The Broad Street Pump

The Landscape Epidemiology of Ross River Virus Disease Outbreaks in Australia

By Michael Walsh[1] and Cameron Webb[1,2]

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Ross River virus (RRV) is Australia's most significant vector-borne and zoonotic pathogen, with approximately 5100 reported cases annually[1]. Transmission of this alphavirus involves multiple mosquito vectors, which exhibit diverse vertebrate host preferences in both dryland and wetland ecosystems[3]. This heterogeneity modulates the dynamics of enzootic, epizootic and zoonotic RRV transmission, imparting a unique infection ecology to each. Furthermore, reservoir and amplification hosts among Australian wildlife and other non-native mammalian hosts have been shown to influence the landscape epidemiology of RRV, particularly with respect to human spillover[4]. While macropods are typically identified as the main reservoir hosts [3] the contribution of specific mammalian hosts to RRV epidemiology remains ill-defined despite several decades of human surveillance and wildlife sampling across Australia[1]. Perhaps most importantly, the impact of anthropogenic alteration of the biotic (e.g. vectors and hosts) and abiotic (e.g. hydrology and land cover) environmental features relevant to RRV infection ecology may be instrumental in generating high risk landscapes[5], and ultimately driving human outbreaks[6]. Understanding the complexities associated with transmission cycles of RRV in the ever changing Australian environment, especially at the margins of evolving metropolitan regions, is critical to managing the risks of future outbreaks.

We summarize here recent work[7] examining the landscape epidemiology of RRV in anthropogenic space with a particular focus on the influence of the ecological niches of mammalian hosts and hydrological features on human outbreaks (https://doi.org/10.1186/s13071-018-2776-x).

Dr Michael Walsh

Dr Cameron Webb

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Methods

Reports of epidemic RRV in humans across Australia from 1 January, 1996 to 1 July, 2016 were obtained from the International Society of Infectious Diseases' ProMED-mail electronic surveillance system (promedmail.org). While the coverage of epidemics by this system is generally good in Australia[8], they ultimately represent a sample of large events occurring in landscapes of significant human influence. As a consequence the scope of this study does not apply to the full spectrum of human RRV experience (e.g. sporadic cases in remote locations). However, we did correct for this potential reporting bias by weighting the sampling of background points by the human footprint[9] in the landscape as a proxy for accessibility and reporting capacity[10].

The distributions of vertebrate hosts of RRV were modelled based on observations recovered from the Global Biodiversity Information Facility (GBIF) (http://www.gbif.org/). Host niche models comprised *Macropus giganteus* (n = 31,293), *M. fuliginosis* (n = 8844), *M. rufus* (n = 15,940), *M. robustus* (n = 17,998), *M. agilis* (n = 1840), *M. rufogriseus* (n = 27,568), *M. parryi* (n = 264), *Wallabia bicolor* (n = 347,082), *Trichosurus vulpecula* (n = 1754), *Isoodon obesulus* (n = 4563), *Perameles nasuta* (n = 82), *Pteropus poliocephalus* (n = 2421), *Pteropus alecto* (n = 1144), *Hydromys chrysogaster* (n = 840), *Rattus sordidus* (n = 75), and *Pseudomys novaehollandiae* (n = 993), which have been identified as RRV hosts either by serology or viral isolation[11–19]. Observations were limited to the same period as the occurrence of RRV epidemics (1996 – 2016) to maintain continuity between host niches and RRV epidemics.

Abiotic features comprised warm and cold quarter mean temperatures obtained from Worldclim[20], the Priestley-Taylor alpha coefficient (P-Tα) as a robust indicator of water-soil balance (this is the ratio of actual evapotranspiration to potential evapotranspiration and represents water stress in each 1 km^2 by capturing both water availability in the soil and water requirements of the local vegetation)[21], vegetation cover represented by the MODIS-based Maximum Green Vegetation Fraction (MGVF)[22], surface water classifications obtained from the Global Lakes and Wetlands Database[23], hydrological flow accumulation obtained from Hydrological Data and Maps based on SHuttle Elevation Derivatives at multiple Scales (HydroSHEDS) information system[24], the position of all controlled water reservoirs and dams in Australia from the Global Reservoir and Dam Database[25, 26].

