undertook an analysis of the results from 191 studies, reporting on 26 signs, symptoms and risk factors of coeliac disease.

Around one in 100 people in the UK have coeliac disease, where a person's immune response to gluten attacks the tissues in their digestive system. Diagnosing the disease can be difficult. Some patients may not have symp-

toms, while others have non-specific symptoms such as indigestion or bloating. It's thought only one in three people with coeliac disease are actually diagnosed. The only treatment available is a gluten free diet.



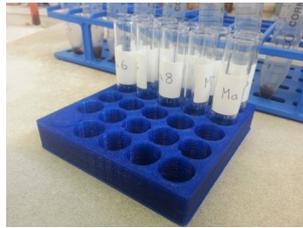
The study aimed to identify which symptoms indicate a higher risk of coeliac disease, and therefore who would benefit from further testing. They found strong evidence that people with family histo-

ry of coeliac disease, dermatitis herpetiformis, anaemia, type 1 diabetes, migraines, HLA DQ2/8 risk genotype, osteoporosis, or chronic liver disease are more than twice as likely to have coeliac disease than the general population. Additionally, close relatives of people with coeliac disease are three times as likely to have it themselves. These signs and symptoms could therefore help identify patients who would benefit from testing.

Elwenspoek MC *et al.* (2021). [The accuracy of diagnostic indicators for coeliac disease: a systematic review and meta-analysis.](#) *PLOS ONE*.

Rapid sexual health testing, diagnosis and treatment

A rapid sexual health service designed to improve access and delivery of care is welcomed by staff and patients, National Institute for Health Research (NIHR)-funded researchers at the Applied Research Collaboration West have found. Demand for HIV and sexually transmitted infection (STI) testing is on the rise, but local authority budgets are shrinking. Patients typically waited over a week for chlamydia and gonorrhoea test results, and then had to return to the clinic for treatment. An interview-based



study examines the experiences of implementing a first-of-its-kind rapid STI testing, diagnosis and treatment service delivered in Unity Sexual Health which provides sexual health services for Bristol, North Somerset and South Gloucestershire. Samples are checked with new rapid testing equipment, so that results, treatment and advice can be given within hours. As most STIs do not cause any symptoms, early detection and treatment can help stop infections spreading and prevent serious disease developing.

Patients valued the faster results, infection-specific treatment and avoiding unnecessary treatment. The rapid results meant that patients could be treated based on their test results, rather than being prescribed antibiotics ‘just in case’ of an infection. Staff welcomed being able to provide treatment based on results and both staff and patients valued avoiding unnecessary antibiotic prescribing.

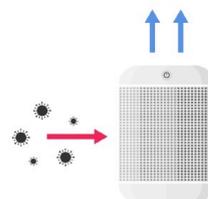
Lorenc A *et al.* (2021). [What can be learnt from a qualitative evaluation of implementing a rapid sexual health testing, diagnosis and treatment service?](#) *BMJ Open*.

Can air filters prevent respiratory infections in care homes?

A major new randomised controlled trial is investigating the effectiveness of air filtration systems in preventing respiratory infections (such as coughs, colds and flu) and COVID-19 among care home residents in England. The AFRI-c ([Air Filters to Prevent Respiratory Infections including COVID-19 in Care Homes](#)) study, which received funding from the National Institute for Health Research, is led by Prof [Alastair Hay](#).

There are currently 220,000

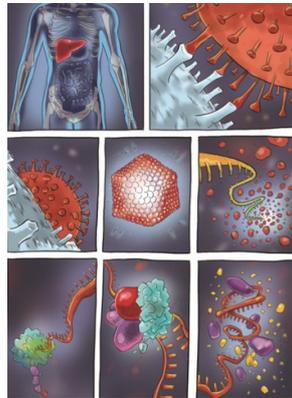
people living in UK care homes, with numbers predicted to double by 2040; reducing the spread of infections in care homes is a research priority. Many infections are spread via droplets produced when people sneeze or cough. Portable air filters seem an obvious solution to reduce the spread of infections since those that contain high efficiency particulate air (HEPA) filters can



quickly remove germs from the air. For years, they have been built into hospital operating theatres and transplant wards to prevent infections. HEPA filters are now built into some portable units available for domestic use, and can be placed in care homes with relative ease. Care home staff will record the number of infections their residents experience during the winter and the results from the two groups (with and without filters) will be compared.

