

HEALTH PROTECTION RESEARCH UNIT  
IN EMERGING AND ZOO NOTIC INFECTIONS

  
*National Institute for  
Health Research*



# **BOOK OF ABSTRACTS AND PRESENTATION OF KEYNOTE SPEAKERS**

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# KEYNOTE SPEAKERS

Keynote speakers for the 2017 National Institute for Health Research (NIHR) Health Protection Research Unit (HPRU) in Emerging and Zoonotic Infections (EZI) annual conference, on 'Meeting the Challenges and Thinking Ahead' are: Dr Ana Maria Bispo de Filippis, Professor Daniel Bausch and Professor Tom Solomon.



***Dr Ana Maria Bispo de Filippis: 'Zika infection in Brazil: where are we now?'***

Ana Maria Bispo de Filippis has a MSc in Molecular and Cellular Biology (1997) and a PhD in Virology. She has been a researcher part of the Virology Department of the Oswaldo Cruz Foundation since 1983 and has worked in various research topics within the areas of surveillance and molecular epidemiology of Poliovirus and other Enterovirus, yellow fever virus, dengue and other arbovirus. From 2004 until 2010, she worked as Regional Consultant of the Pan-American Health Organization (OPAS/OMS) in Washington DC (USA), coordinating the network of regional laboratories that support the immunization programs in the American region, specifically, the network of laboratories that work with measles, rubella, polio, rotavirus and HPV. In March 2010, Ana returned to the Flavivirus laboratory in the Oswaldo Cruz Institute (Fiocruz), working again with virological surveillance, serology, molecular epidemiology, pathogenesis, and atypical clinical presentation of dengue and other arbovirus with epidemiological importance within the state of Rio de Janeiro and Brazil. In November 2015, she led the team that detected for the first time in the world the presence of Zika in amniotic fluid of two pregnant women with foetus presenting microcephaly. This represented the first strong evidence that associated the Zika Virus and the microcephaly. Ana is the main investigator of various projects in the areas of Zika virus with funding from the European Union, WHO, Wellcome Trust, the Brazilian Health Department, IDRC (Canada) and MRC (UK).

Ana has a continuous role in training human resources at different levels, technical professionals and academics (undergraduates, master students and PhDs). Ana's laboratory collaborates with Institutes from Brazil, Europe and United States. Ana is a permanent consultant for the Brazilian Health Department, Regional and Municipal Health Secretariat, OPAS/WHO.



***Professor Daniel Bausch: 'Outbreaks: The Slow Road to Rapid Control'***

Daniel Bausch is the Director of the United Kingdom Public Health Rapid Support Team (UK PHRST), a joint effort by Public Health England and the London School of Hygiene and Tropical Medicine to respond and conduct research to prevent and control outbreaks of dangerous infectious diseases around the world. He is trained in internal medicine, infectious diseases, tropical medicine, and public health. Dr. Bausch specializes in the research and control of emerging tropical viruses, with over 20 years' experience in sub-Saharan Africa, Latin America, and Asia combating viruses such as Ebola, Lassa, hantavirus, and SARS coronavirus. He places a strong emphasis on capacity building in all his projects and also has a keen interest in the role of the scientist in promoting health and human rights.



***Professor Tom Solomon: 'The Health Protection Research Unit in Emerging and Zoonotic Infections - A Year of Challenges and Successes'***

Professor Tom Solomon studied medicine at Oxford, did a PhD in Vietnam and postgraduate virology in the United States, before training as a neurologist.

He is Professor of Neurology at the Walton Centre NHS Foundation Trust and Director of the HPRU in Emerging and Zoonotic Infections. He studies emerging viral infections, particularly those that affect the brain, has published more than 200 scientific papers, and was awarded the Royal College of Physicians Triennial Moxon medal in 2014.



# **ORAL ABSTRACTS**



1

LYME SESSION

**Host-derived markers of Lyme disease and their diagnostic potential**

Greg Joyner

PhD Student

Clinical Surveillance theme

Lyme disease (LD) is a multisystem infection caused by tick-borne spirochaetes of the *Borrelia burgdorferi sensu lato* group. UK laboratory diagnosis of LD involves the two-tier serological approach. The negative predictive value of the test has been challenged, particularly in early stage LD. There is considerable interest, therefore, in the development of improved diagnostic tests. The main aim of the project is to identify new markers that could form the basis for improved tests. The project is part of collaboration between the University of Liverpool and Public Health England that aims to improve diagnostic testing for several infectious diseases.

A mass spectrometry biomarker discovery study was undertaken on LD positive and negative residual diagnostic samples from UK LD testing by Public Health England. A control group of healthy subjects serum samples (from NHS blood transfusion service) were also included. To ensure differences were specific to LD rather than genetic to infection, a "related-disease control group" including serum samples from syphilis, leptospirosis and chronic fatigue syndrome were included. A total of 50 human samples were compared by label-free quantitative mass spectrometry.

Surprisingly, Lyme seropositive and seronegative groups were found to have very few proteins that were significantly different when directly compared. One protein, Lipocalin-2 was found at a significantly higher abundance in the LD-positive patients compared with those that were LD-negative. This is of interest due to involvement in innate immunity. Lipocalin-2 has been found in mice exposed to *B. burgdorferi*. Leptospirosis samples showed increased levels of several proteins involved in host-immune response including neutrophil defensin-1. Several key differences were also found in CFS and syphilis patients.

The results of the mass spectrometry run have generated several proteins of interest that will be further investigated by Western blot analyses on larger sample groups to further investigate their diagnostic potential.

**Author and Affiliations:**

Greg Joyner<sup>1,2</sup>, Nick Beeching<sup>2,3</sup>, Amanda Semper<sup>4</sup> and Julian Hiscox<sup>1,2</sup>

<sup>1</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Liverpool School of Tropical Medicine, Liverpool, UK.

<sup>4</sup>Public Health England, PHE Porton, Porton Down, Salisbury, UK.

2

LYME SESSION

**The incidence and demographics of Lyme disease in UK primary care, 1998-2015**

John Tulloch

PhD Student

Epidemiological Approaches theme

Lyme disease is a tick-borne disease of increasing global public health interest. Clinical presentation is varied, posing challenges for case definition. Current incidence data in England and Wales are based solely upon Public Health England laboratory confirmed cases. The reported national annual incidence in 2016 was 1.95 per 100,000. Many cases of Lyme disease do not require laboratory diagnostics; it is therefore likely that this figure is an under-estimate.

The Health Improvement Network (THIN) is a database of primary care electronic health records, containing over 11 million unique patients across the UK. We searched the THIN database between 1998 and 2015 for patient records that had at least one of twenty-eight Read codes concerning Lyme disease. We captured information on date of diagnosis and patient demographics. Using these data we describe the Lyme disease incidence, patient characteristics and management in primary care at a national level.

These electronic health records suggest an overall incidence of 4.23 cases per 100,000 person years. This varied between nations; Scotland 10.69, England 3.34, Wales 1.80 and Northern Ireland 1.27 per 100,000 person years. Over the study period incidence rates rose overall and in each nation, except Northern Ireland. There was no significant difference in incidence between sexes. English patients were significantly more likely to live in rural rather than urban areas. In England, the number of cases increased as the level of deprivation decreased. Cases were seen year round, and peaked in July.

These results provide an estimate of the incidence of Lyme disease in the UK. There is significant variation between nations. Demographic analysis indicates that certain sections of society are at relatively higher risk of presenting with disease. This will impact the public health messaging and management of Lyme disease. Our future work will focus on the management of Lyme disease patients in primary care.

**Author and Affiliations:**

John SP Tulloch <sup>1</sup>, Rob M Christley <sup>1,2</sup>, Alan D Radford <sup>1,3</sup>, Jenny C Warner <sup>1,4</sup> and Roberto Vivancos <sup>1,5</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, UK.

<sup>2</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>3</sup>Institute of Infection and Global Health, University of Liverpool, Leahurst Campus, Chester High Road, Neston, S. Wirral, CH64 7TE, UK.

<sup>4</sup>Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>5</sup>Health Protection Agency, Cheshire and Merseyside Health Protection Unit, Liverpool, UK.

3

LYME SESSION

**The *Ixodes ricinus*  
tick –  
investigating  
*Borrelia*  
prevalence and  
microclimate  
influence in  
England**

Liz McGinley

PhD Student

Vector Biology & Climate  
Modelling theme

*Ixodes ricinus* (the Sheep Tick) is a vector of many pathogens of human and veterinary importance. In the UK it is the primary vector of *Borrelia burgdorferi*.l., the causative agent of Lyme borreliosis - the most common vector-borne disease of humans in the temperate northern hemisphere. Three genospecies of this bacterial complex which are associated with Lyme borreliosis are known to circulate in the UK. Changing land use, human activity, wildlife distributions and weather patterns influence human exposure to this tick species.

The aim of this study was to investigate seasonal peak activity of *Ixodes ricinus*, specifically the microclimate factors which influence when peak activity commences and ends. In addition; the spatial and temporal prevalence of *Borrelia burgdorferi*.l. was investigated across different land cover types and geographical regions.

Longitudinal surveying of twelve sites in England over two years, accompanied by repeated seasonal surveying of twenty four sites across six different land cover types, resulted in comprehensive data on *I. ricinus* activity, habitat and microclimate variables. A proportion of ticks collected from each of the survey sites were tested for the presence of pathogenic *Borrelia* genospecies.

