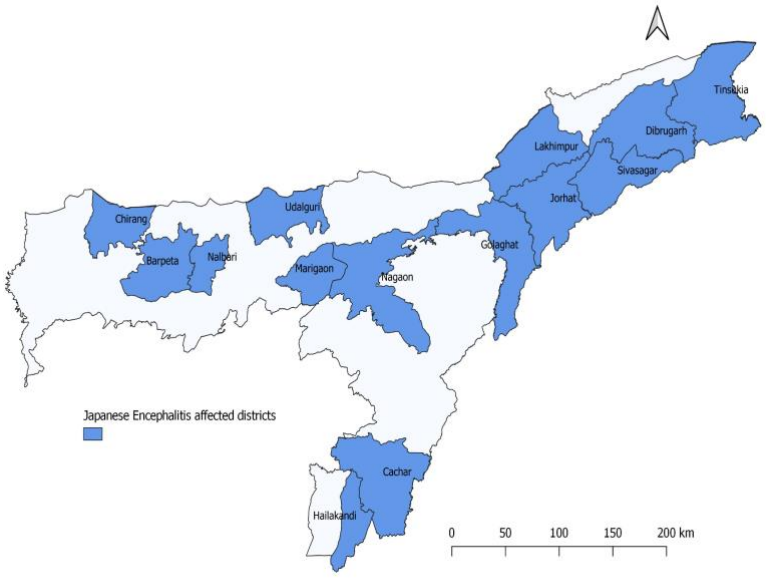
Watching brief

Title	Japanese encephalitis outbreak in Assam, Northeast India, January to August 2022.
Authors	Punam Bandodkar, Murali Umapathy, Ramya Murugesan and Malsawmtluangi Ralte
Date of first report of the outbreak	1st July 2022 (1)
Disease or outbreak	Japanese encephalitis virus (JEV) infection which is caused by Japanese encephalitis virus, a flavivirus, and is transmitted to humans through the bite of infected culicine mosquitoes (2).
Origin (*country, city, region*)	Assam, Northeast region, India.
Suspected Source (specify food source, zoonotic or human origin or other)	Japanese encephalitis is a mosquito borne zoonotic disease. The risk of acquiring infection was found to be high in areas close to paddy fields and water bodies, along with the presence of pig's habitats. Pigs and wading birds are the amplifying hosts (or the natural reservoirs) of JEV (2).
Date of outbreak beginning	1st July 2022 (1)
Date outbreak declared over	Ongoing - the most recent report on Japanese encephalitis in Assam was published on 23rd September 2022 (3).

Affected countries & regions	Figure1. Assam, a northeast state in India affected by the Japanese encephalitis outbreak, 2022 (4).  Figure 2. Districts in Assam, India, affected by Japanese encephalitis outbreak, 2022 (4).  *Upper Assam*: Golaghat, Sivasagar, Dibrugarh, Tinsukia, Lakhimpur, Jorhat, Majuli, Cachar. *Southern Assam*: Hailakandi *Central Assam*: Nagaon, Hojai, Morigaon. *Lower Assam*: Barpeta, Nalbari, Baksa, Chirang and Udalguri. Golaghat in upper Assam is the worst affected district.

Number of cases	434 confirmed cases reported from 1st July to 23rd September 2022 (3).
Clinical features(2)	Incubation period: 5-15 days. Symptoms*:* ● Most people infected with JEV are asymptomatic or develop only mild symptoms. ● Initial symptoms may include fever, headache and vomiting. Mental status changes, neurologic symptoms and weakness and movement disorders might develop over the next few days. Seizures are also common, especially among children. ● Less than 1% of those infected with JEV develop neurologic illness, with a case fatality rate (CFR) of 20%-30%. About 1 in 4 cases are fatal (2). ● Around 30%-50% of survivors continue to have post illness sequelae (i.e., neurologic, cognitive or psychiatric symptoms). ● A small percentage of infected people develop inflammation of the brain (encephalitis), with symptoms including sudden onset of headache, high fever, disorientation, coma, tremors and convulsions.
Mode of transmission (dominant mode and other documented modes)	JEV, a flavivirus, is transmitted to humans through the bite of infected Culicine mosquitoes. The *Culex vishnui* group. *C. tritaeniorhynchus, C. vishnui* and *C. pseudo vishnui* are the main vectors of JEV reported in different parts of India. *C. tritaeniorhynchus* has been reported as the most prominent vector in India (5). It is found in Tamil Nadu, Karnataka and Kerala. *C. vishnui* subgroups are common, widespread and breed in water with luxuriant vegetation, mainly in paddy fields. The abundance of JEV in these areas is related to rice cultivation, shallow ditches and pools in Tamil Nadu, Karnataka and West Bengal. The other species of *Culex* mosquitoes are variably isolated from states such as Tamil Nadu, Karnataka, West Bengal, Andhra Pradesh and Goa. There is no evidence of human-to-human transmission to date (6).

