

I&I NETWORK NEWSLETTER



2023 - ISSUE 2



New pathway to prevent kidney failure

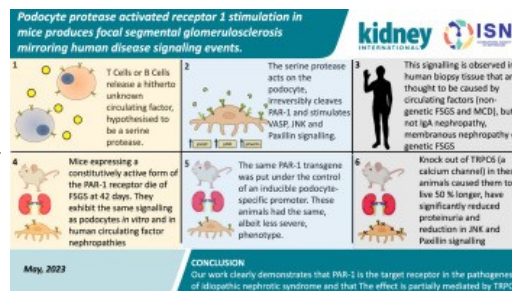
With funding from charity [Kidney Research UK](#), Profs [Moin Saleem](#) and [Gavin Welsh](#) from Bristol Medical School and their team have identified a new treatment pathway for patients with non-genetic (idiopathic) nephrotic syndrome (INS), targeting a still unknown factor that causes the progression towards kidney failure.

[Nephrotic syndrome](#) causes kidneys to leak protein into the urine. This is caused by faults in the organ's filtration system and in some cases, can lead the patient to develop kidney failure. While it is a rare disease, it affects around 10,000 people each

year in the UK with the majority of cases related to non-genetic causes.

The team knew there might be one of more factors in the blood that caused the kidneys to fail, but have so far been unable to identify it. They looked to identify how the factor worked and attempt to block it. Using plasma from the blood of INS patients who were being treated with dialysis, they wanted to confirm if a

receptor known as PAR-1 works in conjunction with the unknown factor. Using plasma from patients, they separated an activator of PAR-1 to investigate their effects on kidney cells in the lab. Both treatments caused distress in the kidney cells. Having confirmed the link between PAR-1 and the unknown factor, results suggest that medications to block the receptor could be a viable option.



May CJ *et al.* (2023). [Podocyte protease actuated receptor 1 stimulation in mice produces focal segmental glomerulosclerosis mirroring human disease signaling events](#). *Kidney International*.

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EVENTS

Working with Industry for Technical Specialists - Industry Engagement

8 June 2023, 12.00 - 14.00, location TBC (UoB only)

Building better treatments for type 1 Diabetes based on understanding human pathogenesis

8 June 2023, 16.00 - 17.00, Prof Matthias von Herrath (Director of Diabetes Research Institute, University of Miami), online

Working with Industry for Technical Specialists - How to communicate with Industry

9 June 2023, 10.00 - 12.00, online (UoB only)

Launch webinar for BBSRC 2023 transformative research technologies (23TRT) call

9 June 2023, 10.00 - 11.00, online

How can we meet growing 'same day' demand in primary care?

12 June 2023, 12.30 - 13.30, Dr Matthew Booker (Centre for Academic Primary Care, University of

Climate Change and Health Symposium

21 June 2023. Chemistry Building

An inclusive and collaborative exploration of the wider effects of climate change on health, including engineering interventions, modelling of disease transmission, impacts on nutrition and food systems, entomology, and mental health consequences on animals and humans.

Posters still being accepted

MORE INFORMATION AND TO REGISTER

ALL WELCOME

Bristol), online

Identification and investigation of novel platelet disorders

12 June 2023, 13.00 - 14.00, Prof Neil Morgan (University of Birmingham), C42 Biomedical Sciences Building and online

Research Culture and Practice Forum

13 – 14 June 2023, online

Three Minute Thesis finals

14 June 2023, 15.00 - 17.00, Priory Road Complex main lecture theatre

Let's Talk Digital Conference 2023

15 June 2023, 9.00 - 17.00, Park Campus, The Park, Gloucestershire University Hospital, Cheltenham GL50 2RH and online

NEWS

Aspirin and reducing stroke risk of people with pneumonia

The research study 'Aspirin after hospitalisation with Pneumonia to prevent cardiovascular Events randomised Controlled Trial' (ASPECT) led by the University of Bristol, sponsored by [North Bristol NHS Trust](#) and supported by the [Bristol Trials Centre](#), has been awarded funding of over £2.3 million by the [National Institute for Health and Care Research](#).

The randomised controlled trial will recruit 22,600 patients from over 60 hospitals across England. Findings

from the four-year study will support future treatment guidelines, if appropriate, for patients with pneumonia. If aspirin is shown to be effective it could prevent up to 3,000 heart attacks and strokes a year in England alone.

Adults over 50 years of age admitted to hospital with pneumonia will be invited to take part in the trial. Those who agree will be split into two groups. One group will be prescribed a three-month course of low-dose aspirin,

the other will not. In all other respects, both groups will receive the standard pneumonia treatment. Participants will be followed up after three months.

The researchers will assess the participants recovery, specifically whether they have had a heart attack or stroke, or any serious side effects from the aspirin. This will be done by reviewing the 'usual care' health records of participants held by NHS hospitals.