Monitored field sites located in the south of England tended to exhibit a distinctive spring peak in *I. ricinus* activity, followed by much reduced activity. Northern field sites exhibited a spring peak, followed by more prolonged activity through summer. Molecular analysis for *Borrelia* was carried out for regional field sites which yielded a minimum of fifty *Ixodes ricinus* specimens. *Borrelia* was detected in all of these sites, with prevalence ranging from 2-6%. At a landscape scale, *Borrelia* prevalence was found to be highest in broadleaf woodland.

**Author and Affiliations:**

Liz McGinley<sup>1,2</sup>, Andy Morse<sup>2,3</sup>, Jolyon Medlock<sup>1,2</sup>, Matthew Baylis<sup>2,4</sup> and Steve Torr<sup>2,5</sup>

<sup>1</sup>Medical Entomology & Zoonoses Ecology Group, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, UK.

<sup>3</sup>School of Environmental Sciences, University of Liverpool, Liverpool, UK.

<sup>4</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>5</sup>Liverpool School of Tropical Medicine, Liverpool, UK.

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**EBOLA SESSION**

**Elucidation of  
the cellular  
interactomes of  
EBOV VP35 and L  
for targeting the  
function of  
essential host  
factors with  
repurposed  
antiviral  
therapies**

Jordana Muñoz-  
Basagoiti

PhD Student

Pathogen Discovery &  
Characterisation theme

Ebola virus disease (EVD) is a deadly disease in humans characterized by severe immunosuppression, high virus replication and a case-fatality rate of up to 90%. Neither vaccine nor treatment is currently available. As RNA viruses have a high mutation rate, host factor-targeting therapies are arising as an alternative. Previous studies have shown that the lower the viral load, the higher the chance for a patient to survive. Therefore, a better understanding of the viral processes of transcription and replication by elucidating the cellular interactomes of the viral RNA polymerase (L) and its co-factor (VP35) can help developing new drugs to treat Ebolavirus disease (EVD).

In this study, the cellular interactomes of EBOV VP35 and L were elucidated by using a label free LC-MS/MS proteomic approach, indicating that histones, stress response proteins, components of the ribosome, transcription and translation factors, chaperones, cell motility proteins and nucleic acid binding proteins are potential interacting partners of these viral proteins.

The validation of these interactions make them good candidates for drug-targeting antiviral therapies with siRNA and small molecule inhibitors in cells where a reverse genetics system that mimics the transcription and replication of Ebola virus can be used as part of high throughput screening assays.

**Author and Affiliations:**

Jordana Muñoz-Basagoiti<sup>1,2,3</sup>, Isabel García-Dorival<sup>2</sup>, Stuart Armstrong<sup>1,2</sup>, Miles W Carroll<sup>1,3</sup> and Julian Hiscox<sup>1,2</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, UK.

<sup>2</sup>Institute of Infection and Global Health, University of Liverpool, UK.

<sup>3</sup>National Infection Service, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

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EBOLA SESSION

## Characterisation of convalescent plasma using an EBOV GP HIV-1 pseudo-typed assay

Charlene Adaken

PhD Student

University of Liverpool

Invited HPRU Member

### Background

Studying survivors of the West African EBOV 2014-16 epidemic provides a unique opportunity to delineate immune responses controlling viral replication. These individuals provide a bank of convalescent plasmas (CP) that can be used for comprehensive characterisation. We sought to develop an HIV-1 EBOV GP pseudo-typed assay which could analyse antibody (Ab) neutralisation.

### Methods

Single-round infectious EBOV GP pseudo-typed viruses were produced by co-transfecting a HIV-1 envelope deficient backbone with a plasmid expressing the 2015 GEBOV GP envelope into 293T cells. Produced virus was quantified via measuring HIV-1 p24 levels and infection monitored by measuring luciferase activity within infected cells. We utilised our pseudo-typed assay in inhibition assays where limiting dilutions of CP were tested for the capacity to restrict viral entry. Eighty-five CP samples were selected for analysis where total EBOV GP binding responses had been characterised using the DABA assay.

### Results

We developed and generated stable GP pseudo-typed single-cycle infectious virus stocks for use in CP neutralisation assays. Inhibition assays to restrict viral entry into cells by CP, showed broad neutralisation potential against EBOV with an inhibitory trend ranging between low to high.

Further study of longitudinal CP samples from a set of donors showed correlation between two assays; the EBOV pseudo-typed particle neutralisation assay and total GP antibody binding. It was shown CP samples with high Ab titres neutralised EBOV to a greater capacity compared to lower titres ( $P < 0.005$ ). Preliminary data also demonstrated a correlation between CP neutralisation within an EBOV replication competent assay and the EBOV pseudo-typed particle assay.

### Conclusion

We have developed a robust EBOV neutralisation assay that has shown to correlate with total EBOV GP Ab binding. This assay can be used in future characterisation of EBOV Ab responses in both survivors as well as vaccine recipients.

### Author and Affiliations:

C. Adaken<sup>1</sup>, J.T. Scott<sup>1,2</sup>, T. Edwards<sup>3</sup>, S. Dicks<sup>4</sup>, S. Gevao<sup>5</sup>, C.P. Cole<sup>5</sup>, S. Baker<sup>5</sup>, O. Kargbo<sup>5</sup>, P. Kamara<sup>5</sup>, J.Griensven<sup>6</sup>, R.S. Tedder<sup>4</sup>, W.A.Paxton<sup>1</sup>, M.G. Semple<sup>2</sup> and G. Pollakis<sup>1</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, UK.

<sup>2</sup>Institute of Translational Medicine, University of Liverpool, Liverpool, UK.

<sup>3</sup>Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, London, UK.

<sup>4</sup> Blood Borne Virus Unit, Virus Reference Department, National Infection Service, Public Health England, London, UK.

<sup>5</sup> National Safe Blood Services, Ministry of Health and Sanitation, Republic of Sierra Leone, Freetown, Sierra Leone.

<sup>6</sup>Department of Clinical Sciences, Institute of Tropical Medicine, Antwerp, Belgium.

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EBOLA SESSION

**Elucidating the determinants of patient outcome following acute EBOV infection**

Natasha Rickett

PhD Student

Pathogen Discovery & Characterisation theme

The 2013-2015 outbreak of *Zaire ebolavirus* (EBOV) in West Africa was unprecedented in scale and caused an explosion in the cases of Ebola virus infections. Early symptoms are non-specific and flu-like, but these rapidly dissolve into systemic issues, frequently resulting in death. The distinguishing features of fatal and non-fatal infections have been difficult to elucidate, though an increased viral load is indicative of a poor prognosis. Using transcriptome data from blood samples of both acute and convalescent patients we have identified a myriad of factors influencing patient outcome, including viral load, host immune response and co-infections. The elucidation of these factors could have major therapeutic implications.

Here we demonstrate that higher viral load and malaria co-infection are correlated with poor patient outcome. The RNA-sequencing data allowed us to explore various avenues of research. One such path was the comparison of malaria testing methodology – i.e. co-infection confirmed by RNA-seq or rapid diagnostic test (RDT). The RDT was employed in the field, however, our RNA-seq data suggests this may have led to under-reporting of *Plasmodium spp.*

**Author and Affiliations:**

Natasha Y. Rickett<sup>1,2</sup>, Xuan Liu<sup>1,3</sup>, Sam Haldenby<sup>3</sup>, Miles W. Carroll<sup>4,5</sup> and Julian A. Hiscox<sup>1,2</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>3</sup>Centre for Genomic Research, Institute of Integrative Biology, University of Liverpool, Liverpool, UK.

<sup>4</sup>Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>5</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, Porton Down, UK.

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**EMERGING  
CHALLENGES  
SESSION**

**Disease, disgust  
and dirty work:  
exploring the  
border practices  
of pest control**

Charlotte Robin

PhD Student

Epidemiological Approaches  
theme

A major preventive measure for hantavirus is control of rats in domestic and work environments; therefore the pest control industry has an important role in managing rodent populations and their impact on public health. Despite this, little is known about this profession's practices and beliefs, particularly in relation to zoonotic disease risk. This study used in-depth semi-structured interviews with pest control technicians to reveal new insights into this little-researched profession.

The border practices of pest control enable technicians to restore order by repairing the physical and conceptual boundaries ruptured by the rats when they enter the home. Pest control technicians are doing 'dirty' work on behalf of society. They act as social agents, subject to the moral opprobrium of others. They do not judge how people live their lives; they are aware of the shame associated with having rats in the private space of the home and the impact this has on quality of life for those affected. Pest control is also 'dirty' work because of the stigma of bringing the practices of death and killing into the home. In this context, the use of toxic chemicals to remove pests from the home sanitises the killing process, removing workers from the reality it.

These two concepts of 'dirty work' highlight a paradox, which influences how technicians understand risk. Pest control technicians routinely work in toxic environments, where the contaminant is the rat. Yet because people have been living in this 'contaminated' environment it is not seen as a risk, it is just part of everyday life. Conversely, people have not lived in environments contaminated with the toxic chemicals used in pest removal; this is a new pollutant. Consequently, technicians will routinely use personal protective equipment when using chemicals, but not necessarily for working in environments potentially contaminated with hantavirus or other rodent-borne diseases.