Demographics of cases	• The precise demographics of JEV cases in this outbreak are not yet documented. However, salient findings from studies conducted in the past will enhance our understanding about JEV outbreaks. • Phukan et al. in their analysis of JEV outbreaks from August 2000 to 2002 reported twice the proportion of JEV cases among males than among females. Also, the proportion of cases among children was more than that of adults. Around 96.3% of the cases were from rural areas. Most common symptoms reported were fever, altered sensorium, headache, neck rigidity, abnormal movements, convulsions (7). • An outbreak in Assam in 2008, had a case fatality rate of 24%. The highest proportion (26%) of cases were among 10 to 20 years of age group. All 45 patients had fever and neurological symptoms, namely headache, altered sensorium, focal deficits and neck stiffness (8). • Patgiri et al. in their study 2011-12 found that the JEV infection was higher in adults (>15 years) as compared to children (<15 years). Around 89.17% of the cases were from rural areas. Most common clinical features included fever, altered mental status and headache. Patients with comorbid conditions had a higher incidence of unfavourable outcomes. Comorbid conditions included cardiovascular disease, cerebrovascular accidents, renal dysfunction, pregnancy and diabetes mellitus. Neuroimaging had varying findings and included infarction, cerebral oedema, atrophic changes and encephalomalacia (9).
Case fatality rate	Of the 434 JEV cases reported in Assam from July to September 2022, 93 people died (3). The CFR in Assam during this outbreak was 21.43% (3). Underreporting of cases may occur, thus overestimating the case fatality of JE infection.
Complications	Most people infected with JEV do not develop symptoms or have only mild symptoms. However, a small percentage of infected people develop inflammation of the brain(encephalitis), which is the most serious clinical consequence of a JEV infection. Symptoms include sudden onset of headache, high fever, disorientation, coma, tremors and convulsions. About 1 in 4 cases with encephalitis are fatal (2).

Available prevention	The National Health Mission, Assam released advisory on JEV for the public (10). ● Protection from mosquito bites – to avoid visiting rice fields during dusk and dawn, to wear long sleeves shirts, trousers and gears (boots, socks and tents) (2), the use of mosquito nets, insecticide and repellents, prevention of accumulation of water and to keep drains around house clean, pig rearing to be 100 meters away from human settlements, use of pig nets or mosquito nets for pig stay farm and to vaccinate pigs against common diseases at regular intervals. ● Toll free number 104 for health-related queries and 108 for ambulance services. ● An Intensive fogging programme was undertaken. ● Insecticidal treated mosquito bed nets were distributed to affected areas. ● Health department earmarked beds for JEV patients in medical colleges (11). ● Fever survey was initiated in a radius of 3 kms of a reported JEV case (11). ● Prevention of breeding sites: Draining of collected flood water was carried out. ● Vaccination (12): A JEV vaccine was introduced in the Indian Universal Immunization Programme (UIP) in endemic districts following a one-time campaign covering at-risk children (1-15 years). In the UIP, the live attenuated SA-14-14-2 JEV vaccine is administered intramuscularly in the thigh or upper arm at 9-12 months & 16-24 months in children where two doses are required. The World Health Organization (WHO) said in a report, that several studies have shown that the efficacy of this vaccine to be between 80-90% after the first dose and more than 98% after two doses of the vaccine (13). Vaccination coverage in two districts of Assam was estimated to be around 40% (14).
Available treatment	There is no specific treatment for JEV. Treatment is symptomatic and includes rest, fluids, and over-the-counter pain medications. Patients who develop severe disease require hospitalization for supportive care and close observation. In Assam, nine medical colleges and ten district hospitals were designated as JEV treatment centres, following standard guidelines of the National Health Mission.