[Read the full University of Bristol news item](#) Image © Raw Pixel

£1.52 million boost for Halo Therapeutics

Clinical trials of an easy-to-use home therapeutic treatment for SARS-CoV-2 are underway following a [£1.52 million investment](#) led by the Development Bank of Wales alongside Science Angel Syndicate members and the KBA Group, an angel consortium of high net worth individuals co-led by Dr Nikolaos Kostopoulos and Paras Barot.

Based on world-class research carried out at Bristol University, [Halo Therapeutics](#) was established as a spin-out

company in 2020 by Dr Daniel Fitzgerald, Prof Christiane Schaffitzel and Prof Imre Berger (both from the University's School of Biochemistry). Halo Therapeutics has been attracted to Wales following a £1,000,000 equity investment by the Development Bank of Wales and will be initially based at Welsh ICE, Caerphilly.

This first-in-human study of Halo Therapeutic's respiratory antiviral spray for coronaviruses will investigate the

safety and tolerability of the treatment prior to subsequent studies being conducted in patients that are SARS-CoV-2 positive or are at risk of becoming SARS-CoV-2 positive.

The virus enters the body through the nose; after multiplying here for several days, it spreads to the throat and salivary glands and then into the lungs. It can subsequently spread to other organs, causing in some cases acute damage and long-term damage known as long-COVID.

Somerscience Festival

Held in Castle Cary and Bruton on 1 May 2023, the [Somerset Science Festival](#) welcomed a great number of exhibitors, workshops, shows and talks aimed at all age groups between 10.00 – 18.00. Amongst the stalls were Prof [Paul Race](#), PhD students Greg Pollard, Monserrat Manzo Ruiz, Sam O'Halloran, and Research Associate Dr Catherine Back (all based in the School of Biochemistry, see

image) who presented the Race lab's work [discovering antibiotics from the abyss](#)



and useful enzymes.

The event also saw Prof [Dek Woolfson](#) speak on *From dark matter to electronic nos-*

es, which touched on the work that University of Bristol spinout [Rosa Biotech](#) is doing on proteins that mimic the mammalian olfactory system, but with a simpler structure that makes them easier to produce and handle.

Also present were the [AD-Dovenom](#) team who explained how they are working to defeat snake venom using an innovative therapeutic platform.

High caffeine level might reduce risk of type 2 diabetes

Previously published research indicates that drinking 3-5 daily cups of coffee, a rich source of caffeine, is associated with a lower risk of type 2 diabetes and cardiovascular disease. An average cup of coffee contains around 70–150 mg caffeine. But most of the published research to date has concerned observational studies, which can't reliably establish causal effects, because of the other potentially influential factors involved, point out the researchers. What's more, it's difficult to disentangle any specific effects of caffeine from the other compounds included in caffeinated drinks and foods.

To overcome these issues,

researchers used Mendelian randomisation to find out what effect higher blood caffeine levels have on body fat and the long term risks of type 2 diabetes and major cardiovascular diseases—coronary artery disease, stroke, heart failure, and irregular heart rhythm (atrial fibrillation). They looked at the role of two common genetic variants of the CYP1A2 and AHR genes in nearly 10,000 people of predominantly European ancestry, who were taking part in 6 long term studies. The CYP1A2 and AHR genes are associated with the speed of caffeine metabolism in the body. People who carry genetic variants

associated with slower caffeine metabolism drink, on average, less coffee, yet have higher levels of caffeine in their blood than people who metabolise it quickly to reach or retain the levels required for its stimulant effects. The results of the analysis showed that higher genetically predicted blood caffeine levels were associated with lower weight and body fat. Higher genetically predicted blood caffeine levels were also associated with a lower risk of type 2 diabetes.

Larsson S et al. (2023). [Appraisal of the causal effect of plasma caffeine on adiposity, type 2 diabetes, and cardiovascular disease...](#) *BMJ Medicine*.

New Fellow of the Academy of Medical Sciences

Athimalaipet V Ramanan, FRCPCH, FRCP, Professor of Paediatric Rheumatology at Bristol Medical School, is among the latest group of influential biomedical and health scientists from UK institutions to be elected to the Academy.

Professor Ramanan is a Consultant Paediatric Rheumatologist at Bristol Royal Hospital for Children, where he is the joint lead for research (Division of Women and Children).

He is a medical advisor for registered charity [Olivia's](#)

[Vision](#), established in 2010 to provide information, support and advice for anyone affect-



ed by uveitis. Every year, an estimated 9,000 new case of

uveitis are diagnosed in the UK, with uveitis now the third leading cause of avoidable blindness.

Prof Ramanan was awarded the British Society of Rheumatology's Innovation in Clinical Practice Award in 2010. He also received the University of Bristol Vice Chancellor's Health Impact award in 2017 and Royal College of Physicians/ National Institute for Health and Care Research Clinical Research Network Award for outstanding contribution to research in 2018.