**Author and Affiliations:**

Charlotte Robin<sup>1,2</sup>, Elizabeth Perkins<sup>2,3</sup>, Francine Watkins<sup>2,4</sup> and Robert Christley<sup>1,2</sup>

<sup>1</sup>Department of Epidemiology and Population Health, Institute of Infection and Global Health, School of Veterinary Science, University of Liverpool, Leahurst Campus, Neston, CH64 7TE, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup> Health Services Research Department, Institute of Psychology Health and Society, University of Liverpool, Liverpool, UK.

<sup>4</sup> Department of Public Health & Policy, Institute of Psychology Health and Society, University of Liverpool, Liverpool, UK.

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**EMERGING  
CHALLENGES  
SESSION**

**Understanding  
agricultural  
antibiotic use  
and their policies  
in the UK dairy  
industry**

Stephanie Begemann

PhD Student

Epidemiological Approaches  
theme

This PhD has used a qualitative study design to explore how the UK dairy industry develops and implements antibiotic policy, and how this is perceived by veterinarians and farmers. A multi-sited ethnographic methodological framework has been used which includes policy document analysis, in-depth interviews with key dairy stakeholders, participant observation of veterinarians in practice and the observation of policy transfer during farmer meetings from retailers to farmers. With data being analysed through thematic coding in N-vivo software, initial results indicate that antibiotic policies in the dairy industry only partially address the complex network of people, animals and the environment in which antibiotics circulate. Although UK milk processors and UK retailers have taken up the lead to produce dairy antibiotic policies, the policies are fragmented and seem to rather benefit market purposes than address structural issues in UK dairy production systems. At the same time, the policies fail to assess the complex interplay of antibiotic exchange between veterinarians and farmers. Drivers such as the veterinary business model (that is still largely dependent on the sales of veterinary medicines), uncertain milk markets due to fluctuating milk prices, and farmers self-regulating their sick animals, have a large impacts on antibiotic dispensing and their use in practice. Some of the policies co-produce new travel routes of antibiotics between systems, such as for example by forbidding to feed antibiotic contaminated milk to calves, it is now disposed into the slurries through which it can end back into the environment and into the food chain. Hence, the former examples show how the governance of agricultural antibiotics entails more than accomplishing antibiotic reduction targets; it demands to explore how antibiotics are part of different worlds that co-produce the circulation of antibiotics and their effects. As such, the concept of One Health is not only about integrating leadership on animal and human level to produce antibiotic policies; it is about exploring both the heterogeneity as relationality of antibiotic realities, and the impact of those processes on antibiotic futures.

**Author and Affiliations:**

Stephanie Begemann<sup>1,2</sup>, Rob Christley<sup>2,3</sup>, Elizabeth Perkins<sup>2,4</sup>, Roberto Vivancos<sup>2,5</sup> and Francine Watkins<sup>2,6</sup>

<sup>1</sup>Institute of Infection and Global Health, University of Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Department of Epidemiology and Population Health, Institute of Infection and Global Health, School of Veterinary Science, University of Liverpool, Leahurst Campus, Neston, CH64 7TE, UK.

<sup>4</sup>Health Services Research Department, Institute of Psychology Health and Society, University of Liverpool, Liverpool, UK.

<sup>5</sup>Health Protection Agency, Cheshire and Merseyside Health Protection Unit, Liverpool, UK.

<sup>6</sup>Department of Public Health & Policy, Institute of Psychology Health and Society, University of Liverpool, Liverpool, UK.

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**EMERGING  
CHALLENGES  
SESSION**

**Quantitative  
analysis of the  
attraction and  
feeding  
behaviour of UK  
mosquito  
species**

Aislinn Currie-Jordan

PhD Student

Vector Biology & Climate  
Modelling theme

Mosquito-borne viruses pose a global threat with increasing numbers of cases being recorded in Europe. Several mosquito species in the United Kingdom could act as vectors for viruses such as West Nile (WNV) and Japanese encephalitis (JEV). However, despite the risk posed, our knowledge of the behaviour and feeding preferences of UK species of mosquito is limited. Gaining such knowledge will improve our ability to quantify risk and provide a basis for rational development of appropriate vector control strategies. This study is focused on analysing the ecology of mosquitoes on the Wirral, particularly *Aedes detritus* which breeds in salt marshes around the coast of UK and has previously been shown to be a potential vector of pathogenic viruses. The distribution and abundance of mosquitoes has been assessed using (i) a network of traps ('Mosquito Magnets') to monitor adult mosquitoes and (ii) a drone to map potential breeding sites on the marsh supported by sampling of breeding sites for mosquito larvae. Further studies have quantified the relationship between trap catches and the numbers of mosquitoes biting humans. The results show that a Mosquito Magnet and novel Human Decoy Trap provide reliable estimates of the numbers of *Ae. detritus* biting humans. Further work is focusing on the effects of environmental temperature on development of JEV in *Ae. detritus*.

**Author and Affiliations:**

Aislinn Currie-Jordan<sup>1,2</sup>, Matthew Baylis<sup>1,3</sup>, Philip McCall<sup>2</sup> and Jolyon Medlock<sup>1,4</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Department of Vector Biology, Liverpool School of Tropical Medicine, Liverpool, UK.

<sup>3</sup>Department of Epidemiology and Population Health, Institute of Infection and Global Health, University of Liverpool, UK.

<sup>4</sup>Medical Entomology & Zoonoses Ecology Group, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

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ZIKA SESSION

## Climate-driven models for mosquito-borne disease risk in China and Europe

Soeren Metelmann

PhD Student

Vector Biology & Climate Modelling theme

The spread of disease vector species is a major health issue for the human population. One of these invasive species, the Asian tiger mosquito *Aedes albopictus*, is able to transmit diseases such as dengue, chikungunya, and Zika, and has been involved in many major and minor outbreaks globally. Originating in south-east Asia, the mosquito has spread remarkably in the last few centuries and is now present on all continents except Antarctica. Here we compare the situation of *Ae. albopictus* in two different regions: China, where the mosquito has long since established, and Western Europe where it has only been introduced in the 1990s. We use two different climate-driven mathematical models to analyse the general vector suitability and disease transmission risk, as well as the spatial vector spread in these regions. Preliminary results suggest that *Ae. albopictus* is at the edge of its possible range in China but will probably spread further in Europe. However, its suitable area is further expanding due to climate change in both regions.

### Author and Affiliations:

Soeren Metelmann<sup>1,2</sup>, Liang Lu<sup>3</sup>, Xiaobo Liu<sup>3</sup>, Matthew Baylis<sup>1,2</sup>, Andy Morse<sup>1,2</sup> and Qiyong Liu<sup>3</sup>

<sup>1</sup>Institute of Infection and Global Health, University of Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Chinese Center for Disease Control and Prevention, Beijing, China.

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ZIKA SESSION

**The direct detection of dengue, chikungunya and Zika from whole blood using the QuRapID, a molecular platform for the point of care**

Dr Thomas Edwards

Postdoctoral Researcher

Liverpool School of Tropical Medicine

Invited HPRU Member

During 2015-2017 the America's experienced large outbreaks of chikungunya and Zika viruses, against a background of endemic dengue transmission. These arboviruses share the same *Aedes* vectors, and have similar clinical features, meaning diagnostic testing is required in order to differentiate these viruses.

Multiplex molecular testing for all three viruses is beneficial, as this avoids the retesting of samples for multiple viruses, and identifies co-infections; we have shown in Guatemala during 2015 that 32% of chikungunya or dengue RT-qPCR positive samples were also positive for the other virus, and that these patients were more likely to be hospitalized than those with chikungunya mono-infection ( $p=0.002$ ).

Alongside our industrial collaborator BioGene (Cambridge, UK) we have developed an RT-qPCR based assay capable of detecting dengue, chikungunya and Zika virus, directly from whole blood, using their point of care molecular platform the QuRapID LV.

During the assay a 15 $\mu$ l volume of whole blood is added to a 250 $\mu$ l vessel, containing a propriety RT-qPCR reaction buffer. Viral lysis is mediated via the action of a detergent mix, and a 70 $^{\circ}$ C heat step. A reverse transcription is then carried out, followed by 40 cycles of PCR. We will show some early development data showing the detection of live cultured dengue, chikungunya and Zika viruses, and compare the detection limit of the system with the currently recommended CDC RT-qPCRs.

Such a test will enable the simultaneous detection of all three arboviruses from whole blood, with a single liquid handling step, and can provide results within one hour, at the point of care. We will be performing a small-scale evaluation of the prototype test in Sergipe, Brazil, in January 2018.

**Author and Affiliations:**

Thomas Edwards<sup>1,5</sup>, Kavita Shah<sup>2</sup>, Christopher Williams<sup>1</sup>, Adam Tyler<sup>2</sup>, David Edge<sup>2</sup>, Leticia del Carmen de Castillo<sup>3</sup>, Ricardo Gurgel<sup>4</sup>, Luis E. Cuevas<sup>1</sup> and Emily R. Adams<sup>1</sup>

<sup>1</sup>Research Centre for Drugs and Diagnostics, Liverpool School of Tropical Medicine, Liverpool, UK.

<sup>2</sup>BioGene Ltd., 8 The Business Centre, Harvard Way, Harvard Industrial Estate, Kimbolton, UK.

<sup>3</sup>Laboratorio Nacional de Salud, Guatemala.