Comparison with past outbreaks	• The first outbreak in India was in 1955, after which outbreaks on a regular basis have been reported. The epidemic in 2005 in Uttar Pradesh reported 6061 cases with 1500 deaths. JEV cases have been reported annually in Northeast states from 2010 to 2014. Reports suggest that the increase in JEV cases in 2022 could be due to prolonged floods resulting in water stagnation in Assam (3). • Previous outbreaks have a similar clinical profile and are more common in rural areas (7–9). • The case fatality of the current and the first outbreak of JEV in Assam (1978) are similar (15). • During the current outbreak, JEV cases were also reported sporadically across upper and lower districts of Assam, which had not been observed in the preceding two years (3).
Unusual features	• JEV has a high case fatality rate: Neurological involvement and non-availability of specific treatment may be a cause of high deaths among those having symptomatic JEV infection. Also, JEV infection being asymptomatic among most may result in underdiagnosis of underreporting of cases, and therefore may inflate the CFR. • It was observed by Dev et al. that, in Assam, the case prevalence by age has shifted from less than 15 years to more than 15 years, unlike other JEV endemic states in the country (16). • Clinical features of JEV infection are similar to infection with West Nile Virus, another arbovirus and transmitted by Culex mosquitoes (16). • In 2018, JEV and Acute Encephalitis Syndrome (AES) killed 277 people in Assam. The numbers of deaths in 2019, 2020 and 2021 were 514, 147 and 131 respectively. After the Silchar flood which claimed around 195 lives with 19 landslides, an upsurge of JEV from January 2022 was observed. • JEV can affect all age groups, but more cases occur in peri-urban regions. The distribution of cases in terms of the demographic characteristics is not available for this outbreak, as most of the information is available only by means of media. This may restrict our understanding about the co-morbidity conditions associated with mortality.

Critical analysis	● Information about private health facilities responding to the infected people is also not available. ● Prevalence of JEV in swine in Assam was 51.6% and 47.1% among the farm pigs and those at slaughter premises respectively. This was associated with the monsoon season and water logging near pig shelters (17). Risk factors for the current JEV outbreak: ● The Silchar flood - prolonged stagnant water provides an ideal place for the breeding of culex mosquitoes (3). ● The rising temperature along with the stagnant water makes the environment conducive for the development of the mosquitoes (18) and the rising humidity increases the lifespan of the adult mosquitoes (18). ○ Low vaccination coverage (40%) of JE vaccine among the people of Assam may also be attributed to high susceptibility to JEV. ○ Abundance of Culex species of mosquitoes in Assam (5) is another risk factor. ● Culex mosquito species: culex mosquitoes lay eggs in stagnant and contaminated water sources namely ditches, pools, rice fields, pit latrines, treeholes and grassy pools. C. *tritaeniorhynchus, C. vishnui* and *C. pseudo vishnui* are the main vectors of JEV reported in Assam. ● Background rates of human cases in the past years- In Assam, every year, there is an upsurge of JEV cases from June to August months, but there is also an increase in the number of cases in the subsequent years from 2010 to 2013 during these months (16). The annual burden has also increased over the years from 2016 to 2019, slightly decreased in 2020, but resurged in 2022 (National Vector Borne Disease Control Programme) (23). Incidence may be more than 10 per 100000 during an outbreak (WHO) (19). ● Issues with vaccinations: According to a report published in August, 2022, health officials said that of 67 deaths, only four were vaccinated, 46 were not and the status of remaining 14 remained unclear (20). Low immunisation coverage increases the susceptibility of the population to JEV infection. The Government of Assam launched a massive vaccination drive to cover around 4,000,000 people. The pace of this drive will be a crucial preventive measure to control the outbreak, and authorities expect a good response, secondary to high acceptance of COVID-19 vaccination. However, the lack of sufficient vaccine availability has resulted in prioritizing the 1 to 15 years age group due to increased susceptibility to JEV (21). ● Since there is no documented human-to-human transmission, vaccination of pigs, identification of symptomatic pigs and their isolation or any other necessary steps becomes important. Both JEV inactivated