A New Era for Synthetic Carbohydrate Receptors

Professor [Anthony Davis](#) in the School of Chemistry has been awarded a European Research Council Advanced Grant of nearly €2.5 million for a project entitled *After GluHUT – A New Era for Synthetic Carbohydrate Receptors (POSTGLUHUT)*, which aims to transform the lives of diabetics.

Molecules which bind carbohydrates can have a range of medical uses. An important example is the application of glucose-binding molecules in glucose monitors for diabetics, and potentially in glu-

cose-sensitive insulin which becomes more active as glucose levels increase.

Anthony's group developed a high effective glucose-binding molecule called [GluHUT](#) (Glucose-binding Hexaurea Temple), which could find use in insulin delivery systems and devices for monitoring blood glucose levels in diabetics. It has been commercialised through a start-up company, Ziyllo, which was bought out by global healthcare company Novo Nordisk in 2018 in an \$800 million deal.

POSTGLUHUT aims to exploit GluHUT in a number of new ways, and also to develop the underlying science so that other carbohydrates can be targeted. The funds will provide the team with the resources required to make the most of GluHUT itself, and to move towards synthetic antibodies binding a range of medically important carbohydrates. Ultimately they hope to develop a range of other medical applications through binding to the carbohydrate units which control many biological processes.

model of 3
+ glucose

World-leading epidemiology research continues

The Medical Research Council Integrative Epidemiology Unit (MRC IEU) at the University of Bristol has been awarded funding to enable a further five years of world-leading research.

MRC IEU, which was established in 2013, is a leading centre for research into methods for causal inference, and evidence triangulation. It is also a leading centre for the application of causal methods to answer important questions about

diseases in populations. Research from IEU enables valuable insight into many key challenges for population health, with important impact for further research, policy and practice.



MRC Integrative Epidemiology Unit

The new funding, which began in April 2023, totals £11,637,000. It covers work spanning six key programme themes:

- Mendelian randomization

- Statistical methods for causal inference
- Data mining epidemiological relationships
- Molecular drivers and predictors of pregnancy complications and future health
- Immunopsychiatry
- Behavioural, social and environmental determinants of physical and mental health

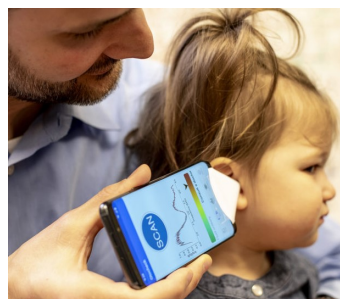
The award will expand the methods the IEU develop and their application into new fields.

Associations between child ENT problems and autism

Young children with ENT (ear, nose and throat) problems relating to the ears, hearing and upper respiratory system, were found to be more common in those with a subsequent diagnosis of autism or who demonstrated high levels of autism traits found a study at the University of Bristol and Aston University.

Researchers looked at data from over 10,000 young children aged between birth and 4 years old from Bristol's [Children of the 90s study](#), to investigate whether early ear and upper respiratory signs are associated with the development of autistic traits.

The team analysed responses to three questionnaires in which mothers had recorded the frequency of nine different signs and symptoms re-



lating to the ears, hearing problems and upper respiratory system when their child was aged 18 to 42 months.

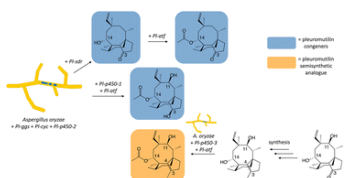
Their results found the frequency of these symptoms was associated with high

scores on each of the autism traits: social communication, coherent speech, sociability and repetitive behaviours, plus those with a clinical diagnosis of autism. Pus or sticky mucus discharge from the ears was especially associated with autism (an increased risk of 3.29) and for impaired hearing during a cold (an increased risk of 2.18).

Hall A. *et al.* (2023). [Associations between autistic traits and early ear and upper respiratory signs: a prospective observational study of the ALSPAC geographically defined childhood population](#). *BMJ Open*.

Biosynthesis of pleuromutilin congeners

Pleuromutilin is an antibiotic diterpenoid made by *Clitopilus passeckerianus* and related fungi, and it is the progenitor of a growing class of -synthetic antibiotics used in veterinary and human medicine. Its antibacterial properties rely on the inhibition of protein synthesis by interfering with the peptidyl transferase centre of the bacterial ribosome and subsequently preventing the formation of peptide bonds between amino acids. To harness the biotechnological potential of



this natural product class, an understanding of its biosynthetic pathway is essential. Numerous efforts have been made to modify the structure of pleuromutilin with the aim to improve its bioactivity and pharmacokinetic properties. Studies have looked at seven

enzyme-coding genes including *Pl-sdr* and *Pl-atf*. The team report on two pathways involving these two genes. Three novel pleuromutilin congeners were isolated, and their antimicrobial activity investigated.

It was observed that the absence of various functional groups - 3 ketone, 11 hydroxyl group or 21 ketone - from the pleuromutilin framework affected the antibacterial activity of pleuromutilin congeners. This study expands our knowledge on the biosynthesis of pleuromutilin and provides avenues for the development of novel pleuromutilin analogues.