<sup>4</sup>Federal University of Sergipe, Brazil.

<sup>5</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

12

ZIKA SESSION

**The spectrum of neurological disease associated with Zika and chikungunya viruses in adults in Rio de Janeiro, Brazil: a case series**

Dr Ravi Mehta

Clinical Research Fellow

Clinical Surveillance theme and Pathogen Discovery & Characterisation theme

**Background**

During 2015-16 Brazil experienced the largest epidemic of Zika virus ever reported. This arthropod-borne virus (arbovirus) has been linked to Guillain-Barré syndrome (GBS) in adults but other neurological associations are uncertain. Chikungunya virus has caused outbreaks in Brazil since 2014 but associated neurological disease has rarely been reported here. We investigated adults with acute neurological disorders for Zika, chikungunya and dengue, another arbovirus circulating in Brazil.

**Methods**

We studied adults who had developed a new neurological condition following suspected Zika virus infection between 1<sup>st</sup> November 2015 and 1<sup>st</sup> June 2016. Cerebrospinal fluid (CSF), serum, and urine were tested for evidence of Zika, chikungunya, and dengue viruses.

**Results**

Of 35 patients studied, 22 had evidence of recent arboviral infection. Twelve had positive PCR or IgM for Zika, five of whom also had evidence for chikungunya, three for dengue, and one for all three viruses. Five of them presented with GBS; seven had presentations other than GBS, including meningoencephalitis, myelitis, radiculitis or combinations of these syndromes. Additionally, ten patients positive for chikungunya virus, two of whom also had evidence for dengue virus, presented with a similar range of neurological conditions.

**Conclusions**

Zika virus is associated with a wide range of neurological manifestations, including central nervous system disease. Chikungunya virus appears to have an equally important association with neurological disease in Brazil, and many patients had dual infection. To understand fully the burden of Zika we must look beyond GBS, and also investigate for other co-circulating arboviruses, particularly chikungunya.

**Author and Affiliations:**

Ravi Mehta<sup>1,15\*</sup>, Cristiane Nascimento Soares<sup>3\*</sup>, Raquel Medialdea-Carrera<sup>1,15\*</sup>, Mark Ellul<sup>1,2,15</sup>, Marcus Tullius Teixeira da Silva<sup>4,5</sup>, Anna Rosala-Hallas<sup>6</sup>, Marcia Rodrigues Jardim<sup>7</sup>, Girvan Burnside<sup>6</sup>, Luciana Pamplona<sup>8</sup>, Maneesh Bhojak<sup>2</sup>, Radhika Manohar<sup>2</sup>, Gabriel Amorelli Medeiros da Silva<sup>3</sup>, Marcus Vinicius Adriano<sup>9</sup>, Patricia Brasil<sup>10</sup>, Rita Maria Ribeiro Nogueira<sup>11</sup>, Carolina Cardoso Dos Santos<sup>11</sup>, Lance Turtle<sup>1,2,15</sup>, Patricia Carvalho de Sequeira<sup>11</sup>, David W Brown<sup>12,13</sup>, Michael J Griffiths<sup>1,14,15</sup>, Ana Maria Bispo de Filippis<sup>11</sup> and Tom Solomon<sup>1,2,15</sup>

\* Contributed equally

<sup>1</sup>NIHR Health Research Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Walton Centre NHS Foundation Trust, Liverpool, UK.

<sup>3</sup>Hospital Federal dos Servidores do Estado, Rio de Janeiro, Brazil.

<sup>4</sup>Instituto Nacional de Infectologia Evandro Chagas, Laboratório de Pesquisa em Neuroinfecção, Rio de Janeiro, Brazil.

<sup>5</sup>Hospital de Clínicas de Niterói, Niterói, Brazil.

<sup>6</sup>Department of Biostatistics, Institute of Translational Medicine, University of Liverpool, Liverpool, UK.

<sup>7</sup>Hospital Universitário Pedro Ernesto, Rio de Janeiro, Brazil.

<sup>8</sup>Hospital Geral de Bonsucesso, Rio de Janeiro, Brazil.

<sup>9</sup>Hospital Barra D'or, Rio de Janeiro, Brazil.

<sup>10</sup>Instituto Nacional de Infectologia Evandro Chagas, Laboratório de Pesquisa Clínica em Doenças Febris Agudas, Rio de Janeiro, Brazil.

<sup>11</sup>Flavivirus Reference Laboratory, Oswaldo Cruz Institute, Rio de Janeiro, Brazil.

<sup>12</sup>Influenza Reference Laboratory, Oswaldo Cruz Institute, Rio de Janeiro, Brazil.

<sup>13</sup>Virus Reference Department, National Infection Service, Public Health England, London, UK.

<sup>14</sup>Neurology Department, Alder Hey Children's NHS Foundation Trust, Liverpool, UK.

<sup>15</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

13

**PUBLIC ENGAGEMENT  
SESSION**

**Catching them  
young:  
Developing  
resources for  
HPRU public  
engagement  
activities in  
schools**

Dr Hannah Williams

Senior Mathematical  
Modeller

Public Health England

Invited HPRU Member

Public and patient engagement and involvement is an important aspect of HPRU work. This project facilitated collaboration across the Emerging and Zoonotic Infections, Modelling Methodology, and Emergency Preparedness and Response HPRUs to engage in highly effective PPE. We identified a need for science resources that cover topics outside the immediate scope of the national curriculum. Building on two workshops that we then delivered to a local primary school, we developed resources boxes based around infectious disease outbreaks (“Operation Outbreak”) and tick awareness (“Tricky Ticks”), to enable teachers and STEM ambassadors to deliver their own sessions.

The resources are intended to be stand-alone, off-the-shelf packs, enabling teachers to deliver engaging science activities for Key Stages 1 and 2. Designed in collaboration with school science teachers and Imperial College London, the packs contain curriculum-based activity plans along with supporting information and equipment. Additionally there are digital versions of the resources to widen their reach and flexibility. Through these resources, we hope to create a platform to promote STEM topics, inspire the younger generation, and encourage the dissemination of public health messages and research.

**Author and Affiliations:**

Emma Bennett<sup>1</sup> and Hannah Williams<sup>1,2</sup>

<sup>1</sup>Emergency Response Department, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

**PUBLIC ENGAGEMENT  
SESSION**

**The importance  
of public  
engagement in  
an epidemic such  
as Zika**

Raquel Medialdea  
Carrera

PhD Student

Clinical Surveillance theme

During 2015-16, Brazil experienced the largest outbreak of Zika virus ever reported. Infection with Zika virus during pregnancy has been linked to the occurrence of congenital birth defects such as microcephaly, hydrocephaly, or abnormalities in the brain. Brazil reported thousands of suspected and confirmed cases of microcephaly associated with Zika virus.

Due to the severity and the impact of this epidemic in Brazil our project, funded by the Wellcome Trust and the HPRU aimed to provide a better understanding of the science behind Zika virus among the people that had been the most affected: families with children suffering from Congenital Zika syndrome. We also aimed to increase awareness on when to seek diagnostic testing for Zika virus, the science behind the disease and public health information on how to improve the conditions for children and their families.

We organized workshops both in Rio de Janeiro and in Recife (North of Brazil) with families of children affected by Congenital Zika Syndrome reaching more than 200 families. The workshops offered a better understanding about Zika virus, diagnosis on Zika virus and the science behind the effect of Zika bringing together a range of specialists: physiotherapist, neurologists, researchers, virologists, immunologist, paediatrician, infection biologist, nutritionist, occupational therapist, public health specialist, psychologist and nurse.

The workshops had a very positive success rate with 100% positive feedback. The attendees reported having benefited and improved their understanding about Zika and the complications that affected their children (100%). Attendees reported that attending this science dissemination and public engagement workshops have had a very positive impact for their lives.

This public engagement work highlights the importance of researchers conducting public dissemination activities involving the general public and the patients affected by large epidemics such as Zika virus.

**Author and Affiliations:**

Raquel Medialdea-Carrera<sup>1,2</sup>, David W. Brown<sup>1,2,3</sup>, Tom Solomon<sup>1,2,4</sup> and Mike Griffiths<sup>1,2,5</sup>

<sup>1</sup>NIHR Health Research Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>3</sup>Influenza Reference Laboratory, Oswaldo Cruz Institute, Rio de Janeiro, Brazil.

<sup>4</sup>Walton Centre NHS Foundation Trust, Liverpool, UK.

<sup>5</sup>Neurology Department, Alder Hey Children's NHS Foundation Trust, Liverpool, UK.



# **POSTER ABSTRACTS**



1

**EBOLA SESSION**

**Transcriptomic  
and proteomic  
analysis of THP-1  
macrophages  
infected with the  
Ebolavirus,  
Makona variant  
compared with  
Reston virus**

Andrew Bosworth

PhD Student

Pathogen Discovery &  
Characterisation theme

The host response to the Ebola virus, Makona variant was compared with that induced by Reston virus using a differentiated THP-1 cell model. High resolution RNASeq was used to profile the transcriptomic changes during infection and this data was then combined with SILAC proteomic data to identify significantly changing host factors. Validation experiments were performed in THP-1, A549 and HEPG2 cell lines to confirm observed transcript and protein abundance changes. Analysis identified networks of host factors regulated by nuclear factor kappa-beta, tumour necrosis factor and toll-like receptor 4. Subnetworks of genes showing significant differences in Reston virus and Ebola virus infected cells were also identified, which were involved in the antiviral response. Upstream regulator activity was manipulated using inhibitory compounds and the effects on Ebola virus and Reston virus lifecycle assessed by mini-replicon.