Eliminating hepatitis C in Pakistan

Pakistan has one of the highest rates of hepatitis C virus (HCV) infection in the world, accounting for over 10% of global HCV infections. A new modelling study led by the University of Bristol suggests that achieving the World Health Organization goal of eliminating HCV as a public health problem by 2030 in Pakistan is likely to be highly cost-effective by 2030, cost-



saving by 2031, and could deliver US\$9.10 billion in savings to the Pakistan national economy by 2050.

The [study](#), a collaboration across the University of Bristol, the [Burnet Institute](#) in Australia, and [Aga Khan University](#) in Pakistan, found that achieving HCV elimination in Pakistan could yield

substantial societal health and economic benefits. These benefits include saving 333,000 lives and averting considerable morbidity due to ill health, leading to improvements in health-related quality of life and workforce productivity.

Lim AG *et al.* (2021). [Health and economic benefits of achieving hepatitis C virus elimination in Pakistan: A modelling study and economic analysis](#). *PLOS Medicine*.

Non-invasive breathing support and infection risk

The use of non-invasive breathing support, commonly known as CPAP or HFNO, to treat moderate to severe COVID-19 infection, isn't linked to a heightened infection risk, as currently thought. Both assisted breathing methods produced little measurable air or surface viral contamination, and not more than simple oxygen therapy, while coughing produced far more aerosol than either method, two studies show.

The findings have prompted a call for a thorough reassessment of the infection control measures deployed for these respiratory support methods, both of which have been cate-

gorised as 'aerosol generating procedures' that expose healthcare staff and other patients to a heightened infection risk.

Unlike mechanical ventilation, which requires intubation and sedation, CPAP and HFNO aren't invasive. But they are thought to generate viral particles capable of contaminating the air and surfaces nearby, necessitating additional infection control precautions. These include segregating patients and the use of high grade FFP3 masks for healthcare workers to curb the risk of aerosol transmission, both of which have implications for costs and capac-

ity. UK data from 2020 estimates that 17% of all emergency COVID-19 hospital admissions required non-invasive respiratory support or mechanical ventilation.

Winslow R *et al.* (2021). [SARS-CoV-2 environmental contamination from hospitalised patients with COVID-19 receiving aerosol-generating procedures](#). *Thorax*.

Hamilton F *et al.* (2021). [Aerosol emission from the respiratory tract: an analysis of aerosol generation from oxygen delivery systems](#). *Thorax*.
Arnold D *et al.* [Coughs and sneezes spread diseases – but do "aerosol generating" procedures?](#). *Thorax*.

Blood pressure drugs could protect against type 2 diabetes

Lowering high blood pressure is an effective way to reduce a person's risk of developing type 2 diabetes in the future, according to research funded by the British Heart Foundation. Doctors already prescribe blood pressure-lowering drugs to reduce a person's chance of having a heart attack or stroke, but whether these drugs can help to stave-off diabetes has been unknown. This study revealed that their protective effects are wider reaching than previously thought and may directly reduce a per-



son's risk of type 2 diabetes. In the most detailed study to date of over 145,000 people from 19 randomised clinical trials across the world, researchers at the Universities of Oxford and Bristol found that a 5 mmHg reduction in systolic blood pressure reduced the risk of type 2 diabetes by 11%. All participants were followed up for an average of 4.5 years and 9,883 people developed type 2 diabetes. People with genetically influenced lower blood pressure levels had a 12% lower risk of type 2 diabetes, compared to those without the genetic associa-

tions.

Prof [Kazem Rahimi](#) and his team then investigated the effects of five major types of blood pressure drugs from 22 clinical trials compared to a placebo. They found angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor-II blockers (ARBs) had the strongest protective effect, both reducing a person's relative risk of developing diabetes by 16%.