Alberti F *et al.* (2023). [Biosynthesis of pleuromutilin congeners using an *Aspergillus oryzae* expression platform](#). *Chemical Science*.

Rosa Biotech accelerates NASH clinical trial in liver disease

Following its latest funding round, [Rosa Biotech](#) has announced plans to accelerate development of its pioneering bio-sensing technology, designed to enable cost effective screening of a range of life-threatening diseases with high accuracy at an early stage.

The company - spun out from the University of Bristol in 2019, based on more than 10 years of research in the lab of protein designer Prof [Dek Woolfson](#) - is initially targeting the early identification

of non-alcoholic fatty liver disease (NAFLD) which, if left untreated, can develop into steatohepatitis (NASH) leading to liver failure. The Western world has experienced a

100% increase in NASH cases during the last 30 years and this

trend is expected to accelerate in the coming decades.

Since incorporation, Rosa's multidisciplinary team has demonstrated that its innovative sensing platform, Pandra,

can detect life-threatening diseases with high accuracy in patient samples. The Pandra platform is particularly relevant given the tsunami of chronic diseases expected to affect large parts of the developed world in the coming decade, and the current difficulties in cost effectively diagnosing these at scale early enough for interventions and lifestyle changes to positively impact patient outcomes.

The company has attracted [£415,000 from angel investors](#) to pursue the project.

rosa
biotech

Rapid diagnostic tests in veterinary practice

Rapid, low-cost and readily available diagnostics that specifically identify pathogens and their antimicrobial susceptibility profiles have been identified as essential, yet questions over the assumed utility of novel rapid technology as a cornerstone of tackling agricultural antimicrobial use (AMU) still exist. This study qualitatively examined the discourse between veterinarians, laboratory representatives, veterinary researchers and (cattle) farmers within three participatory events

concerning diagnostic testing on UK farms, to offer a critical examination of the interaction between veterinary diagnostic practice and agricultural AMU.

Veterinarian-led discussion suggested that veterinary rationales for engaging with diagnostic testing are nuanced and complex, where veterinarians (i) were driven by both medical and non-medical motivators; (ii) had a complex professional identity influencing diagnostic-test

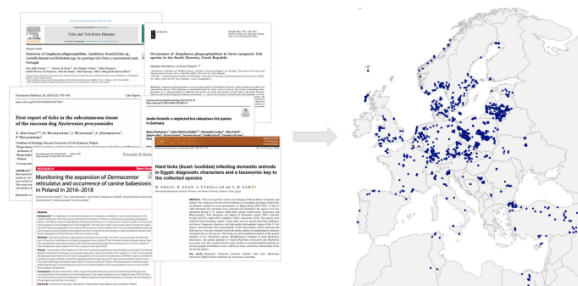
engagement; and (iii) balanced a multitude of situated contextual factors that informed “gut feelings” on test choice and interpretation. It is suggested that data-driven diagnostic technologies may be more palatable.

Bard AM *et al.* (2023). ‘I Believe What I’m Saying More Than the Test’: The Complicated Place of Rapid, Point-of-Care Tests in Veterinary Diagnostic Practice. *Antibiotics*.

Distribution of ticks in the Western Palearctic

The distributions of ticks and tick-borne pathogens are thought to have changed rapidly over the last two decades, with their ranges expanding into new regions. This expansion has been driven by a range of environmental and socio-economic factors, including climate change. Spatial modelling is being increasingly used to track the current and future distributions of ticks and tick-borne pathogens and to assess the associated disease risk. However, such analysis is dependent on high-resolution occurrence data for each species. To facilitate such analy-

sis, in this review the authors have compiled georeferenced tick locations in the Western Palearctic, with a resolution



accuracy under 10 km, that were reported between 2015 and 2021.

The data presented provides a collection of recent high-resolution, coordinate-referenced tick locations for use in spatial analyses, which

in turn can be used in combination with previously collated datasets to analyse the changes in tick distribution and research in the Western Palearctic. In the future it is recommended that, where data privacy rules allow, high-resolution methods are routinely used by researchers to geolocate tick samples and ensure their work can be used to its full potential.

Noll M, Wall R *et al.* (2023). Distribution of ticks in the Western Palearctic: an updated systematic review (2015–2021). *Parasites and Vectors*.

Blood cells with therapeutic benefit

New technology to develop red blood cells (RBCs) that carry additional proteins within them to provide therapeutic benefit which can reach all parts of the body, has received funding to progress the innovation.

The platform, developed by University of Bristol spin-out [Scarlet Therapeutics](#), has raised seed funding from [Science Creates Ventures](#) and [Meltwind](#) to build a pipeline of novel therapies to treat patients with a wide range of diseases, particularly metabolic disorders.