**Author and Affiliations:**

Andrew Bosworth<sup>1</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

2

**EMERGING  
CHALLENGES  
SESSION**

**Focus on  
*Chlamydia  
psittaci*  
(psittacosis)**

Dr Vicki Chalker

Head of Respiratory &  
Vaccine Preventable  
Bacteria Reference Unit

Public Health England

Invited HPRU Member

Psittacosis, caused by *Chlamydia psittaci* can be severe in outcome. Human infection is associated with close contact with birds; via contaminated aerosol inhalation from urine/faeces. Infected patients can be bird handlers with occupationally or recreational exposure or sporadic cases associated with avian contact in the home or workplace. Infection presents in humans as a non-specific flu-like illness or community-acquired pneumonia (CAP). Psittacosis is not often considered in cases of CAP and specific tests are not frequently undertaken. Therefore the proportion of CAP cases caused by *C. psittaci* remains unclear. Recent meta-analysis indicates approximately 1% of CAP may be caused by *C. psittaci* (Hogerwerf et al., 2017). The RVPBRU PHE pPCR service from August 2012-October 2017 tested 36 specimens that were referred for *C. psittaci* qPCR. Specimens were from patients aged 8-80 years (mean 46 years), 21 (58%) were male. *C. psittaci* was detected by qPCR using the method by Pantchev et al., 2009 in 5/36 (14%) specimens. This PCR detects *C. psittaci /abortus* and cannot distinguish species. Limited clinical information was provided with the specimens. However, positive referred specimens included BAL (3), sputum (1) and throat swab (1) of which 4/5 were from male patients. One positive patient was a known pigeon handler, another had acute respiratory failure and was on ECMO. A further qPCR positive patient was associated with a serologically confirmed cluster of 5 cases *C. psittaci* with feral pigeon faeces exposure in office workers. This reflects a low number of positive cases overall, nonetheless 14% referred specimens had detectable *C. psittaci* DNA. It is likely that this infection is vastly under detected and is not always considered as a potential cause of respiratory tract infection.

Pantchev, A., Sting, R., Bauerfeind, R., Tyczka, J., Sachse, K. (2009) New real-time PCR tests for species-specific detection of *Chlamydophilapsittaci* and *Chlamydophilaabortus* from tissue samples. *Vet J*, 181: 145-150.

Hogerwerf L, DE Gier B, Baan B, VAN DER HOEK W (2017) *Chlamydia psittaci* (psittacosis) as a cause of community-acquired pneumonia: a systematic review and meta-analysis. *Epidemiol Infect.*

**Author and Affiliations:**

Derren Ready<sup>1,2</sup>, Jessica Townley<sup>1</sup>, Lalita Vaghji<sup>1</sup>, Sarah Philips<sup>1</sup>, Baharak Afshar<sup>1</sup>, Massimo Mentasti<sup>1</sup>, Colin Brown<sup>1</sup> and Vicki Chalker<sup>1,2,3,4</sup>

<sup>1</sup>Public Health England, Colindale, London, NW9 5EQ, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>NIHR Health Protection Research Unit in Respiratory Infections, London, UK.

<sup>4</sup>Respiratory Infections Section, National Heart and Lung Institute, Department of Medicine, Imperial College London, UK.

3

EMERGING  
CHALLENGES  
SESSION

Tick borne  
viruses in the UK  
and risk of tick  
borne  
encephalitis  
virus  
importation by  
migratory birds

Maya Holding

PhD Student

Vector Biology & Climate  
Modelling theme

Louping ill virus (LIV) is currently the only tick borne virus in the UK known to cause disease in vertebrates. Although very rare, LIV can cause encephalitis in humans and can be fatal. Prevalence and distribution of LIV in questing ticks in much of the UK is not known. Tick-borne encephalitis virus (TBEV) is highly pathogenic to humans, causing several thousand cases in Europe each year. TBEV is present across much of Europe and Asia; it is not thought to be present in the UK. During autumn millions of migratory birds arrive in the UK from Europe including TBEV endemic counties, many of which may carry ticks, which might therefore provide a route of entry of TBEV into the UK.

Aims were to investigate prevalence of LIV in the questing *I. ricinus* in southwest England and to screen for TBEV. Secondly to investigate the risk of autumn migratory birds importing TBEV infected ticks to the UK.

Forty two sites across southwest England were surveyed for questing ticks in 2016. Ticks were processed, pooled and screened by RT-PCR for LIV and TBEV. Birds were screened for ticks in the east and south of England autumn 2017. Ticks were removed and bird information recorded. The ticks will be identified, processed and screened for TBEV.

Of the 2434 screened UK questing ticks, no LIV or TBEV virus was detected, further work is needed to seek to further understand its ecology and develop a greater understanding of the distribution of LIV across the UK.

Surveying of migratory birds is on-going; thus far 154 ticks have been collected from 59 birds, from a total of 418 screened. Preliminary results will be presented, summarising the ecology of ticks on migratory birds, including the key bird species and species of ticks imported by the birds.

**Author and Affiliations:**

Maya Holding<sup>1,3</sup>, Roger Hewson<sup>1,3</sup>, Jolyon Medlock<sup>1,3</sup>, Stuart Dowall<sup>1</sup> and Matthew Baylis<sup>2,3</sup>

<sup>1</sup>Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>2</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>3</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

## 4

### EMERGING CHALLENGES SESSION

## Determining the Host Response to Enterovirus 71 Infection in Human Rhabdomyosarcoma Cells

George Lock

PhD Student

Clinical Surveillance theme

Enterovirus 71 (EV71) of the *Picornaviridae* family is the leading cause of hand, foot and mouth disease globally and coined as the next pathogen to supersede poliovirus after its eradication. Viral growth curves allow each stage of the virus life cycle to be determined and can allow changes in the host response to be monitored over time using a variety of assays.

In parallel RD cells were infected with either a circulating UK EV71 strain or with one of two Malaysian strains; samples were taken at every six hours for 24 hours. Supernatant was aspirated and saved for virus titration and the cells, lysed and the supernatant recovered for virus and cellular protein analysis via western blot. Immunofluorescence (IF) enabled visualization of intracellular virus replication the cell at each time point as well as changes in the production of key innate inflammatory markers.

At 3 hours post infection, no virus protein was visualized within the cells or noted in western blot. At 6 hours post infection, virus protein could be visualized in the cells via IF with minimal virus protein detected in western blot. Virus was first released at 6 hours post infection (p.i.) and any virus released at a later dated could be a result of progeny virus infecting neighbouring cells. Hours 18 to 24 p.i. show an exponential increase in the virus released from the cells. As infection progresses, the amounts of ISG15, a pro-inflammatory protein, remains largely unchanged between the infected and uninfected. However a key protein in transcription and activation of the innate immunity, STAT1, decreased during the later stages of infection. This reduction of STAT1 was greater in cells infected with the severe virus, indicating the virus' potential for reducing the immune response, aiding replication and potentially the production of more severe forms of infection.

#### Author and Affiliations:

George Lock<sup>1,2</sup>, Lisa Ng<sup>1,2,3</sup>, Julian Hiscox<sup>1,2</sup> and Tom Solomon<sup>1,2</sup>

<sup>1</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Singapore Immunology Network, A\* STAR, Singapore.

5

EMERGING  
CHALLENGES  
SESSION

The **epiC** study:  
Investigating  
household  
transmission of  
*Cryptosporidium*

Caoimhe McKerr

PhD Student

Epidemiological Approaches  
theme

This poster outlines the proposal for a collaborative study between Public Health Wales, Public Health England, and the Health Protection Research Units at the University of Liverpool.

**Rationale**

*Cryptosporidium* is a major contributor to human diarrhoeal illness worldwide and infection with this parasite causes over 4,000 cases of diagnosed illness in England and Wales every year. Outbreaks can be large but may only represent a small proportion of actual cases, and how much sporadic disease there is has not been sufficiently established.

Secondary infection may represent an underestimated and unreported amount of sporadic disease which could be prevented with tailored advice and public health messages.

There are no published household-level studies in England and Wales which ascertain likely risk factors or pathways to secondary spread.

**Objectives**

- To calculate secondary transmission rate within households
- To estimate the prevalence of asymptomatic carriage
- Identify risks for secondary transmission

**Approach**

This project will be a year-long observational study to identify secondary transmission in households exposed to a case of *Cryptosporidium*, and also to elicit information on risk factors and likely mechanisms for spread.

We will recruit 400 households across England and Wales where someone has had a positive diagnosis of *Cryptosporidium*, ask general questions about the household composition and behaviours, and retrieve stool samples from each household member for testing, speciation, and further molecular typing.

We anticipate that the addition of the specialist molecular typing will help to accurately describe the epidemiology of sporadic and secondary disease and identify specific risks for spread by species.

**Author and Affiliations:**

Caoimhe McKerr<sup>1,2,3</sup>, Rachel Chalmers<sup>4</sup>, Robert Christley<sup>1,5</sup>,  
Sarah O'Brien<sup>2,3</sup> and Roberto Vivancos<sup>1,2,6</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit In Gastrointestinal Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Institute of Infection and Global Health, The Farr Institute@HeRC, University of Liverpool, Waterhouse Building (2<sup>nd</sup> Floor, Block F), 1-5 Brownlow Street, Liverpool, UK.