Davey Smith G *et al.* (2021). [Blood pressure lowering and risk of new-onset type 2 diabetes: an individual-level meta-analysis of 145,000 randomized participants.](#) *The Lancet.*

The epigenetic atlas

Epigenetic variation exists but it is unclear what causes this variation – is it genetic or is it the environment? It is also unclear how genetic differences that occur between individuals' impact on our epigenomes. The atlas of genetic effects on DNA methylation (DNAm) was produced by the [Genetics of DNA Methylation Consortium](#) (GoDMC) of 50 universities and institutes and more than 150 scientists, including the University of Bristol, University of Exeter Medical School, King's College

London and Leiden University Medical Center. The analysis focused on the natural differences between individuals in their DNAm levels across the genome. DNAm plays a central role in gene regulation. It helps to define how cells respond to environmental signals and, ultimately, contributes to health or susceptibility to disease. However, the amount and the effects of differences in DNAm from one person to another is poorly understood.

The consortium analysed 32,851 participants from across the world; by providing a world-wide platform for collaboration and combining genetic and epidemiological expertise, the scientists of GoDMC established a large resource of genetic effects on DNAm and how this [atlas](#) can be used to understand the genetic basis of DNAm variation.

Min JL *et al.* (2021). [Genomic and phenotypic insights from an atlas of genetic effects on DNA methylation.](#) *Nature Genetics*

Regular exercise to prevent pneumonia

Previous research has suggested that regular exercise might be associated with a reduced risk of pneumonia, but the studies have had mixed findings with some reporting evidence of a relationship and others no evidence. Researchers at Bristol carried out a pooled analysis of all published studies to re-evaluate the relationship between regular exercise and the risk of developing pneumonia. They found that people who exercise regularly

have a lower risk of developing pneumonia and pneumonia-related death compared to those who were the least or not physically active. The relationship was shown for pneumonias that did not result in death and those that resulted in death. The results did not change on taking into account known factors that can affect pneumonia such as age, sex, body mass index, socioeconomic status, alcohol consumption, smoking, and pre-existing diseases.

The strength of the association did not vary by age or sex. The research does not prove cause and effect and further studies are needed to show if the associations demonstrated are causal.

Kunutsor SK *et al.* (2021). [Physical activity reduces the risk of pneumonia: systematic review and meta-analysis of 10 prospective studies involving 1,044,492 participants](#). *GeroScience*.

School staff not at higher risk of death from COVID-19

The aim of the study was to estimate occupational risk from COVID-19 among school staff – teachers, teaching and lunchtime assistants - using Office for National Statistics (ONS) mortality data from England and Wales between 8 March - 28 December 2020. The researchers found across occupational groups there was a strong correlation between COVID-19 mortality and non-COVID-19 mortality. The mortality rates for deaths with COVID-19 were low among people working in schools (ten per 100,000 in female primary school teachers to 39 per 100,000 in male secondary school teachers) compared to many other oc-

cupations (nine to 50 per 100,000 in women; from ten to 143 per 100,000 in men). The study found there were fewer deaths than the five-year average among female primary and secondary school



teachers and the number of deaths among male teachers were similar to the five-year average. There were more deaths among teaching assistants compared to the five-year average, but only around half of the excess deaths were

thought to be attributable to COVID-19. For all women working in schools combined there was a small increase in the number of deaths (5%) compared with the five-year average, but the number of deaths from COVID-19 was larger than the excess, suggesting that some people who died with COVID-19 may have died in a normal year from other causes.

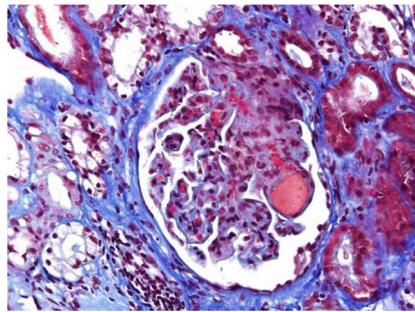
Lewis SJ *et al.* (2021). [Was the risk of death among the population of teachers and other school workers in England and Wales due to Covid-19 and all causes higher than other occupations during the pandemic in 2020?... BMJ Open](#).