Red blood cells have pervasive reach throughout the body and a long life of up to 120 days, and expressing therapeutic proteins inside the therapeutic RBCs (tRBCs) keeps them hidden from the immune system. Previous attempts to develop tRBCs have been hindered by the level of therapeutic proteins contained in the RBCs, thus impacting efficacy, and the technical constraints around manufacturing these therapies. Scarlet's technologies aim to address these issues by ensuring a high level of therapeutic proteins inside the

tRBCs, enabling more efficacious and thus effective therapies and improving the manufacturing by being able to generate the tRBCs from cell lines rather than from donated stem cells.

Scarlet is initially targeting two rare metabolic diseases: hyperammonemia and hyperoxaluria. The platform also has the potential to treat other metabolic diseases requiring enzyme replacement therapy, as well as cancer and autoimmune diseases.

[Read the full University of Bristol news item](#)

Intervention for the management of antibiotics for children

This trial aimed to assess whether an easy-to-use multifaceted intervention for children presenting to primary care with respiratory tract infections would reduce antibiotic dispensing, without increasing hospital admissions for respiratory tract infection.

A two arm randomised controlled trial clustered by general practice, using routine outcome data, with qualitative and economic evaluations was designed and launched in English primary care practices using the EMIS

electronic medical record system.

No evidence was found that antibiotic dispensing differed between intervention practices and control practices. Prespecified subgroup analyses suggested reduced dispensing in intervention practices with fewer prescribing nurses, in single site (compared with multisite) practices, and in practices located in areas of lower socioeconomic deprivation, which may warrant future investigation. The team concluded that this stewardship intervention did not re-

duce overall antibiotic dispensing or increase respiratory tract infection-related hospital admissions. Evidence suggested that in some subgroups and situations (for example, under non-pandemic conditions) the intervention slightly reduced prescribing rates but not in a clinically relevant way.

Blair PS *et al.* (2023). [Multifaceted intervention to improve management of antibiotics for children presenting to primary care with acute cough and respiratory tract infection \(CHICO\)...](#) *BMJ*.

Bacterial bonding to surfaces

Bacterial fibrillar adhesins are specialised extracellular polypeptides that promote the attachment of bacteria to the surfaces of other cells or materials. Adhesin-mediated interactions are critical for the establishment and persistence of stable bacterial populations within diverse environmental niches and are important determinants of virulence. The fibronectin (Fn)-binding fibrillar adhesin CshA, and its paralogue CshB, play important roles in host colonisation by *Streptococcus goro-*

donii. The team probed the early stages of structural and functional divergence in Csh proteins by determining the X-ray crystal structure of the CshB adhesive domain NR2 and characterising its Fn-binding properties. Despite sharing a common fold, CshB_NR2 displays an ~1.7-fold reduction in Fn-binding affinity relative to CshA_NR2. Complementary bioinformatic studies reveal that homologues of CshA/B_NR2 domains are widely distributed in both Gram-positive and

Gram-negative bacteria, where they are found housed within functionally cryptic multi-domain polypeptides. The findings are consistent with the classification of Csh adhesins and their relatives as members of the recently defined polymer adhesin domain (PAD) family of bacterial proteins.

Barringer R *et al.* (2023). [Domain shuffling of a highly mutable ligand-binding fold drives adhesin generation across the bacterial kingdom.](#) *Proteins.*

Macrocyclic lactone resistant cyathostomins

In recent years, resistance to the benzimidazole (BZ) and tetrahydropyrimidine (PYR) anthelmintics in global cyathostomin populations, has led to reliance on the macrocyclic lactone drugs (ML-of which ivermectin and moxidectin are licensed in horses) to control cyathostomins, a worm parasite. Recently, the first confirmed case of resistance to both ivermectin (IVM) and moxidectin (MOX) was reported in the USA in yearlings imported from Ireland. This suggests that ML resistance in cyathostomins has emerged, and raises the possibility that regular move-

ment of horses may result in rapid spread of ML resistant cyathostomins. Resistance may go undetected due to a lack of surveillance for ML efficacy.

In this article, the team report anthelmintic efficacies in cyathostomins infecting UK Thoroughbreds on four studs using faecal egg count reduction tests. Resistance to MLs was not found in yearlings or mares on studs B, C or D with FECR after MOX OR IVM treatment; although yearlings on studs B, C and D all had an egg reappearance period (ERP) of six weeks for MOX and stud C had a four-week ERP for IVM.

This study describes the first confirmed case of resistance to both licensed ML drugs on a UK Thoroughbred stud and highlights the urgent need for a) increased awareness of the threat of ML resistant parasites infecting horses, and b) extensive surveillance of ML efficacy against cyathostomin populations in the UK, to gauge the extent of the problem.