	and live-attenuated vaccines derived from cell cultures are used, and pig vaccination has been reported in Japan, Nepal, Taiwan, and South Korea, but to a limited extent and only in order to protect pregnant sows from reproductive disorders. Moreover, since the transmission cycle is complex, a single measure of pig vaccination is less likely to be effective. However, the impact of mass vaccination in pigs on human disease has not yet been demonstrated (22). ● Measures to prevent the breeding of mosquitoes needs to be targeted while controlling the outbreak of JEV. For containment of JEV spread, provisions are made for thermal malathion fogging in high-risk areas and distribution of insecticide treated bed nets, introduction of larvivorous fish for control of mosquito breeding; and health-education/awareness programmes for community action have been carried out (21). ● As per the World Health Organisation (WHO) factsheet on JEV, there is very little evidence available to support reduction in JEV disease burden from interventions other than the vaccination of humans. Hence, the WHO recommends prioritization of vaccination of humans over vaccination of pigs and mosquito control measures (19).
Key questions	● What is the demographic distribution of JEV cases in Assam? ● Is the health workforce sufficiently prepared to combat this outbreak? ● What is the JEV vaccine coverage in Assam? ● How protective is the JEV vaccine? ● What measures are taken to identify or control infection among pigs? ● What measures have been deployed to prevent breeding of *Culex* mosquitoes? ● Are there strategies in place to improve JEV vaccination rates amongst the wider population?
Acknowledgements	This Watching Brief is an output of an epidemiology workshop between The National Institute of Epidemiology and EPIWATCH.

References	1. Pallav Bora. Japanese Encephalitis claims 23 lives in 15 days in Assam. India Today. (16 July 2022). https://www.indiatoday.in/india/story/japanese-encephalitis-vlaims-23-lives-assam-1976201-2022-07-15 (accessed 30 January 2023). 2. CDC. Transmission of Japanese Encephalitis Virus | Japanese Encephalitis | CDC. (07 December 2022). https://www.cdc.gov/japaneseencephalitis/transmission/index.html (accessed on 30 January 2023). 3. Kangkan Kalita. Prolonged floods double Japanese encephalitis cases, deaths in Assam. The Times of India. (23 September 2022). https://timesofindia.indiatimes.com/city/guwahati/prolonged-floods-double-je-cases-deaths-in-assam/articleshow/94387857.cms (accessed on 08 February 2023). 4. Bora PK. Assam: Outbreak of Japanese Encephalitis now a major threat. EastMojo. (25 July 2022). http://www.eastmojo.com/assam/2022/07/25/assam-outbreak-of-japanese-encephalitis-now-a-major-threat/ (accessed 01 February 2023). 5. Japanese encephalitis vectors in India. National Center for Vector Borne Diseases Control, Mohfw, GoI. (14 February 2023). https://ncvbdc.mohfw.gov.in/index4.php?lang=1&level=0&linkid=479&lid=3756 (accessed 14 February 2023). 6. Question and answers about Japanes encephalitis. National Center for Vector Borne Diseases Control, Mohfw, GoI. (30 January 2023). https://nvbdcp.gov.in/index4.php?lang=1&level=0&linkid=480&lid=3763 (accessed 30 January 2023). 7. Phukan A, Borah P, Mahanta J. Japanese encephalitis in Assam, Northeast India. Southeast Asian J Trop Med Public Health. 2004;35(3):618-22. DOI: https://pubmed.ncbi.nlm.nih.gov/15689077/ 8. McNaughton H, Singh A, Khan S. An Outbreak of Japanese Encephalitis in a Non-Endemic Region of North-East India. J R Coll Physicians Edinb. 2018 Mar 1;48(1):25–9. DOI: https://doi.org/10.4997/jrcpe.2018.105 9. Patgiri SJ, Borthakur AK, Borkakoty B, Saikia L, Dutta R, Phukan SK. An appraisal of clinicopathological parameters in Japanese encephalitis and changing epidemiological trends in upper Assam, India. Indian J Pathol Microbiol. 2014 Jul 1;57(3):400-406. DOI: 10.4103/0377-4929.138732 10. Protect and prevent. Continue the fight against Japanese encephalitis. National Health Mission, Assam. https://nhm.assam.gov.in/sites/default/files/swf_utility_folder/departments/nhm_lipl_in_oid_6/this_comm/je_half_page_ad_2022_english.pdf (accessed 01 February 2023). 11. Kangkan Kalita. Stagnant water after floods increases JE threat in rural Assam | Guwahati News - Times of India. (07 July 2022). https://timesofindia.indiatimes.com/city/guwahati/stagnant-water-after-floods-increases-je-threat-in-rural-assam/articleshow/92710522.cms (accessed 09 February 2023). 12. Operational guide Japanese Encephalitis.pdf. Immunization division, Mohfw, GoI. (November 2012).