COVID-19 vaccines and very rare blood clotting

A group of 11 institutions, led by the University of Liverpool and including the University of Bristol, is seeking to understand the very rare, but very serious, condition of blood clotting with low platelets in the general population, in COVID-19 infection, and potentially following vaccination.

The vast majority of people who experience a side effect from COVID-19 vaccination have only mild reactions lasting for two or three days. However, in March 2021 reports of small numbers of people being admitted to hospital predominantly after the Oxford/AstraZeneca vaccine

with what could potentially be a very rare side effect of vaccination began to emerge. These people had blood clots in the major veins in the brain, abdomen, or elsewhere in the body, but at the same time a low level of platelets in the blood.



The researchers, supported by a wide range of collaborators within the NHS and national agencies, will work together to

study the mechanisms underlying the occurrence of blood clots with low platelets – known as thrombotic thrombocytopenia syndrome (TTS). This project is supported by the National Institute for Health Research and backed by £1.6 million of government funding from the [Vaccine Taskforce](#).

Bristol's involvement in the study, led by Prof [Jonathan Sterne](#) (Bristol Medical School), will be to look at the association of COVID-19 vaccination with cardiovascular events after vaccination by analysing very large (population-level) datasets.

Parent-collected nose swabs

Respiratory tract infections in children, such as coughs, colds, flu and COVID-19, are some of the most common illnesses treated in primary care. The study, which was conducted before the pandemic, compared the quality and performance of parent-collected nose and saliva swab samples with nurse-collected samples.



Both parent-collected and nurse-collected samples were sent to a clinical testing laboratory for the detection of

over 40 common respiratory pathogens. While parent-collected nose swabs performed well compared to those collected by nurses (91.6% inter-rater agreement for viral infections and 91.4% inter-rater agreement for bacterial infections), parent-collected saliva swabs did not perform as well (69% and 78.1% for viral and bacterial infections respectively).

Results showed that parents

collected a higher number of human cells on the nose swabs compared to the nurses, which suggests that children are more tolerant of a parent performing the swabbing technique, and parents should have the confidence to take the swabs if requested.

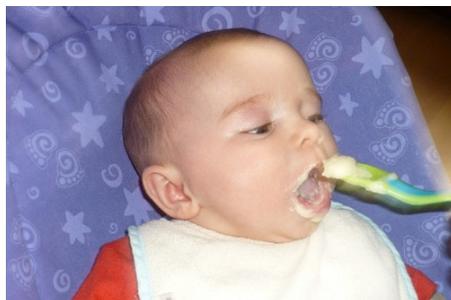
Woodall C *et al.* (2021). [Performance of parent-collected nasal and saliva swabs compared with nurse-collected swabs for the molecular detection of respiratory microorganisms: a prospective study.](#) *Microbiology Spectrum*.

Over-diagnosis of cow's milk allergy in infants

Cow's milk allergy can present with either acute or delayed symptoms. Delayed symptoms are more varied and include gut and skin symptoms, such as possetting and vomiting, colic, loose stools or constipation, and flaring of eczema. Many of these symptoms are already known to be common in infants, making delayed cow's milk allergy difficult to diagnose.

Researchers found that one in four parents reported two or more possible "mild to

moderate" symptoms every month. Symptoms were most numerous at three months of age, when all children were



fully breastfed and not directly consuming cow's milk. At six months of age, there was no difference in the number

of children with two or more symptoms between those consuming and not consuming cow's milk. Together, these findings suggest that the majority of symptoms listed in cow's milk allergy guidelines are common, normal and not caused by cow's milk allergy.

Vincent R *et al.* (2021). [Frequency of guideline-defined cow's milk allergy symptoms in infants: secondary analysis of EAT trial data.](#) *Clinical and Experimental Allergy*.