The Maxent machine learning algorithm, which estimates the density of predictor variables conditional on observed occurrences[27, 28], was used to model both the host niches and the RRV epidemic landscape suitability. Maxent has become a popular approach to modeling the ecological niches of many zoonotic infectious diseases[29–31], and has been shown to perform better than other machine learning algorithms[31, 32]. Ten thousand background points were sampled proportional to HFP to corrected for sampling bias, as described above. Unique background point datasets were sampled for each host species and human outbreak occurrence datasets. All Maxent models (for reservoirs and RRV epidemics) were cross-validated using 5-fold cross-validation with the cross-validation mean area under the curve (AUC) reported as a percentage. Landscape features used in the Maxent models were ranked according to their permutation importance, which randomly permutes the values of the landscape factors between background and presence points.
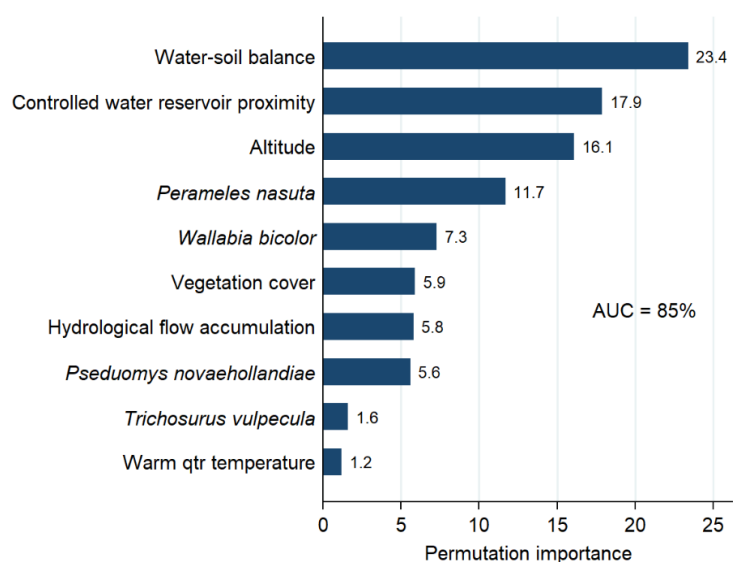

Figure 1. Relative influence of each feature to epidemic RRV landscape suitability as derived from their permutation importance in the Maxent model. Landscape features are ranked from most influential to least with the permutation importance listed at the top of each bar. The area under the curve (AUC) reported as a percentage is also presented to indicate model performance https://doi.org/10.1186/s13071-018-2776-x *[7]*

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Results and Discussion

The ten most influential environmental features and their associated rank RRV landscape suitability model are presented in Figure 1. Together these features explained 96% of the variation in the data, while the remaining 15 features accounted for only 4% combined. Water-soil balance (permutation importance (PI) = 23.4%) and proximity to controlled water reservoirs (PI = 17.9%) ranking first and second, respectively, while flow accumulation (PI = 5.8%) ranking seventh, demonstrated the importance of hydrological features to landscape suitability. The ecological niches of four wildlife hosts (long-nosed bandicoots (*Perameles nasuta*), swamp wallabies (Wallabia bicolor), New Holland mice (*Pseudomys novaehollandiae*), and common brushtail possums (*Trichosurus vulpecula*)), proved influential to RRV landscape suitability with an overall contribution to the loss function of 26.2%. Altitude (PI = 16.1%) and vegetation cover (PI = 5.9%) also demonstrated significant influence on RRV habitat suitability.

The response curves presented in Figure 2 showed that closer proximity to controlled water reservoirs was associated with greater RRV landscape suitability. Increasing soil-water balance (i.e. diminishing water stress) was strongly associated with increasing risk, but only along the spectrum from the most arid soil-water balance conditions up to a point halfway to the least arid soil-water balance conditions (P-T α ≈ 50%), after which risk did not markedly change. Each wildlife host niche was associated with at least a doubling of RRV risk even at modest predicted niche probabilities. The AUC for the RRV landscape suitability model was 85%, suggesting good prediction against testing data.

The current investigation modelled landscape suitability of RRV epidemics in anthropogenic environments across the Australian continent between 1996 and 2016. This is the first investigation of the relationship between RRV epidemics and hydrological dynamics and structure, as well as the most thorough interrogation of the relevance of wild mammalian hosts on human epidemic risk. Moderate soil-water balance, proximity to controlled water reservoirs, altitude, and the ecological niches of *P. nasuta* and *W. bicolor* were the primary delineators of high-risk landscapes.