Bull KE *et al.* (2023). [The first report of macrocyclic lactone resistant cyathostomins in the UK.](#) *International Journal for Parasitology: Drugs and Drug Resistance.*

Cost-effectiveness of Hepatitis C virus self-testing

Globally, there are approximately 58 million people with chronic hepatitis C virus infection (HCV) but only 20% have been diagnosed. HCV self-testing (HCVST) could reach those who have never been tested and increase uptake of HCV testing services. The research team compared cost per HCV viraemic diagnosis or cure for HCVST versus facility-based HCV testing services. They used a decision analysis model with a one-year time horizon to examine the key drivers of economic cost per diagnosis or cure following the introduction of HCVST in China (men who

have sex with men), Georgia (men 40–49 years), Viet Nam (people who inject drugs, PWID), and Kenya (PWID). HCV antibody (HCVAb) prevalence ranged from 1%–60% across settings.

Cost per HCV viraemic diagnosis without HCVST ranged from \$35 2019 US dollars (Viet Nam) to \$361 (Kenya). With HCVST, diagnosis increased resulting in incremental cost per diagnosis of \$104 in Viet Nam, \$163 in Georgia, \$587 in Kenya, and \$2,647 in China. Differences were driven by HCVAb prevalence. Switching to blood-based

HCVST (\$2.25/test), increasing uptake of HCVST and linkage to facility-based care and NAT testing, or proceeding directly to NAT testing following HCVST, reduced the cost per diagnosis. HCVST increased the number of people tested, diagnosed, and cured, but at higher cost. Introducing HCVST is more cost-effective in populations with high prevalence.

Walker JG *et al.* (2023). [Cost-effectiveness of Hepatitis C virus self-testing in four settings](#). *PLoS Global Public Health*.

Needle and syringe programmes reduce HIV and Hep C risk

Although the Netherlands, Canada and Australia were early adopters of harm reduction for people who inject drugs (PWID), their respective HIV and hepatitis C (HCV) epidemics differ. A research team measured the pooled effect of needle and syringe program (NSP) and opioid agonist therapy (OAT) participation on HIV and HCV incidence in these settings.

They observed 94 HIV seroconversions and 81 HCV seroconversions among 2023 and 430 participants, respectively.

Comprehensive NSP/OAT led to a 41% lower risk of HIV acquisition and a 76% lower risk of HCV acquisition compared with no/partial NSP/OAT, with little heterogeneity between studies for both infections.

The findings determined that in the Netherlands, Canada and Australia, comprehensive needle and syringe program and opioid agonist therapy participation appears to substantially reduce HIV and hepatitis C acquisition compared with no or partial needle and

syringe program/opioid agonist therapy participation. The results from an emulated trial design reinforce the critical role of comprehensive access to harm reduction in optimising infection prevention for people who inject drugs.

Van Santen DK *et al.* (2023). [Comprehensive needle and syringe program and opioid agonist therapy reduce HIV and hepatitis c virus acquisition among people who inject drugs in different settings: a pooled analysis of emulated trials](#). *Addiction*

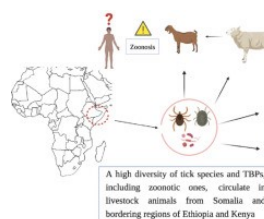
Pathogens of domestic animals in Somalia

Ticks and tick-borne pathogens (TBPs) of domestic animals in Somalia and neighbouring regions of Ethiopia and Kenya were reviewed to identify knowledge gaps in these regions, where unrestricted livestock movements across borders are common.

Thirty-one tick species representing six genera

(*Rhipicephalus*, *Hyalomma*, *Amblyoma*, *Haemaphysalis*, *Ornithodoros* and *Argas*) were reported to infest domestic animals, mainly live-

stock. In addition, 18 TBPs, including zoonotic pathogens (e.g., Crimean-Congo haemorrhagic fever virus), were detected, with *Babesia* spp., *Theileria* spp., and *Rickettsia* spp. being the most commonly reported. Generally, ticks and TBPs in the region are under-studied, and the infection intensity and herd prevalence of ticks and TBPs is unclear due to insufficient data and poor ap-



proaches to quantitative analysis, making it difficult to propose management policies in the region.

There is an urgent need, therefore, for more and better studies so that sustainable

control strategies against them can be planned.

Jimale KA, Wall R & Otranto D (2023). [Ticks and tick-borne pathogens of domestic animals in Somalia and neighbouring regions of Ethiopia and Kenya](#). *Acta Tropica*.

Inhibitors of *Mycobacterium tuberculosis*

In 2020, the number of people dying from tuberculosis (TB) caused by *Mycobacterium tuberculosis* increased to a total of 1.5 million, with an estimated 9.9 million people worldwide falling ill with TB. Successful TB treatment is threatened by the spread of drug-resistant *M. tuberculosis* strains, including multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant (XDR-TB). In consequence, new anti-tubercular agents are needed

for *M. tuberculosis* treatment to overcome drug-resistant TB strains.