Early warning signals could help monitor disease outbreaks

Using a novel, sequential analysis combined with daily COVID-19 case data across 24 countries, new research suggests that Early Warning Signals (EWSs) can predict COVID-19 waves. The team found that warnings were regularly detectable prior to exponential cases changes, but the reliability of these signals depended on the amount of time between successive waves of infection and the mathematical likelihood of a critical transition. Consequently, EWSs showed highest accuracy for waves that experienced a sup-

pressed R number over a long period before the outbreak. As the ongoing pandemic has shown, being able to identify rapid increases in cases before they occur is important



for people to modify their behaviours, and to inform government actions.

The research found that hotly debated early warning signals were most reliable before the

second COVID-19 wave that was experienced by many, and whilst these signals performed less well for the first and third waves, any rapid increase in cases could be identified well in advance. There is a lot of conflicting evidence surrounding EWS use in epidemiology and ecological monitoring in general; the team hope the methodological points raised in this work helps others disentangle the complicated behaviour of these warnings.

O'Brien DA and Clements CF (2021). [Early warning signal reliability varies with COVID-19 waves.](#) *Biology Letters*.

Asymptomatic testing and vaccination at universities

By adapting an existing mathematical model of COVID-19 transmission in universities, researchers at Bristol were able to show that case numbers can be kept low when a high percentage of students are vaccinated and are using lateral flow testing twice a week.

The study was the first of its kind to look at the impact both these factors have on the incidence, scale and timing of COVID-19 outbreaks on campus. It's hoped the findings will help universities set policies to protect their students and wider university community while minimising

any disruption to education.

At low levels of vaccination uptake (30% vaccinated and with no asymptomatic testing) there could be more than twice as many students infected this term as there were in the autumn term of 2020, with 53% to 71% of students infected during the first term. Under the best-case scenario, where 90% of students are vaccinated and are using a lateral flow test, twice a week, four days apart, this drops to 7 to 9%, with around 80% of these cases estimated to be asymptomatic. At 30% vaccination uptake, asymptomatic testing is particularly effective and can

reduce the number of cases by up to half if 90% of students are participating. At high levels of vaccination uptake (70% to 90%), the trajectory of the case numbers in the student population is mainly influenced by the level of infection that is circulating in the surrounding community. The [Office for National Statistics](#) reported earlier this month 91% of students have had at least one dose and by late last month, 85% had had two vaccine doses.

Nixon E *et al.* (preprint). [Impacts of vaccination and asymptomatic testing on SARS-CoV-2 transmission dynamics in a university setting.](#) *medRxiv.*

GW4 PhD programme for health professionals

The GW4 Alliance is a consortium of four of the most research-intensive and innovative universities in the UK: Bath, Bristol, Cardiff and Exeter. It is set to launch a new PhD programme for health professionals after receiving a £7m grant from the Wellcome Trust.

The GW4 Clinical Academic Training Programme for Health Professionals (GW4-CAT HP) will fund five annual intakes of five fellows, starting in Autumn 2022. PhD fellows will have access

to exceptional support, training and guidance from world-leading academics and research environments across



the GW4 member universities; this will include supportive mentorship and as-

sisting with the transition to a post-doctoral clinical academic role. The programme is dedicated to identifying and nurturing talent by delivering an outstanding mentored and supported research training experience to establish an academic career for clinical leaders of the future.

Further information on the programme is available on the [GW4-CAT website](#).

Funding for the School of Public Health Research

The National Institute for Health Research (NIHR) awarded a third round of funding to the [NIHR School for Public Health Research](#) (SPHR). The next round of the school, which has been awarded £25 million from April 2022, will advance and extend the school's current research themes of children, young people and families; public mental health; and places and communities.



Established in April 2012, the renewed School is an extended partnership between Bris-

tol University and eight other leading centres of academic public health research excellence across England. The School aims to build the evidence base for effective public health practice by bringing together England's leading

public health research expertise in one virtual organisation. The school conducts applied public health research to increase the volume and quality evidence on cost-effective interventions and supports local public health practitioners and policy makers to engage with research and seek out research evidence to inform their decisions.