In conclusion, features mediating the movement of water through the landscape and the ecological niche of wildlife hosts appear to promote landscapes suitable to RRV epidemics in anthropogenically impacted environments. These findings highlight environmental features that may help direct geographically targeted vector and wildlife surveillance in concert with human syndromic surveillance. Careful monitoring of key wildlife populations and protection of their habitat in peri-urban spaces may be warranted and, as such, presents unique opportunities for One Health prevention initiatives to be integrated with urban planning and environmental conservation strategies.
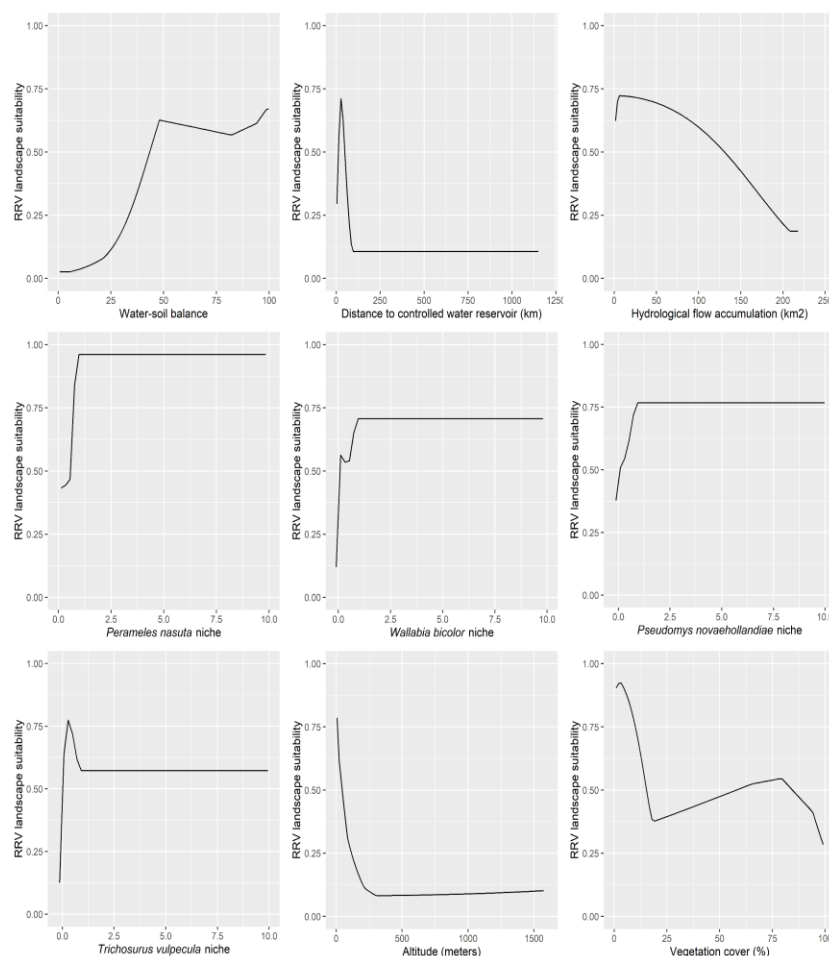

Figure 2. Variable response curves for the hydrological features, the ecological niches of wildlife hosts, altitude and vegetation cover (https://doi.org/10.1186/s13071-018-2776-x)[7].

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Staff Profile

DR JUSTIN BEARDSLEY

Justin is an infectious disease specialist, fellow of the Royal Australasian College of Physicians, and clinical researcher. He completed his PhD at the Oxford University Clinical Research Unit in Ho Chi Minh City. His research in Vietnam was focussed on fungal infections where he conducted a multi-national randomised clinical trial into adjunctive steroid therapy for Cryptococcal Meningitis in South East Asia and Africa (Beardlsey *et al*, NEJM 2016). He was also interested in the epidemiology of fungal infections, immune responses in Cryptococcal Meningitis, pharmacokinetics of anti-fungal drugs in the central nervous system, and temporal trends in cryptococcal drug susceptibility. He was involved in several other clinical trials in Cryptococcal Meningitis and hepatitis C, and is a co-author on the Lancet Global Burden of Disease series in his capacity as GBD specialist on Vietnam and HIV.