<sup>4</sup>Cryptosporidium Reference Unit, Public Health Wales Microbiology ABM, Singleton Hospital, Swansea, UK.

<sup>5</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>6</sup>Health Protection Agency, Cheshire and Merseyside Health Protection Unit, Liverpool, UK.

## 6

### EMERGING CHALLENGES SESSION

# The use and reporting of airline passenger data for infectious disease modelling: a systematic review

Margaux Mesle

PhD Student

Epidemiological Approaches  
theme

Understanding the likely international spread of infectious diseases and the risks posed through air passenger movement are an important aspect of public health needs, especially for novel or emerging infectious diseases. Mathematical modelling studies attempting to address these issues currently employ a wide range of data sources to parameterise models of air passenger movement. Questions exist, however, as to the suitability and validity of data sources used for this purpose. We conducted a systematic literature search to identify the sources and efforts to assess the validity of airline passenger data used in modelling studies of infectious disease and international spread.

Articles matching our search and inclusion criteria were downloaded from three databases, selected based on our defined inclusion criteria. From each of the final selection of 68 articles, information detailing the type and source of airline passenger data used was extracted, and data validation and reproducibility assessed.

We found that commercial data, more specifically from International Air Transport Association (IATA) and Official Airline Guide (OAG) accounted for 60% of articles, followed by open source governmental data (15%). The data type most frequently used was that containing origin-destination pairs (45%), followed by passenger numbers (28%), and data validation was done in only three papers. Given our set of reproducibility guidelines, no article was fully reproducible, and only four were partially reproducible.

Based on our review, we make several recommendations to the field for modelling of airline passenger movement for infectious disease modelling purpose. More effort is needed to assess the validity and potential bias of data sources used, particularly when modelling efforts are informing national and international public health policies. We also recommend that the standard of reporting is improved to permit greater reproducibility of results. Finally, we highlight the need for an open access validated data source of airline passenger movement.

#### Author and Affiliations:

Margaux Mesle<sup>1,2</sup>, Ian Hall<sup>1,3</sup>, Robert Christley<sup>1,4</sup>, Steve Leach<sup>1,3</sup> and Jonathan Read<sup>1,4,5</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Institute of Infection and Global Health, The Farr Institute@HeRC, University of Liverpool, Waterhouse Building (2<sup>nd</sup> Floor, Block F), 1-5 Brownlow Street, Liverpool, UK.

<sup>3</sup>Emergency Response Department, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>4</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>5</sup>Centre for Health Informatics Computation and Statistics, Lancaster Medical School, Lancaster University, UK.

7

EMERGING  
CHALLENGES  
SESSION

**Bunyavirus  
VSVΔG  
Pseudoviruses  
for Detection of  
Neutralising  
Antibodies**

Dr Gillian S Slack

Research Scientist

Public Health England

Invited HPRU Member

**Background**

Crimean-Congo haemorrhagic fever (CCHF) is a severe tick-borne disease with case fatality rate of 5-40%. Principally vectored by *Hyalomma* ticks CCHF is endemic in parts of Africa, Asia and Southern and Eastern Europe, with ongoing outbreaks in Turkey, Kosovo, Greece, Iran, Tajikistan and Pakistan, including new introductions to India and recently Spain. The aetiological agent of CCHF, CCHF *orthonairovirus* (CCHFV), a member of the *Nairoviridae* family and *Bunyavirales* order, is a tripartite negative sense RNA enveloped virus, which due to the severity of disease, lack of treatment options and potential for human to human transmission is classified by ACDP as a Hazard Group 4 agent. Research into anti-CCHFV therapeutics and vaccines is consequently heavily restricted due to the requirement for work to be carried out in containment level (CL) 4 laboratories. The development and implementation of non-infectious minigenome and pseudovirus assays is therefore vital, as they enable the efficacy of potential antivirals and vaccine candidates to be assessed at low containment, expediting research into this pathogen. Here we present data on the optimisation of VSVΔG pseudovirus assays for the detection of CCHFV neutralising antibodies in clinical samples.

**Methods**

The VSVΔG pseudovirus system was optimised and used to produce *Rift Valley fever phlebovirus*, *SFTS phlebovirus* and CCHFV pseudoviruses. VSVΔG(GFP)CCHFV and VSVΔG(luc) CCHFV pseudoviruses were then used to test convalescent sera for neutralising antibodies. Results were validated by comparison to FRNT assays (focus reduction neutralisation titres) that were carried out at CL 4 using wild type CCHFV.

**Results**

Luciferase pseudoviruses had a larger dynamic range than their GFP counterpart, and gave comparable results to FRNT assays with wtCCHFV.

**Conclusions**

The VSVΔG pseudovirus system is highly versatile allowing the rapid preparation and quantification of a panel of pseudoviruses at CL 2, which can then be used to detect neutralising antibodies in patient sera.

**Author and Affiliations:**

Gillian S Slack<sup>1,2</sup>, John Chamberlain<sup>1</sup>, Anitha Varghese<sup>1</sup>, Robert Watson<sup>1</sup>, Stuart Dowall<sup>1</sup>, Yuto Suda<sup>3</sup>, Masayuki Shimojima<sup>3</sup> and Roger Hewson<sup>1,2</sup>

<sup>1</sup>National Infection Service, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>National Institute of Infectious Diseases, Tokyo, Japan.

## 8

### EMERGING CHALLENGES SESSION

# Using Big Data to improve animal disease surveillance: investigating the Enhanced Infectious Diseases (EID2) database and WAHIS

Dr Maya Wardeh

Postdoctoral Researcher

Risk Assessment of  
Emerging and Zoonotic  
Threats theme

Few studies have examined global animal disease distributions. We investigate whether combining repositories of animal diseases can improve occurrence understanding. The OIE's WAHIS describes global distributions of confirmed reports of infectious animal diseases. The Enhanced Infectious Disease database (EID2) mines metadata records accompanying genetic sequences and scientific publications to explain where, when and in which hosts pathogens occur.

Reports describing the global incidence of Foot and Mouth Disease (FMD), Leishmaniosis, Newcastle Disease (ND), and West Nile (WN) were obtained from WAHIS. The data was subsequently cleaned and matched to EID2 spatial layer. Evidence of the geographical distribution of the selected diseases was extracted from EID2. Quantitative comparisons of the two sources were made of pathogen presence/assumed absence (using Cohen's kappa coefficient, and diagnostic potential of sources).

The reported presence of FMD was similar at country/sub-country-level in WAHIS, compared to higher and much lower in EID2, respectively. Reporting rates were similar to FMD at country-level for Leishmaniosis, and low for both resources at sub-country-level. Country-level ND reporting was higher in WAHIS compared to EID2, and comparative to FMD at sub-country-level for both, respectively. Finally, WN at country-level was least reported in both, and reporting was low at sub-country-level.

In all cases except WN, agreement between sub-country-level presence was lower than country-level. WAHIS only captured 24-60% of EID2 country-level presence, and 10-32% for sub-country-level except FMD (75%); EID2 captured higher-levels of WAHIS country-level presence except WN, but was less good at sub-country-level (except Leishmaniosis). Neither resource was obviously better at capturing absence.

These results suggest some agreement in the presence of disease identified using both sources but that neither resource overlaps well. This indicates there is merit in combining both data sources for global mapping of infection diseases. This work is a scoping tool to help investment in disease surveillance and control.

#### Author and Affiliations:

Maya Wardeh<sup>1,2</sup>, Marie McIntyre<sup>1</sup> and Matthew Baylis<sup>1,2</sup>

<sup>1</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, UK.

9

LYME SESSION

**Prevalence of  
*Borrelia*  
Infections in the  
United Kingdom  
and the  
Development of  
an Enhanced  
Testing Regime**

Daniel Carter

PhD Student

Public Health England

Invited HPRU Member

The Rare and Imported Pathogens Laboratory (RIPL) at Public Health England (PHE), Porton Down provides a reference service for the laboratory diagnosis of *Borrelia* infections in the United Kingdom. The assays in use at RIPL currently focus on the diagnosis of Lyme Borreliosis with limited capability of diagnosing infections with the Relapsing Fever clade of *Borrelia*. The specificity of the assays in use to be able to detect infection with UK circulating strains of *Borrelia* has also not been ascertained.

One area of interest is to determine the prevalence of Relapsing Fever in locally acquired infections as well as infections in returning travellers. Recombinant Glycerophosphodiester Phosphodiesterase (GlpQ) protein specific to the Relapsing Fever clade of *Borrelia* will be used to develop an ELISA assay which has been previously demonstrated by TG Schwan et al. (1996). A panel of samples from the RIPL sample archive will then be tested using the GlpQ ELISA to determine seroprevalence in UK endemic cases and cases in returning travellers. After initial identification of antibodies, further work will look at other variable membrane proteins to determine immunodominance and their potential benefit for early/late diagnosis of Relapsing Fever.