[Read the full press release](#)

COVID-19 studies should record menstrual changes

Researchers from the universities of Bristol, Edinburgh and Oxford sought to evaluate the existing anecdotal and scientific literature on menstrual cycle feature changes in the COVID-19 pandemic and provide suggestions for future research. They conducted a comprehensive review of current literature and found just 12 studies that had reported on menstrual changes in relation to the pandemic in general and/or COVID-19 specifically. None of the COVID-19 vaccine trials has collected data on menstrual changes.

Anecdotes shared online and data from the MHRA's Yellow Card scheme for adverse drug

reactions, suggested that many women and people who menstruate have experienced disruptions to their menstrual cycles since the start of the pandemic, either due to pandemic-related factors like



stress and behaviour changes and/or due to COVID-19 illness itself or COVID-19 treatments and vaccines.

However, the researchers say from what is known about how the menstrual cycle

works and how it can be disrupted by factors like stress, weight changes, infection, and inflammation (e.g. following vaccination), they strongly suspect that any pandemic-related changes will be short term with no serious or lasting effect on health and fertility. Further research into the effects of COVID-19 and other health related exposures on women's menstrual health is urgently needed and any COVID recovery plan needs to consider women's health.

Sharp G *et al.* (2021). [The COVID-19 pandemic and the menstrual cycle: research gaps and opportunities](#). *International Journal of Epidemiology*.

Child deaths during pandemic lowest on record for England

The number of children in England who died fell to 3,067 between April 2020 – March 2021. This is 356 fewer deaths than were recorded in the preceding 12 months (April 2019 – March 2020), and likely represents the lowest level of child mortality on record.

The study, which uses data from the University of Bristol-led [National Child Mortality Database](#) (NCMD) — a first-of-its-kind initiative to collect comprehensive and timely data on every child death in England — sought to quantify the relative risk of childhood deaths across England during the first year of the COVID

pandemic, compared to a similar period of 2019.

Findings from the analysis showed that deaths from non-COVID infections and other underlying medical conditions fell, and there is some evidence that deaths from substance abuse also reduced. In addition, the reduction in mortality appeared to occur during the winter months, where the seasonal increase, often caused by infections other than COVID-19, was not apparent. This period coincided with the prolonged lockdown in England from January to April 2021; suggesting that public health measures may be able

to modify a significant number of childhood deaths every year. The reduction in child deaths was most prominent in children under ten years old. These findings stand in stark contrast to overall mortality for England's population, which was 14% higher than the previous year – and suggest that widespread changes in the delivery of healthcare during the pandemic may have prevented child deaths.

Odd D *et al.* (2021). [Child mortality in England during the first year of the COVID-19 pandemic](#). *Archives of Disease in Childhood*.

French Embassy visit to COVID-19 research facilities

Dr Rachel Millet and Arthur Belaud from the French Embassy's Innovation Branch, which seeks to drive France-UK business enterprise, met with scientists Prof Imre Berger and Frederic Garzoni, founders of Imophoron Ltd, the biotech start-up developing ADDomer™ that uses technology developed at an institution in France. ADDomer™ is a thermostable vaccine platform being developed by

Bristol scientists to combat emerging infectious diseases.

During the visit, the delega-



tion took a tour of labs in the University's [Max Planck-Bristol Centre for Minimal Biology](#) (MPBC), the GW4/

Wellcome Trust Cryo-EM facility led by Prof Christiane Schaffitzel, and [Science Creates](#), the Bristol-based incubator, which is operated in partnership with the University and supports scientists and engineers in commercialising ground-breaking innovations.

Pictured are L to R: Arthur Belaud, Dr Anne Westcott from the University of Bristol, Dr Rachel Millet, and Prof Imre Berger.

ELIZABETH BLACKWELL FUNDING

Nurturing
Research.
Improving
Health.



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. This scheme is currently closed to submissions for any projects focusing on face to face engagement.