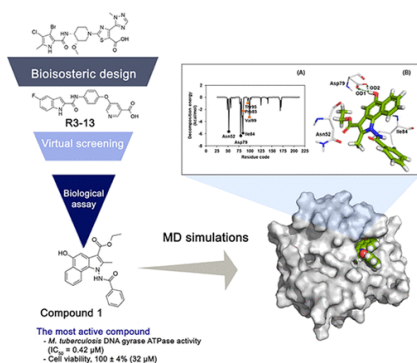
Mutations in DNA gyrase confer resistance to fluoroquinolones, second-line antibiotics for *M. tuberculosis* infections. Identification of new agents

that inhibit *M. tuberculosis* DNA gyrase ATPase activity is one strategy to overcome this. Here, bioisosteric designs using known inhibitors were employed to

define novel inhibitors of *M. tuberculosis* DNA gyrase

ATPase activity. This yielded the modified compound R3-13 with improved drug-likeness compared to the template inhibitor that acted as a promising ATPase inhibitor against *M. tuberculosis* DNA gyrase. Utilisation of compound R3-13 as a virtual screening template, supported by subsequent biological assays, identified seven further *M. tuberculosis* DNA gyrase ATPase inhibitors.

Kamsri B *et al.* (2023). [Bioisosteric Design Identifies Inhibitors of *Mycobacterium tuberculosis* DNA Gyrase ATPase Activity](#). *Computational Chemistry*.



Do temperature changes cause eczema flares?

It is unclear if ambient temperature changes affect eczema. It is also unclear if people with worse disease are more susceptible to weather-related flares, or specific types of emollient offer protection. Substantiating these links may help inform action plans and patients self-management.



A research team wanted to investigate the effect of short-term temperature variations on eczema symptoms in children. Data

from a UK cohort of 519 children (6 months-12 years) with at least mild eczema, participating in a randomised trial comparing four types of emollients on eczema symptoms, were combined with observed temperature data from the

Hadley Centre's Integrated Surface Database.

Seasonal variation in patient-oriented eczema measure (POEM)

scores was observed, suggesting symptoms worsening with colder weather in winter and improving with warmer

weather in summer. Findings are consistent with previous studies demonstrating either improvements in eczema symptoms or reduced flares in hot weather. Worse disease and different emollient types did not increase susceptibility or provide protection against temperature changes. Further work should investigate the role of sunlight, humidity, air pollution and other environmental factors.

Chan J *et al.* [Do temperature changes cause eczema flares? An English cohort study.](#) *Clinical and Experimental Dermatology*.

Monkey pox barriers to public health measures

The 2022-23 Mpox epidemic is the first-time sustained community transmission had been reported in countries without epidemiological links to endemic areas. During that period, the outbreak almost exclusively affected sexual networks of gay, bisexual, or other men who have sex with men (GBMSM) and people living with HIV. In efforts to control transmission, multiple public health measures were implemented, including vaccination, contact tracing and isolation. This study examines knowledge, attitudes, and perceptions of Mpox among a

sample of GBMSM during the 2022-23 outbreak in the UK.

Interviews were conducted with 44 GBMSM between May and December 2022. Most interviewees were well informed about Mpox transmission mechanisms and were either willing to or currently adhering to public health measures, despite low perceptions of Mpox severity. Measures that aligned with existing sexual health practices and norms were considered most acceptable. Although social media was a key mode of information sharing,

there were preferences for timely information from official sources to dispel exaggerated or misleading information. Future public health interventions and campaigns should be co-designed in consultation with key groups and communities to ensure greater acceptability and credibility in different contexts/communities.

May T *et al.* (preprint). [Mpox knowledge, behaviours and barriers to public health measures among gay, bisexual and other men who have sex with men in the UK...](#) *MedRxiv*.

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**

British Thyroid Foundation

[Research award on thyroid disorders](#)

Closing date: 2 July 2023

Award amount: £35,000

This supports research projects on thyroid disorders. Researchers working on projects in the UK may apply. Funding may be used to supplement existing projects or to get new research started.

Bureau of International Security and Nonproliferation

[Prevention and Mitigation of High Consequence Pathogen Spillover in Southeast Asian Live Animal Markets and Supply Chains](#)

Closing date: 3 July 2023

Award amount: USD \$1,750,000

For projects that will advance the mission of NDF's project on the prevention and mitigation of zoonotic spillover stemming from high-risk live animal markets and associated supply chains in Southeast Asia.

National Institutes of Health

[Enhancement or Sustainment of Data Science Tools for Infectious and Immune-Mediated diseases \(U24 Clinical Trial Not Allowed\)](#)

Closing date: 6 July 2023

Award amount: USD \$600,000

For the enhancement and/or sustainment of high-value data science research software to improve the acquisition, management, analysis, visualization, and dissemination of data and knowledge across the immune-mediated, and infectious-disease research continuum. This includes infectious diseases, emerging infections, or immune-mediated diseases that include allergy, autoimmunity, or immune reactions associated with transplantation.

As a part of the trans-NIAID data science program, this call focuses on enhancement and/or sustaining operations and improving the user experience and availability of existing, widely adopted informatics tools and resources.