https://dhsfw.assam.gov.in/sites/default/files/swf_utility_folder/departments/dirfw_lipl_in_oid_5/menu/document/JE%20Ops%20Guide%2029%20Nov%202012_0_0.pdf (accessed 01 February 2023).
13. Live attenuated SA-14-14-2 Japanese encephalitis (JE) vaccine. World Health Organization. https://www.who.int/groups/global-advisory-committee-on-vaccine-safety/topics/japanese-encephalitis-vaccines/sa-14-14-2-vaccine (accessed 14 February 2023).
14. Khan SA, Choudhury P, Kakati S, Doley R, Barman MP, Murhekar MV, et al. Effectiveness of a single dose of Japanese encephalitis vaccine among adults, Assam, India, 2012-2018. Vaccine. 2021 Aug 16;39(35):4973–4978. DOI: https://doi.org/10.1016/j.vaccine.2021.07.041
15. Deka NC, Hussain S a. W, Laskar JC. Japanese encephalitis in Assam. (Report of the clinical profile of nine cases). J Assoc Physicians India. 1980;28(8):233–237. DOI: https://pubmed.ncbi.nlm.nih.gov/6257633/
16. Dev V, Sharma V, Barman K. Mosquito-borne diseases in Assam, north-east India: current status and key challenges. WHO South-East Asia J Public Health. 2015;4(1):20. DOI: https://doi.org/10.4103/2224-3151.206616
17. Hussain M, Dhanze H, Mehta D, Kumar MS, Gandham RK, Gupta M, et al. Prevalence and risk factors associated with Japanese encephalitis virus infection in swine population of Assam, India. Asian Pac J Trop Med. 2022 Nov 1;15(11):503-510. DOI: https://doi.org/10.4103/1995-7645.359788
18. Gaurav Das. Fear of Japanese encephalitis adds to continuing flood woes. The Times of India. (01 August 2016). https://timesofindia.indiatimes.com/city/guwahati/fear-of-japanese-encephalitis-adds-to-continuing-flood-woes/articleshow/53487708.cms (accessed 08 February 2023).
19. Japanese encephalitis. WHO. (09 May 2019). https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis 9accessed 14 February 2023).
20. Kangkan Kalita. Stress on vaccines to counter Japanese Encephalitis in Assam. The Times of India. (10 August 2022). https://timesofindia.indiatimes.com/city/guwahati/stress-on-vaccines-to-counter-japanese-encephalitis-in-assam/articleshow/93465951.cms (accessed 09 February 2023).
21. Sentinel Digital Desk. Preventive measures for Japanese Encephalitis - Sentinelassam. (28 July 2022). https://www.sentinelassam.com/editorial/preventive-measures-for-japanese-encephalitis-604672 (accessed 09 February 2023).
22. Ladreyt H, Durand B, Dussart P, Chevalier V. How Central Is the Domestic Pig in the Epidemiological Cycle of Japanese Encephalitis Virus? A Review of Scientific Evidence and Implications for Disease Control. Viruses. 2019 Oct 15;11(10):949. DOI: 10.3390/v11100949
23. State-wise number of AES/JE cases and deaths from 2015-2022.pdf. Directorate of NVBDCP-Delhi. https://nvbdcp.gov.in/WriteReadData/l892s/26436995031670414999.pdf (accessed 02 February 2023).
