

# Japanese Encephalitis Emergence in Australia: The Potential Population at Risk

Laith Yakob,<sup>1</sup> Wenbiao Hu,<sup>2</sup> Francesca D. Frentiu,<sup>3</sup> Narayan Gyawali,<sup>4</sup> Leon E. Hugo,<sup>4</sup> Brian Johnson,<sup>4</sup> Colleen Lau,<sup>5</sup> Luis Furuya-Kanamori,<sup>6</sup> Ricardo Soares Magalhaes,<sup>7</sup> and Gregor Devine<sup>4</sup>

<sup>1</sup>Department of Disease Control, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom; <sup>2</sup>Faculty of Health, School of Public Health and Social Work, Queensland University of Technology, Brisbane, Australia; <sup>3</sup>Faculty of Health, School of Biomedical Sciences, Queensland University of Technology, Brisbane, Australia; <sup>4</sup>Mosquito Control Laboratory, QIMR Berghofer Medical Research Institute, Brisbane, Australia; <sup>5</sup>School of Public Health, University of Queensland, Brisbane, Australia; <sup>6</sup>Centre for Clinical Research, University of Queensland, Brisbane, Australia; and <sup>7</sup>Queensland Alliance for One Health Sciences, School of Veterinary Sciences, University of Queensland, Brisbane, Australia

In Australia, Japanese encephalitis virus circulated in tropical north Queensland between 1995 and 2005. In 2022, a dramatic range expansion across the southern states has resulted in 30 confirmed human cases and 6 deaths. We discuss the outbreak drivers and estimate the potential size of the human population at risk.

**Keywords.** Japanese encephalitis; emerging diseases; zoonoses; transmission pathways.

Japanese encephalitis virus (JEV) is a single-stranded RNA flavivirus transmitted by mosquitoes of the genus *Culex*. Amplifying hosts include wading birds and swine. Most mammals, including humans, do not amplify the virus to the degree needed to infect mosquitoes and facilitate onward transmission. In endemic countries, a small proportion (<1%) of infected people exhibit symptoms, ranging from nonspecific febrile illness to severe encephalitis with convulsions [1]. In regions with no immunity, the proportion of overt infections may be far higher [2]. The fatality rate among symptomatic cases is around 30%, with half of survivors experiencing cognitive or neurophysiological sequelae [1].

Japanese encephalitis is a vaccine-preventable disease but is the leading cause of viral encephalitis in Asia, with an estimated 68 000 cases per year [3]. Until 2022, the southerly limit of the disease was the far north of Australia where, in 1995, there were 3 cases and 2 deaths on Badu Island [4], and a further 2 cases

from that island and Cape York in 1998 (1 recovered, 1 with ongoing cognitive challenges) [5]. An additional death from JEV in the Tiwi Islands, Northern Territory (NT), occurred in 2021 [1]. In north Queensland (QLD), JEV was recovered annually from mosquitoes and/or domestic pigs in 1995–1998 and 2000–2005. JEV surveillance in QLD was then scaled back [6] and subsequent, limited mosquito screening yielded no further detections. In 2020, however, Queensland Health reported the seroconversion of domestic pigs to JEV in Cape York [7].

## THE CURRENT OUTBREAK

On 25 February 2022, JEV was isolated from a commercial pig farm in southern QLD following investigation of high abortion and stillbirth rates in farrowing sows. Notifications from piggeries in New South Wales (NSW), Victoria (VIC), and South Australia (SA) followed [8]. Sampling of piggeries occurred in response to symptoms. The presence of JEV was determined by polymerase chain reaction detection in fetuses, although identification of JEV-specific immunoglobulin M (IgM) was also used. National reference laboratories provided verification [8].

As of 25 August 2022, 40 human Japanese encephalitis cases have been reported by the Australian Department of Health including 30 confirmed (6 dead) and 10 probable. Case definitions are set by the Communicable Disease Network of Australia (Supplementary Table 1A). Their criteria for laboratory confirmation include the unequivocal detection of virus by nucleic acid amplification or isolation. However, most human cases are identified by serological tests [9], which have issues of sensitivity and cross-reactivity with endemic flaviviruses such as West Nile virus subtype Kunjin and Murray Valley encephalitis virus (MVEV). These must be ruled out to confirm a Japanese encephalitis case. Testing for JEV-specific IgM in cerebrospinal fluid (CSF) has high sensitivity and specificity, but assays conducted on JEV-specific immunoglobulin G in CSF or serum must compare acute and convalescent sera and demonstrate  $\geq 4$ -fold increases in titer. The gold standard for those assays is neutralization testing [9]. Japanese encephalitis case identification is confirmed by a public health reference laboratory (Supplementary Table 1A).