During specialist training, Justin worked in rural Zambia, and developed a long-term interest in global health. He believes medical research can be harnessed to reduce global inequalities. With this in mind, he recently joined the Marie Bashir Institute at the University of Sydney to join their mission of reducing the impact of emerging and re-emerging infectious diseases in the Asia-Pacific region. His research focus remains in South East Asia, where he is currently investigating aspergillosis, technological supports for compliance with long-term anti-infective treatment (eg. in fungal infections or tuberculosis), and community level approaches to containing the emergence of anti-microbial resistance.

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DFAT Fellowship Program India Visit

BY MICHAEL WALSH

A delegation of University of Sydney faculty has recently returned from an extended visit to South India as part of the Department of Foreign Affairs and Trade's Australia Awards Fellowship program, funding which was successfully obtained by Dr. Shailendra Sawleshwarkar and Prof Vitali Sintchenko. This trip comprised site visits to Manipal Academy of Higher Education, Manipal, Karnataka and the National Institute for Research in Tuberculosis, an Indian Council for Medical Research Institute based in Chennai, Tamil Nadu, to facilitate Fellows' training in molecular methods to augment India's existing Drug resistant TB and HIV research and disease control programs. Under the leadership of Prof Vitali Sintchenko, and supervision of Dr. Ranjeeta Menon and Dr. Nathan Bachmann, fellows learned how to apply modern genomic methods, including whole genome sequencing and bioinformatics, to investigate infection transmission networks within communities. Prof Ben Marais conducted a seminar on childhood tuberculosis and Dr Sawleshwarkar discussed opportunities for HIV drug resistance studies. In addition to training and capacity building, the visit also assessed inter-faculty research interests and current capacities to develop specific plans for ongoing collaborative educational and research projects. Following from this conference, Dr. Michael Walsh is currently developing a zoonoses surveillance project with colleagues at Manipal Academy of Higher Education and the Karnataka State Veterinary Health Services focusing on One Health research capacity and, in further collaboration with Dr. Sawleshwarkar to focus on global health academic networks. Drs. Walsh and Sawleshwarkar will return to Manipal in November, 2018 to initiate the next stage of the project's development.

University of Sydney delegation providing training to fellows at National Institute for Research in Tuberculosis, an Indian Council for Medical Research Institute based in Chennai

DFAT Fellowship Program India Visit

Building Tuberculosis Research Capacity in India

BY NATHAN BACHMANN

Dr Nathan Bachmann has recently spent five months in India and has started several projects with the goals of improving laboratory diagnostics of tuberculosis and our understanding of recurring infections. Nathan has focused on the development of a culture independent genome sequencing method to directly sequencing *M. tuberculosis* strains from respiratory samples. He worked in Professor Kiran Chawla's laboratory at the Manipal Academy for Higher Education in Karnataka. He also worked with Dr Uma Devi and Dr Siva Kumar from the National Institute for Research in Tuberculosis in Chennai. He was able to adapt a genome sequencing protocol with DNA extraction methods that are commonly used in Indian laboratories, which will aid introducing directly sample sequencing as part of routine diagnostics.

Apart from the above projects and with funding from the Department of Foreign Affairs and Trade, Dr Bachmann was a member of the organising committee for two international workshops on "Genomics of Tuberculosis" held at Manipal Academy for Higher Education (MAHE) and at the National Institute for Research in Tuberculosis (NIRT) in May 2018. These symposiums were jointly organized by MAHE, NIRT and the University of Sydney with Central TB Division, New Delhi. These meetings brought together scientists, clinicians and public health specialists with expertise in microbiology, public health and clinical aspects of TB and HIV drug resistance. Dr Bachmann's visit to India was supported by the Australia-India Early and Mid-Career Fellowship from the Australia Academy of Science.

Bioinformatics training in pathogen genomics in India

BY RANJEETA MENON

Dr Ranjeeta Menon has been instrumental in organising and providing training in genome sequence analysis for laboratory scientists from Manipal Academy for Higher Education (MAHE), the National Institute for Research in Tuberculosis (NIRT) and other national mycobacterium reference laboratories in India. The training and seminars were conducted at the MAHE and WHO Collaborating Centre for Tuberculosis Research and Training hosted by the NIRT. The seminar started with a welcome note by Dr Soumya Swaminathan, Deputy Director General, WHO. The program focused on whole genome sequencing, metagenomics and advanced bioinformatics of large-scale data generation and analysis using high performance computing. Partners from India were keen to implement best practice models for genomics in tuberculosis control as the Government of India has made a commitment to eradicate tuberculosis from India by 2025, which is five years ahead of a globally-set deadline.