If you would like to apply for funding to support an engagement activity which adheres to social distancing guidance relating to coronavirus, please get in touch to discuss this in more detail. 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). Applications **reviewed all year**.

FUNDING OPPORTUNITIES

Research Professional provides access to an extensive database of funding opportunities. 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 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 [RED website](#).

*Research Professional

Medical Research Council

[New investigator research grant](#)

Closing date: 12 January 2022

Award amount: not limited

This supports researchers who are capable of becoming independent PIs and who are ready to take the next step towards that goal within the areas of infections and immunity. Applicants are expected to combine their time with other activities, such as other research grants or clinical duties, teaching, administration duties, or other time spent in faculty.

National Institute of Allergy and Infectious Diseases, US

[Systems biology for infectious diseases \(U19 clinical trial not allowed\)](#)

Closing date: 14 January 2022

Award amount: USD 10 million

This supports research that employs systems biology approaches to human pathogens, in order to predict disease severity, responses to vaccines and therapeutics, and identifying candidate targets for interventions. The aim is for systems biology for infectious diseases centres to use systems biology approaches to integrate diverse datasets and build predictive models for infectious diseases, including pathogens in the NIAID priority pathogens list.

Digital Innovation Hub Healthcare Robotics

[COVID-19 response open call](#)

Closing date: 15 January 2022

Award amount: €250,000

This accelerates the embedding of robotic applications in healthcare-related settings and enables the smooth deployment of new, effective robotic-based solutions. Proposals must clearly state the relevant clinical demand and the healthcare problem related to COVID-19 to be solved by the robotic application, as well as the added clinical value of the solution. It must be an already existing robotic system that is at technology readiness levels 7 to 8.

European Society for Paediatric Infectious Diseases

[Young investigator award](#)

Closing date: 31 January 2022

Award amount: €250,000

This recognises young investigators in the field of paediatric infectious diseases. Both clinical and basic research is eligible. Applicants must be members of ESPID in good standing and be within 16 years of obtaining their PhD or the highest degree they hold. Up to two awards are available, each including funded attendance at the society's annual meeting, and €5,000 to be paid to the host institution towards research.

Healthcare Infection Society

[Small research grants](#)

Closing date: 1 March 2022

Award amount: £10,000

These support small-scale research projects within the scope of infection prevention and control and nosocomial infections, or possibly the costs associated with the visit of an overseas research fellow.

Horizon Europe: Global Challenges and European Industrial Competitiveness

[HORIZON-HLTH-2022-DISEASE-07 — tackling diseases](#)

Closing date: 21 April 2022

Award amount: €3,000,000

This supports projects that set out a credible pathway to contributing tackling diseases and reducing disease burden. Funding is available under the following topics:

- HORIZON-HLTH-2022-DISEASE-07-01 - support for the functioning of the Global Research Collaboration for Infectious Disease Preparedness (GloPID R)
- HORIZON-HLTH-2022-DISEASE-07-02 - pandemic preparedness
- HORIZON-HLTH-2022-DISEASE-07-03 - non-communicable diseases risk reduction in adolescence and youth, Global Alliance for Chronic Diseases

National Institute of Allergy and Infectious Diseases, US

[Innovation for HIV vaccine discovery \(R01 clinical trial not allowed\)](#)