Another area of interest is the suitability of antigens used in commercially available assays to detect antibodies raised during infection with UK *Borrelia* genospecies. This will be done using a proteomic and genomic approach in order to analyse commercially available antigens and compare the protein sequences with that of local *Borrelia* to determine differences in immunoreactivity. A strain collection of different *Borrelia* genospecies will also be created with input from collaborators within PHE and the NHS in order to provide valuable sequence data for these projects as well as any future research.

**Author and Affiliations:**

Daniel Carter<sup>1,2</sup>, Jackie Duggan<sup>1,2</sup>, Daniel Bailey<sup>1</sup>, Steven Pullan<sup>1</sup>, Sally Mavin<sup>3</sup>, Roger Evans<sup>3</sup>, Julian Hiscox<sup>2,4</sup>, Nicholas Evans<sup>4</sup>, Richard Vipond<sup>1,2</sup>, Matthew Dryden<sup>1</sup> and Tim Brooks<sup>1,2</sup>

<sup>1</sup>Public Health England, PHE Porton, Porton Down, Salisbury, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Raigmore Hospital, Inverness, UK.

<sup>4</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

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LYME SESSION

**Lyme and other tick borne diseases – present and future research in the UK**

Dr Jenny Warner

Postdoctoral Researcher

Clinical Surveillance theme

Lyme disease is the subject of increasing political scrutiny and patient advocacy. At present, advances in Lyme disease research are not keeping pace with demand for an evidence base for the diagnosis, management and prevention of Lyme and other zoonotic tick-borne diseases (TBDs) in the UK.

A one-day workshop was held in Edinburgh, Scotland on June 1<sup>st</sup> 2017, funded by a Strategic Research Fund grant from the NIHR Health Protection Research Unit in Emerging and Zoonotic Infections (HPRU EZI). This workshop brought together UK research groups representing interest areas from tick ecology, through diagnostics to disease epidemiology. The primary objective of the workshop was to review current research across the UK, identifying areas of synergy between different groups and also key research gaps not currently being addressed. The workshop also served to create a networking opportunity for researchers with a common interest who may be seeking collaborators. Information was shared about current capabilities and research goals and a number of key research gaps were identified in each topic area. The event provided a valuable networking opportunity and seeded new collaborations which will be essential to address some of the emerging research priorities around Lyme and TBDs in the UK.

Although tick ecology, diagnostics and epidemiology were all well represented amongst the workshop participants, there were only three clinicians present who actively manage Lyme disease patients. Consequently, there was limited opportunity to form the partner networks necessary to conduct the types of multi-centre clinical studies needed to address key research gaps around treatment strategies. Further clinical partners would be needed from both primary and secondary care in order to move many of the priority clinical research areas forward. In the next stages, patient and public involvement will be beneficial; any future meetings should wherever possible have patient and public representation.

**Author and Affiliations:**

Jenny Warner<sup>1,2</sup>, Amanda Semper<sup>1,2</sup>, John Tulloch<sup>1</sup> and Tim Brooks<sup>1,2</sup>

<sup>1</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Rare and Imported Pathogens Laboratory, Public Health England, PHE Porton, Porton Down, Salisbury, UK.

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ZIKA SESSION

## Potential for Zika virus transmission by mosquitoes in temperate climates

Dr Marcus Blagrove

Postdoctoral Researcher

Vector Biology & Climate Modelling theme

Mosquito-borne Zika virus (ZIKV) transmission has only been detected in the tropics despite the distributions of its primary vectors extending farther into temperate regions. It is unknown whether ZIKV's range has reached a temperature-dependant limit, or if it can spread into temperate climates. Using wild mosquitoes for field applicability, we assessed the vector competence of four common temperate mosquito species, two of which, *Aedes albopictus* and *Ochlerotatus detritus*, were found to be competent for ZIKV. We orally exposed mosquitoes to ZIKV and held them at a wide range of incubation temperatures, estimated the time required for mosquitoes to become infectious at each temperature, estimated the degree-day requirement for ZIKV in each species, and applied these data to a ZIKV spatial risk model. We identified a minimum temperature threshold for the transmission of ZIKV by mosquitoes between 17 and 19°C. Using these data, we generated degree-day based risk maps that show significant risk of ZIKV transmission beyond the current observed range in southern USA, SE China and southern European countries. The model was also applied to projected scenarios of future conditions of climate and human population. Using these scenarios, we predict that the population at risk increases by factors of 1.5 and 6.91 in the USA and Europe by 2080.

### Author and Affiliations:

Marcus S C Blagrove<sup>1,2</sup>, Cyril Caminade<sup>1,2</sup>, Ken Sherlock<sup>1</sup>, Gail E Chapman<sup>1</sup>, Jenny Hesson<sup>1,3</sup>, Soeren Metelmann<sup>1,2</sup>, Philip J McCall<sup>4</sup>, Gareth Lycett<sup>4</sup>, Peter J Diggle<sup>5</sup>, Alessandra della Torre<sup>6</sup> and Matthew Baylis<sup>1,2</sup>

<sup>1</sup>Department of Epidemiology and Population Health, Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Department of Medical Biochemistry and Microbiology, Zoonosis Science Center, Uppsala University, Sweden.

<sup>4</sup>Vector Biology Department, Liverpool School of Tropical Medicine, Liverpool, UK.

<sup>5</sup>Lancaster Medical School, University of Lancaster, Lancaster, UK.

<sup>6</sup>Department of Public Health and Infectious Diseases, Sapienza University of Rome, Laboratory affiliated to Istituto Pasteur Italia – Fondazione Cenci Bolognetti, Rome, Italy.

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ZIKA SESSION

## Climate change impact on vector-borne diseases: an update from the trenches

Dr Cyril Caminade

Tenure Track Fellow

Vector Biology & Climate Modelling theme

Zika, dengue, chikungunya, malaria, yellow fever, Lyme disease, bluetongue, Shmallenberg are vector-borne diseases (VBD) with huge impacts on societies and they are now often mentioned in the news. These diseases are transmitted by exothermic arthropod vectors such as mosquitoes, midges and ticks which are extremely sensitive to external environmental conditions. Rainfall is an important factor as it provides breeding sites for larvae. Temperature impacts a broad range of factors such as vector development, its survival, vector biting rates and the time required for the pathogen to develop inside the arthropod vector. Consequently, anthropogenic climate change is expected to greatly impact the distribution and severity of these vector-borne diseases. This presentation will provide an overview of recent modelling studies carried out in Liverpool about the impact of future climate change on animal and human vector-borne diseases.

We will discuss scientific findings published over the past 5 years, and critically compare them to recently observed trends in VBD burden. The increase in malaria burden simulated over the Tropical highland regions by dynamical disease models is consistent with recent increase in malaria incidence over mountainous regions of Colombia, Ethiopia and North Kivu in DRC. Dynamical models driven by climate parameters solely were also able to anticipate the spread of *Ae. albopictus* (vector of Zika, dengue and chikungunya) in Europe and the USA. Last but not least, climatic conditions were also optimal for mosquito borne transmission of Zika virus in 2015 over South America when the largest outbreak occurred. Similar results were found for the bluetongue (animal disease) outbreak that occurred over northern Europe in 2006.

### Author and Affiliations:

C. Caminade<sup>1,2</sup>, A.E. Jones<sup>1</sup>, J. Turner<sup>1</sup>, S. Metelmann<sup>2,3</sup>, M. Blagrove<sup>1,2</sup>, A.P. Morse<sup>2,3</sup> and M. Baylis<sup>1,2</sup>

<sup>1</sup>Department of Epidemiology and Population Health, Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>2</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>3</sup>Department of Geography and Planning, School of Environmental Sciences, University of Liverpool, Liverpool, UK.

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ZIKA SESSION

**Neuro-  
developmental  
outcomes  
measured in  
congenital  
infections  
including Zika –  
what are we  
measuring?**

Dr Melissa Gladstone

Senior Lecturer  
Neurodevelopmental  
Paediatrics

University of Liverpool

Invited HPRU Member

**Background**

There has been emerging interest in outcomes of children affected by congenital infections since the outbreak of Zika. This has affected many children in LMIC settings where few tools are adapted and standardised to assess children appropriately.

**Methods**

We conducted a systematic review of the literature to identify what outcome measures have been used in children affected by congenital infections (including Zika). We searched Pubmed, Scopus, Google Scholar and Cochrane from 1960 to 2017 to identify studies where outcomes were measured secondary to in-utero viral infections or microcephaly at birth. We collated studies to evaluate coverage of outcomes against the framework of the International Classification of Functioning and Disability (ICF).

**Results**

167 studies were identified with information relating to outcomes measured in children exposed to viral infections in utero from the preterm period to 19 years of age. 65/167 studies concentrated on microcephaly with 47.7% defining microcephaly as OFC  $\leq 2SD$ , 27.7% defining microcephaly as OFC  $< 3SD$ , some (6%) using both definitions and some not providing a definition. Only 24.6% of studies measured other factors. 11/167 studies measured eye structure (microphthalmia, retinopathy, maculopathy) with some measuring visual functioning (6%) (10/167), hearing (15%) (26/167), epilepsy (24/167) 14.4% with a few measuring Precht's motor movements, Gross Motor Function and sleep patterns). The few that focused on cognitive functioning mainly used Bayley Scales of Infant Development (BSID) (13/167) 7.7% for preterm-2 years or Wechsler Intelligence Scale for Children (WISC)(17/167) 10% in 6-17 year olds. No studies looked at any aspects of family functioning, mental health or child participation.