This capacity building has been well received by collaborators in India, and will assist in filling an important existing gap in microbial genomics and bioinformatics. The scientists from India along with the team from Sydney will continue to work together with a plan over the next year to advance the agenda of eliminating TB globally and in Asia Pacific. The team from Australia was funded by DFAT Australia Fellowship and included Professor Vitali Sintchenko, Professor Ben Marais, Dr Ranjeeta Menon, Dr Shailendra Sawleshwarkar, Dr Nathan Bachmann and Ms Danielle Somers. The program has a strong commitment to bilateral exchange of researchers and enhancing the skills and knowledge of scientists in India.

Left: Nathan Bachmann presenting workshop certificates

Right: Ranjeeta Menon with USYD delegation at WHO Collaborating Centre for Tuberculosis Research

Advances in the Biology and Management of Modern Bed Bugs

The First Bed Bug Textbook for 50 years!

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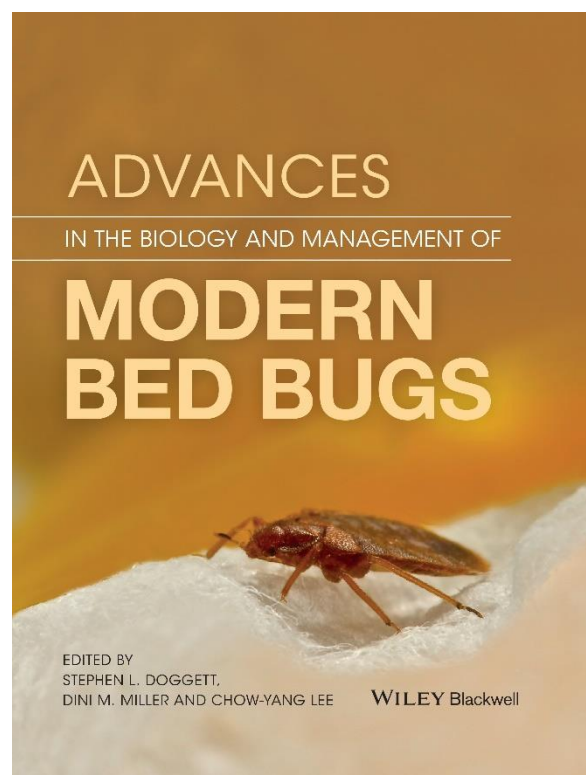[2]Department of Entomology, Virginia Tech, Blacksburg, Virginia, USA
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Over the last two decades, the world has seen an unprecedented resurgence in bed bugs. This has been as unexpected as it has been dramatic, with no sector of society being exempt from a possible infestation. Furthermore, the resurgence has involved huge financial costs; there is no question that these nuisance insects are impacting the world economy billions of dollars annually. In Australia alone, it was estimated that bed bugs had a fiscal cost on our economy of over $200million dollars between the years 2000 to 2012!

Perhaps one of the most unusual aspects of the resurgence is that it has simultaneously involved two species, the Common bed bug, *Cimex lectularius* L., and the Tropical bed bug, *Cimex hemipterus* (F.). The return of these public health pests has prompted a renewed interest in bed bug research and numerous papers have been published in recent years covering a multiple of disciplines. It is now becoming difficult for the average researcher to assimilate all the information available on bed bugs and thus there is a need for a new academic text that reviews all the literature from the past to the present, and offers it in a readily digestible form. Hence the birth of the new text, *Advances in the Biology and Management of Modern Bed Bugs* (*ADVANCES*).

ADVANCES is published by Wiley-Blackwell, released in March 2018 and available from all major book stores.

Front cover of *Advances in the Biology and Management of Modern Bed Bugs*.

For more information and to see sample chapters, abstracts, and a video of the editors discussing the book, go to www.abmmbb.com.

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UPCOMING EVENTS

14 September 2018:

Centenary of the 1918 Pandemic: Advances in Diagnosis and Control of Influenza and Respiratory Viruses Symposium

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