Closing date: 28 July 2022

Award amount: USD 2 million

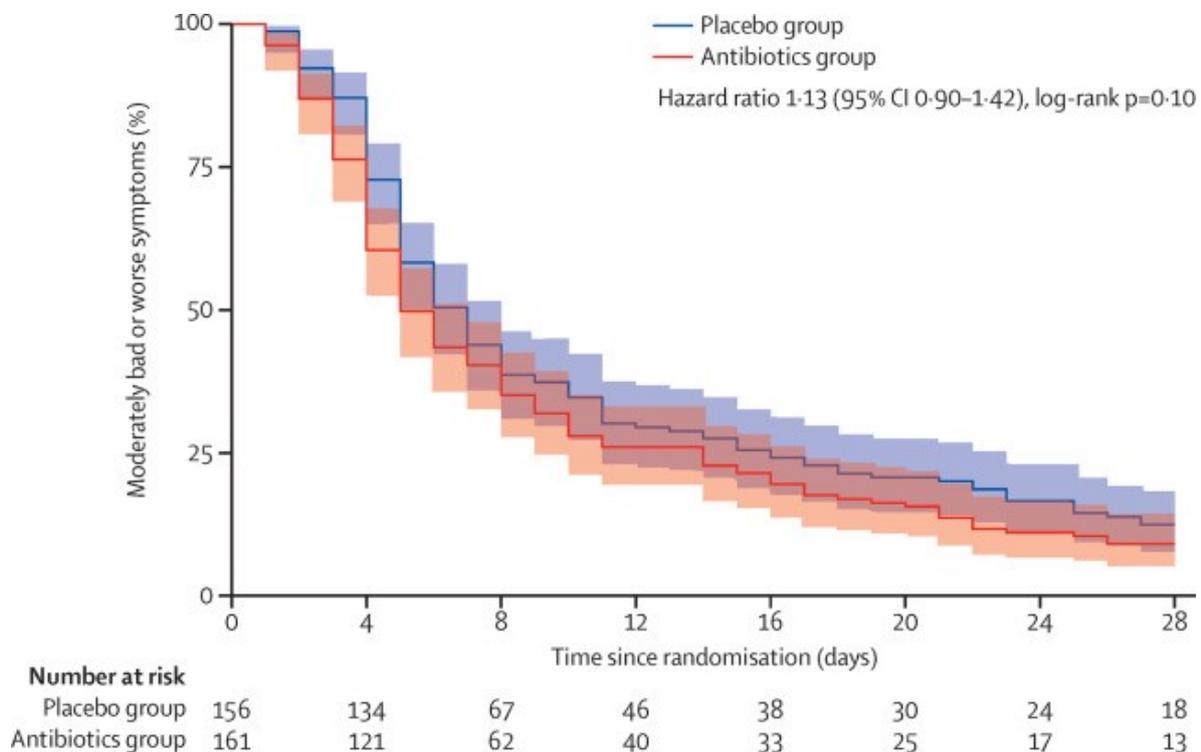
This supports high risk, high impact early discovery research on vaccine approaches to prevent acquisition of or ongoing infection by HIV.

THIS ISSUE'S FEATURED ARTICLE

Antibiotics for lower respiratory tract infection in children presenting in primary care in England (ARTIC PC): a double-blind, randomised, placebo-controlled trial

Little P, Francis NA, Stuart B *et al.* (2021). *The Lancet*.

Researchers at Southampton, Bristol, Oxford and Cardiff sought to test whether amoxicillin reduces the duration of moderately bad respiratory tract symptoms in children. The largest randomised placebo-controlled trial of the antibiotic amoxicillin for treating chest infections recruited 432 children aged six months to twelve years with acute uncomplicated chest infections from primary care practices in England and Wales. They found only a small, non-significant, difference in the duration of symptoms reported between the treated and placebo groups: children given the placebo had symptoms which were rated moderately bad or worse for around 6 days on average after seeing the doctor, and those given antibiotics got better only 13% quicker. This was true even for the groups of children where the doctor heard sounds in the chest, the child had a fever, where the doctor rated the child as more unwell, the child coughed up phlegm or had a rattly chest, or the child was short of



breath. Results suggest that unless pneumonia is suspected, clinicians should provide 'safety-netting' advice such as explaining what illness course to expect and when it would be necessary to re-attend but not prescribe antibiotics for most children presenting with chest infections.

This study confirms that antibiotics (amoxicillin) do not provide a clinically important benefit for symptom duration among children presenting with uncomplicated lower respiratory tract infections, nor in the key clinical subgroups that clinicians commonly prescribe for (those with chest signs, fever, physician rating of unwell, sputum or chest rattle, and shortness of breath).

CONTACTS

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

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Co-Chair (interim): [Angela Nobbs](#)
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- [Borko Amulic](#) - Lecturer in Immunology
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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.

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