The JEV genotype causing the current outbreak is genotype IV [9]. This is associated with the 2021 human case from the Tiwi Islands. It is not the genotype isolated during the 1995 and 1998 Australian outbreaks (genotypes I and II, respectively).

A variety of factors may have caused the recent expansion of JEV in Australia. First, 2021 and 2022 were La Niña years, causing extraordinarily high rainfall during typical Australian

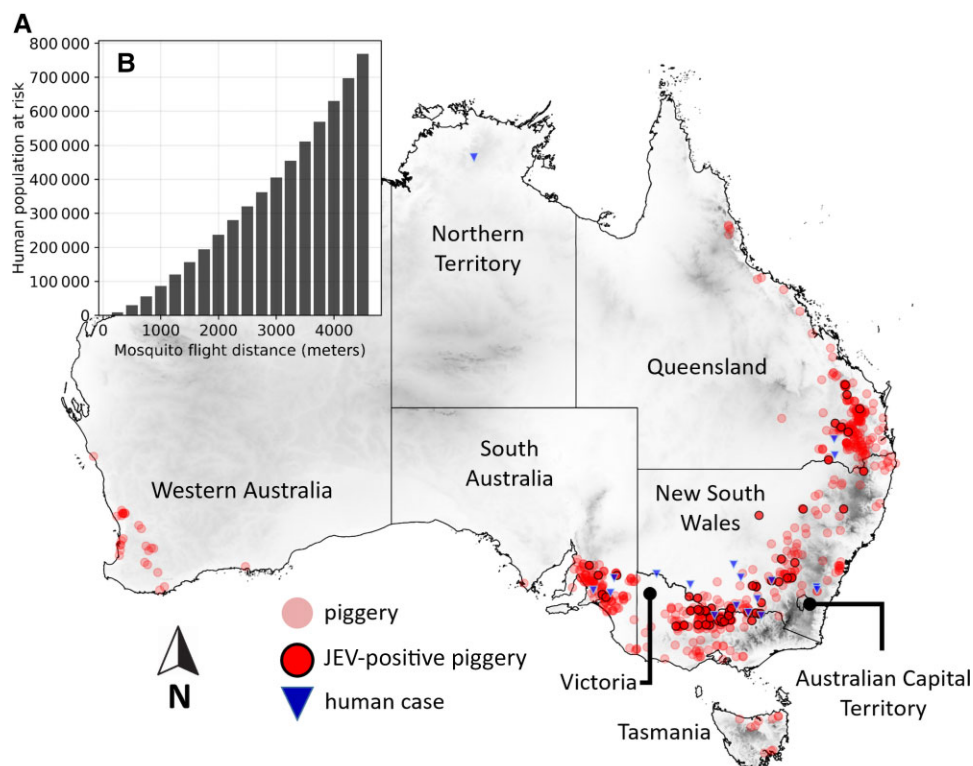
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Correspondence: G. Devine, QIMR Berghofer Medical Research Institute, 300 Herston Road, Brisbane 4006, Queensland, Australia (greg.devine@qimrberghofer.edu.au).

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**Figure 1.** Current distribution of Japanese encephalitis virus (JEV) in Australia and the human population at risk. A, Distribution of piggeries (pink circles), locations of JEV-exposed or -infected piggeries (red circles), and places associated with human JEV cases (blue triangles) in 2022. The map also shows JEV distribution in relation to elevation and the presence of the Great Dividing Range (shaded in gray). B, Human population at risk, assuming that all piggeries can be infected and that mosquitoes have considerable dispersal potential (<https://github.com/lwyakob/JEV>).

summer temperatures (Supplementary Figure 2). In temperate Australia, La Niña is also associated with outbreaks of the similar zoonotic, mosquito-borne MVEV [10]. This climate system created new temporary wetlands across southern Australia, which may have impacted the movement and distribution of JEV-infected wading birds dispersing from the north. It also created optimal habitats for the proliferation of *Culex annulirostris*, which was the key JEV vector in north QLD and is abundant across mainland Australia [6].

Where new wetlands, viremic birds, and high mosquito densities converged near piggeries, the probability of “spillover” and rapid amplification in domestic pigs increased. Infected piggeries may then have become a source of virus for vector-borne transmission to humans. However, other pathways involving feral pigs or wild birds may also sustain JEV infection. In Australia, the geographic spread of JEV in 2022 may have been aided by intensive pig farming and a large feral pig population [1, 6]. Oronasal transmission among domestic pigs presents an additional infection route [11], while JEV exposure in feral pigs was reported from northern Australia in 2022 (Supplementary Table 1B).