**Conclusions**

The study demonstrated lack of cohesiveness and consistency in measurement of outcomes. Studies focus more on health structure and functioning rather than the other relevant social, psychological and participatory parts of the ICF which may actually be more relevant for families and children.

**Author and Affiliations:**

P Rai<sup>1</sup>, A Patel<sup>2</sup>, K Milner<sup>3</sup> and M Gladstone<sup>1,4</sup>

<sup>1</sup>Department of Women and Children's Health, Institute of Translational Medicine, University of Liverpool, Liverpool, UK.

<sup>2</sup>Department of Paediatric Neurology, Boston Children's Hospital, Boston.

<sup>3</sup>MARCH centre, London School of Hygiene and Tropical Medicine, UK.

<sup>4</sup>NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, UK.

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ZIKA SESSION

## Evaluation and comparison of 8 different methods for serologic diagnosis of Zika Virus in Brazil

Raquel Medialdea  
Carrera

PhD Student

Clinical Surveillance theme

The increase in congenital defects and other neurological diseases associated with ZIKV infection in Latin America has made evident the need for highly accurate laboratory testing to detect Zika virus infection. The WHO recommends that diagnosis of ZIKV seven days after symptoms onset should be performed with serologic assays. Serologic assays are based on detection of specific antibodies in bodily fluids such as serum. However, the performance and accuracy of this assays in an extensively flavivirus exposed population such as Brazil, has not been investigated yet.

We performed the evaluation of 8 different serologic assays for Zika IgM and IgG detection: IgM and IgG Euroimmun ELISA, ZIKV PRNTs, IGM CDC Euroimmun, Green-BOB Assay, IgM Novagnost, IgM and the IgG Biomanguinhosrapid test. In addition, IgM and IgG Panbio Dengue ELISAs were also investigated.

Samples were referred for routine diagnostics to the reference Flavivirus laboratory at the Institute Oswaldo Cruz, Rio de Janeiro. Sensitivity was measured using sequential serum samples collected in 2015-2016 from 67 ZIKV PCR positive cases (n=159). Specificity was assessed using sera from subjects with confirmed (PCR and IgM positive) exposure to Dengue (serotypes 1-4 [n=89]), yellow fever infection (n=10) or vaccination (n=9); collected in or before 2013 to exclude ZIKV exposure. ZIKV is estimated to have arrived in Rio in January 2015.<sup>5</sup>

Our findings demonstrate that among the ZIKV IGM methods, the IGM Novagnost has a better overall accuracy compared to the IGM Euroimmun and IGM CDC MAC ELISA.

Among the assays that detect IGG anti-ZIKV, the GreenBOB assay had the most accurate performance compared with the IGG Euroimmun and IgG Biomanguinhos. We also demonstrated a large proportion of false positive results in the Dengue assays.

Our findings demonstrate the importance of diagnostic test validation using samples appropriate to the local population and highlight the need for more accurate diagnostics, especially for ZIKV patients presenting after acute infection.

### Author and Affiliations:

Raquel Medialdea-Carrera<sup>1,2</sup>, Patricia Sequeira de Carvalho<sup>3</sup>, Ana Bispo de Filippis<sup>3</sup>, David Brown<sup>1,4,5</sup>, Tom Solomon<sup>1,2,6</sup> and Mike Griffiths<sup>1,2,7</sup>

<sup>1</sup>NIHR Health Research Health Protection Research Unit in Emerging and Zoonotic Infections, University of Liverpool, Liverpool, UK.

<sup>2</sup>Institute of Infection and Global Health, University of Liverpool, Liverpool, UK.

<sup>3</sup>Flavivirus Reference Laboratory, Oswaldo Cruz Institute, Rio de Janeiro, Brazil.

<sup>4</sup>Influenza Reference Laboratory, Oswaldo Cruz Institute, Rio de Janeiro, Brazil.

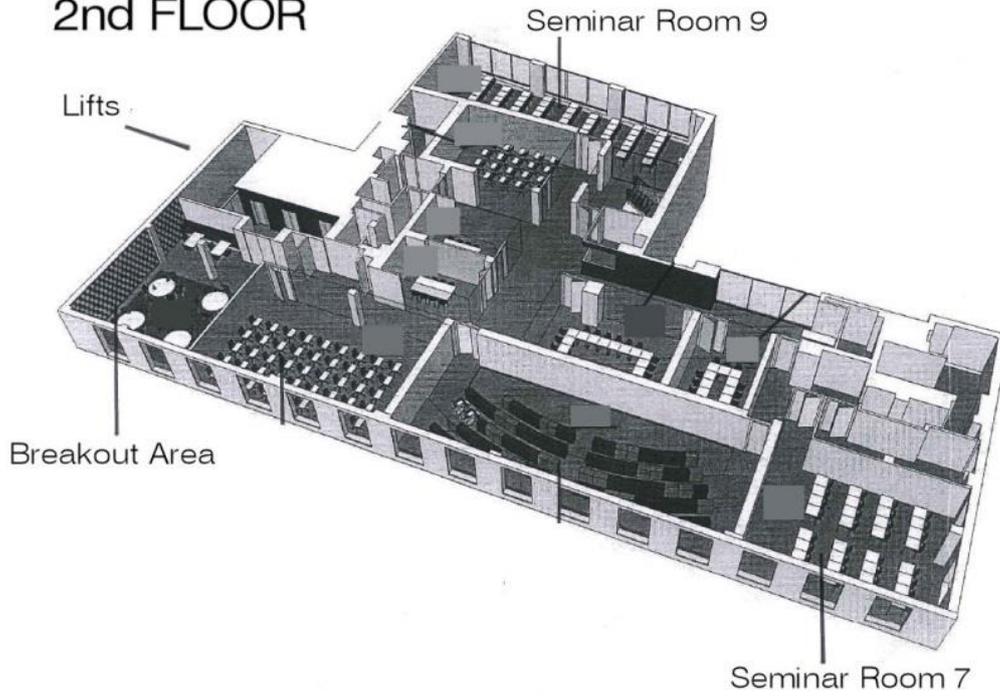
<sup>5</sup>Virus Reference Department, National Infection Service, Public Health England, London, UK.

<sup>6</sup>Walton Centre NHS Foundation Trust, Liverpool, UK.

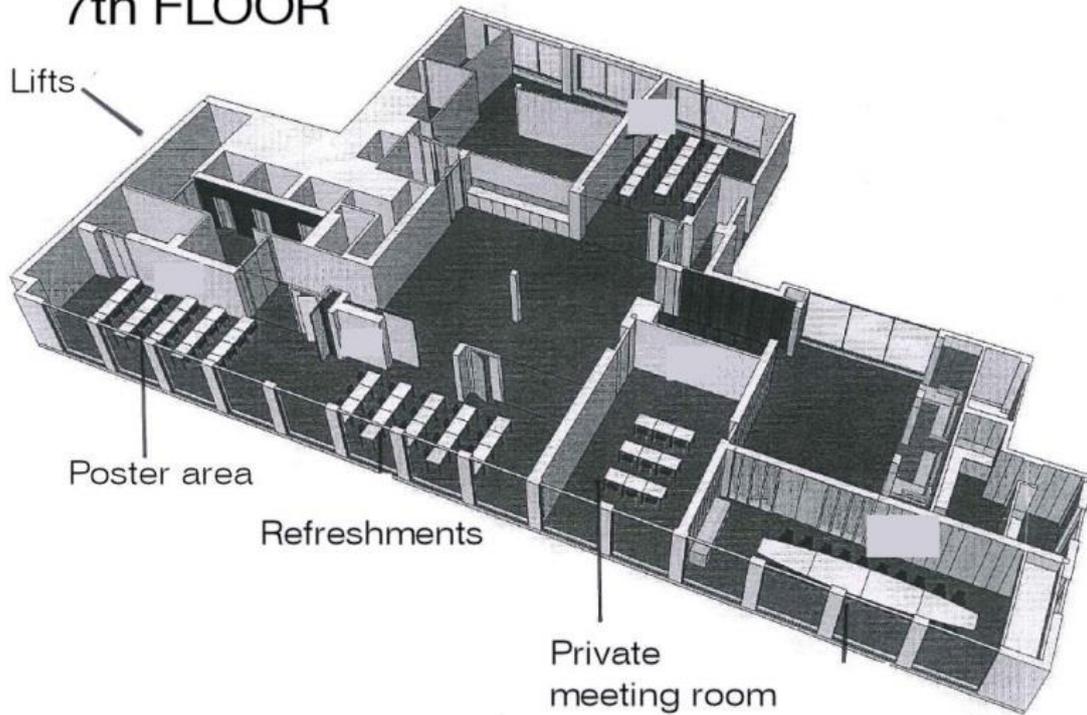
<sup>7</sup>Neurology Department, Alder Hey Children's NHS Foundation Trust, Liverpool, UK.

# FLOOR PLAN

## 2nd FLOOR



## 7th FLOOR



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# NOTES

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**HEALTH PROTECTION RESEARCH UNIT  
IN EMERGING AND ZONOTIC INFECTIONS**

**Website:** <http://hpruezi.nihr.ac.uk>

**Email:** [hpruei@liverpool.ac.uk](mailto:hpruei@liverpool.ac.uk)

**Follow us on Twitter:** [@hpruezi](https://twitter.com/hpruezi)