Department of Health and Social Care

[Small Business Research Initiative \(SBRI\): Vaccine development for potential epidemic diseases stage 1](#)

Closing date: 12 July 2023

Award amount: £2,000,000

The aim of this competition is to support further development of vaccine candidates, technologies and platforms against specified pathogens of epidemic potential including Disease X. The UK Vaccine Network has identified a list of priority pathogens, though applications for work on other pathogens within the same family will be considered. Your proposal can address any part of the development pathway in the UK or in relevant low and middle-income countries (LMICs), including: pre-clinical and non-clinical development; manufacturing process design; phase 1 clinical trials.

International Society of Antimicrobial Chemotherapy

[Project grants](#)

Closing date: 1 September 2023

Award amount: £20,000

These support antimicrobial research in low- to middle-income countries. Projects should address one of the following areas: feasible and effective prevention strategies to prevent transmission of pathogens in low resource settings; basic laboratory support for a healthcare system minimally needed to tackle infectious diseases; improving antimicrobial use worldwide to ensure it is delivered only to those who need it.

Healthcare Infection Society

[Graham Ayliffe training fellowship](#)

Closing date: 1 September 2023

Award amount: £73,000

This enables clinicians working in the field of infection prevention and control to take a one year paid leave of absence to pursue their specialist area by broadening their knowledge base and imparting that knowledge to the wider scientific and medical community.

THIS ISSUE'S FEATURED ARTICLE

Incidence of HIV and hepatitis C virus among people who inject drugs, and associations with age and sex or gender: a global systematic review and meta-analysis

HIV and HCV Incidence Review Collaborative Group. *The Lancet Gastroenterology and Hepatology*.

Countries must intensify efforts to track HIV and hepatitis C virus (HCV) incidence among people who inject drugs, and to prioritise this group in prevention and elimination work.

UNAIDS and the World Health Organization (**WHO**) have recommended targets for ending the HIV/AIDS epidemic and eliminating HCV as a public health threat by 2030. To validate these targets, countries must measure HIV and HCV incidence and document a decline over time. People who inject drugs are one of the key risk groups for HIV and HCV infection, so it is important for countries to track HIV and HCV incidence in this high-risk group.

Bristol Medical School researchers sought to address this by summarising global HIV and primary HCV incidence data among people who inject drugs together with age- and sex- or gender-specific incidence data. They conducted a systematic review and meta-analysis by searching for relevant studies published between 2000 and 2022.

Data on HIV and HCV incidence in people who inject drugs was limited. Globally, only 14% and 12% of countries have at least one estimate on these measures, respectively. In many cases, estimates are not recent, not nationally representative, and were usually constrained to a city within a country.

The availability of estimates was also geographically skewed, with few estimates from middle-income countries for HCV, and only one HIV and HCV incidence estimate from low-income countries.

Although limited, available data suggest that HIV and HCV incidence are high in this population - on average 1.7 per 100 person per year for HIV and 12.1 per 100 person per year for HCV. These figures mean that, on average, if 100 people who inject drugs uninfected with HIV and HCV were followed for one year, nearly 2 would acquire HIV and 12 would acquire HCV. However, there is considerable variability in these estimates: the ranges are 0.1-31.8 per 100 person per year for HIV and 0.2-72.5 per 100 person per year for HCV. Additionally, young people who inject drugs were found to have on average a 1.5-times greater risk of HIV and HCV than older people who inject drugs, and women had a 1.4-times greater risk of HIV and a 1.2-times greater risk of HCV than men.

Their findings suggest there is a pressing need for most countries to scale-up measurement and monitoring of HIV and HCV incidence among people who inject drugs, and to prioritise this population in prevention and elimination efforts. In addition, given that young people who inject drugs and women who inject drugs have higher risk of getting infected with both HIV and HCV, age-appropriate and gender-appropriate prevention measures are urgently needed to reach and engage with these vulnerable risk subgroups.

CONTACTS

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

Co-Chair (non-clinical): [Angela Nobbs](#) - Senior Lecturer in Oral Microbiology
Co-Chairs (clinical): [Julia Colston](#) - Consultant in Infection
[Ed Moran](#) - Consultant in Infectious Diseases

- [Borko Amulic](#) - Senior Research Fellow in Immunology
- [Matthew Avison](#) - Professor of Molecular Bacteriology
- [Charles Beck](#) - Consultant Epidemiologist & Head of Team, Field Service South West, National Infection Service, UK Health Security Agency
- [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
- [Adrian Mulholland](#) - Professor of Chemistry
- [Laura Peachey](#) - Lecturer in Veterinary Parasitology
- [Annela Seddon](#) - Director of the Bristol Centre for Functional Nanomaterials
- [Luca Shytaj](#) - Lecturer in Virology
- [Suzanne Mills](#) - Research Development Associate for the Faculties of Health and Life Sciences
- [Peter Vickerman](#) - Professor of Infectious Disease Modelling
- [Richard Wall](#) - Professor of Zoology
- [Catherine Brown](#) - Network Administrator

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 [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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