An effective JEV vector is one that is highly competent at the viral titers encountered in the serum of viremic birds or swine.

To facilitate transmission to humans, these vectors must display a biting preference for those amplifying hosts and humans. Mosquitoes must also occur at sufficient densities to ensure that a proportion live long enough to feed on an infected host, incubate the virus, and disseminate the infection to their salivary glands.

*Culex annulirostris* is considered the major Australian vector of JEV, although the relative competence of different lineages of that species remains unknown [12]. It feeds opportunistically on a variety of vertebrates, proliferates under optimal conditions, and is capable of dispersing >4 km per day (Supplementary Table 3). Other endemic mosquito species that may play a role include 2 recently established vectors with limited distributions. *Culex gelidus* has been implicated in previous Australian JEV outbreaks, whereas *Culex tritaeniorhynchus* is responsible for the majority of JEV transmission in Asia (Supplementary Table 3).

Currently, none of the human cases reported appear to be associated with an occupational hazard (Supplementary Table 1A). This suggests that it is the dispersal capacity of the mosquito, rather than the occupation of the infected human, that dictates the current risk. This presents a quandary for Australia’s health authorities, who are battling with limited vaccine supplies and the identification of at-risk groups.

## ESTIMATING THE HUMAN POPULATION AT RISK

Currently, Australian health departments have not released the locations of human JEV cases, but the locations of many infected piggeries and humans have been detailed by the World Organisation for Animal Health [8] and by local media organizations. The precise or approximate locations of >50 JEV-exposed piggeries (24 from NSW, 6 from QLD, 6 from SA, and 17 from VIC) (Supplementary Table 1C and Supplementary Figure 1C) and 22 locations associated with human infections (10 from NSW, 2 from QLD, 7 from SA, 2 from VIC, and 1 from NT) (Supplementary Table 1A and Supplementary Figure 1A) are available. Although the majority of reports congregate around the NSW/VIC border, the perimeter of the current JEV outbreak now contains 600 000 km<sup>2</sup> of eastern and southern Australia, on both sides of the Great Dividing Range (Figure 1A).

The well-characterized JEV vector, *Culex annulirostris*, can disperse a considerable distance (4.4 km, Supplementary Table 3). Our aim was to identify the human population within this distance of a piggery and therefore potentially at risk of infection. There is no complete database of all piggery locations available in the public domain, but we downloaded locations from the Farm Transparency Project (<https://farmtransparency.org>). Some of the piggery locations noted in Supplementary Table 1C were not listed by that project, so both datasets (n = 699) were combined and mapped to create Figure 1A.

To estimate the population at risk of being bitten by an infected mosquito dispersing from a piggery (Figure 1B), we downloaded raster data for the Australian human population (resolution of 100 m) updated to 2020 by WorldPop (<https://www.worldpop.org>). The Python code for linking (“masking”) the boundaries of various radii around known piggery locations to the human population raster is available on GitHub (<https://github.com/lwyakob/JEV>).

Our illustrative maps and analyses have major limitations that include an approximation of human case locations, an assumption that all piggeries are equally susceptible to infection, and a poor understanding of true dispersal behaviors of the vector. Nonetheless, if we assume that all mapped piggeries are vulnerable to infection, and that infected vectors fly 4.4 km over their lifetimes (ie, *Culex annulirostris*; Supplementary Table 3), then 740 546 people are potentially at risk of receiving an infective bite (Figure 1B).

## CONCLUSIONS

This initial analysis demonstrates that approximately 3% of the human population in Australia may be vulnerable to JEV infection following its recent range expansion, if piggeries are a major source of virus. Figure 1A suggests that JEV is now endemic over a large part of subtropical and temperate Australia. This

winter, as temperatures declined and floodwaters receded, the virus may have retreated into the wild reservoir. This is the pattern for MVEV, which is also maintained in wading birds and spills over into the human population during La Niña years [10]. The interval until the next JEV outbreak is impossible to predict, but a warming climate and extreme flood events may exacerbate transmission and increase the frequency and severity of outbreaks.

In the future, protection from JEV in Australia may require (1) intensive surveillance of piggeries, (2) targeted vaccination of humans, (3) an understanding of virus movement from northern Australia and Asia, (4) studies on the vectorial capacity of mosquitoes for invading JEV genotypes, and (5) characterization of the epidemiological role of wading birds and feral pigs.

## Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Notes

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