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Research

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Flooding and Arboviral Disease: Predicting Ross River Virus Disease Outbreaks Across Inland Regions of South-Eastern Australia

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Abstract

Flood frequency is expected to increase across the globe with climate change. Understanding the relationship between flooding and arboviral disease can reduce disease risk and associated costs. South-eastern Australia is dominated by the flood-prone Murray-Darling River system where the incidence of Australia's most common arboviral disease, Ross River virus (RRV), is high. This study aimed to determine the relationship between riverine flooding and RRV disease outbreaks in inland south-eastern Australia, specifically New South Wales (NSW). Each study month from 1991 to 2013, for each of 37 local government areas (LGAs) was assigned 'outbreak/non-outbreak' status based on long-term trimmed-average age-standardized RRV notification rates and 'flood/non-flood' status based on riverine overflow. LGAs were grouped into eight climate zones with the relationship between flood and RRV outbreak modeled using generalized estimating equations. Modeling adjusted for rainfall in the previous 1–3 mo. Spring–summer flooding increased the odds of summer RRV outbreaks in three climate zones before and after adjusting for rainfall 1, 2, and 3 mo prior to the outbreak. Flooding at any time of the year was not predictive of RRV outbreaks in the remaining five climate zones. Predicting RRV disease outbreaks with flood events can assist with more targeted mosquito spraying programs, thereby reducing disease transmission and mosquito resistance.

Key words: arboviral, Ross River virus, outbreak, flood, riverine

The incidence of mosquito-borne disease is closely linked to environmental conditions due to their influence on vectors. Flood events, defined as the inundation of normally dry land arising from excessive rainfall, riverine overflow, high tides or high sea levels (GA 2013), may provide additional breeding sites for mosquitoes and stimulate mosquito egg-hatching, promoting mosquito populations and disease transmission (Liehne 1988, Russell 1993, Wilks et al. 2006). Since the 1990s, increases in West Nile virus (WNV) disease in Europe and malaria and dengue in the Americas have been attributed to flooding (Hubalek et al. 1999, WHO 2013).

Descriptive studies indicate that the impact of flooding on arboviral disease is variable. WNV disease incidence increased after flooding in Egypt (Darwish et al. 1994), Sudan (McCarthy et al. 1996), the Czech Republic, Romania, and Italy (Hubalek et al. 1999, WHO 2013) but not after flooding in the South African Highveld, nor in Illinois (Paz and Semenza 2013), Nebraska (Janousek and Kramer 1998) or Kansas in the United States (Harrison et al. 2009). In sub-Saharan Africa and Sudan, Rift Valley fever disease incidence also increased after flooding (McCarthy et al. 1996, Anyamba et al. 2014, Gudo et al. 2016, Sang et al. 2017), as did St. Louis encephalitis in southern California (Reisen et al. 1995) but not in mid-western United States, even after the most extensive flood ever recorded (Anders and Shireley 1994). In Australia, 19 occasions of inland flooding over a period of 60 yr were followed by only seven outbreaks of Murray Valley encephalitis (Forbes 1978). Clearly, not all flooding is a precursor to arboviral disease activity. Indeed, some consider that flooding may reduce mosquito populations and disease transmission through egg flushing and destruction of breeding habitat (Roiz et al. 2015).

While many studies have described the relationship between flooding and arboviral disease, few have statistically analyzed the relationship. Studies using river height (Williams et al. 2009) and river flow (Bi et al. 2009) of the Murray River in Australia, demonstrated a significant and positive association with Ross River virus (RRV) disease incidence. While river height and river flow are surrogates for flooding (Poiani 2006), they do not necessarily indicate that flooding has occurred. Riverine overflow may be a more useful measure for exploring the relationship between flood and arboviral disease activity; however, no studies using this measure have been identified.

RRV is the most common mosquito-borne virus in Australia, with an average of more than 4,700 disease cases recorded each year (DoH 2017). Outbreaks preceded by flooding have occurred in several locations across Australia, with almost three-quarters occurring in the southeast corner of the continent, that is in New South Wales (NSW), Victoria and South Australia (Tall et al. 2014). Of these three states, NSW reports the highest annual average RRV case numbers (DoH 2017); and compared to metropolitan and coastal NSW, inland NSW reports the highest notification rates and antibody prevalence (Boughton et al. 1984, Doggett 2004, Kelly-Hope et al. 2004). Further, RRV outbreaks are more frequent in inland NSW than elsewhere in the State (i.e., 64% compared to 36%, respectively; Kelly-Hope et al. 2004), resulting in a significant public health issue for inland NSW.

Australia's longest continuous river system, the Murray-Darling River system (MDR), dominates the geographical landscape of inland NSW. The MDR experiences a varying frequency of flood events (Poiani 2006), all with the potential to impact mosquito populations and RRV disease activity. Given the high activity of RRV disease and the geographical dominance of the MDR system, inland NSW is an ideal location for exploring the relationship between riverine flooding and arboviral disease.

The primary aim of this study was to investigate whether overflow of the MDR's tributaries was predictive of RRV outbreaks in inland NSW. Secondary aims were to identify the month and specific location in which flooding and outbreaks were associated and to determine the time delay between flood events and RRV outbreaks.

Methods

Study Design, Period, and Area

An observational, retrospective population-based ecological design was used for the study period 1 June 1991 to 31 May 2013 (i.e., 22 yr). The study area comprised inland NSW, west of the Great Dividing Range (a mountain range forming a natural geographical barrier between coastal and inland NSW), and included 50 local government areas (LGAs) representing 75% of NSW land area (GA 2004). This area coincides with Bureau of Meteorology (2011) weather forecast areas 11–12 and 14–16 (Fig. 1) and is dominated by the MDR system (Fig. 2).

Study Data

Estimated resident populations and de-identified RRV notification data were provided by NSW Ministry of Health for the 31 December of each year of the study period and included the variables age, LGA of residence (based on 2011 boundaries), laboratory confirmation status, symptom status, symptom onset date, report date and location of disease acquisition. Notifications were excluded from the dataset if: symptom onset date fell outside the study period; report date fell outside the study period and symptom onset date was not stated; neither symptom onset nor report date was stated; the case was seronegative for RRV antibodies; the individual was ≥12 yr of age and was reported as asymptomatic (Flexman et al. 1998); disease acquisition location was outside the study area for residents or unknown for nonresidents. If a resident's disease acquisition location was not specified, it was assumed to be LGA of residence.

Maximum daily river height recorded by river gauging stations (RGS) was sourced from Department of Primary Industries (http://realtimedata.water.nsw.gov.au/water.stm). LGAs with no RGSs were excluded from the study. Weather data—total rainfall per month per LGA; 30-yr annual averages for total rainfall and daily minimum and maximum temperatures—were sourced from weather stations closest to main population centers (BOM 2014). Additional river height and rainfall data were retrieved for the 3 mo preceding the study period. LGA land area and irrigation data (area

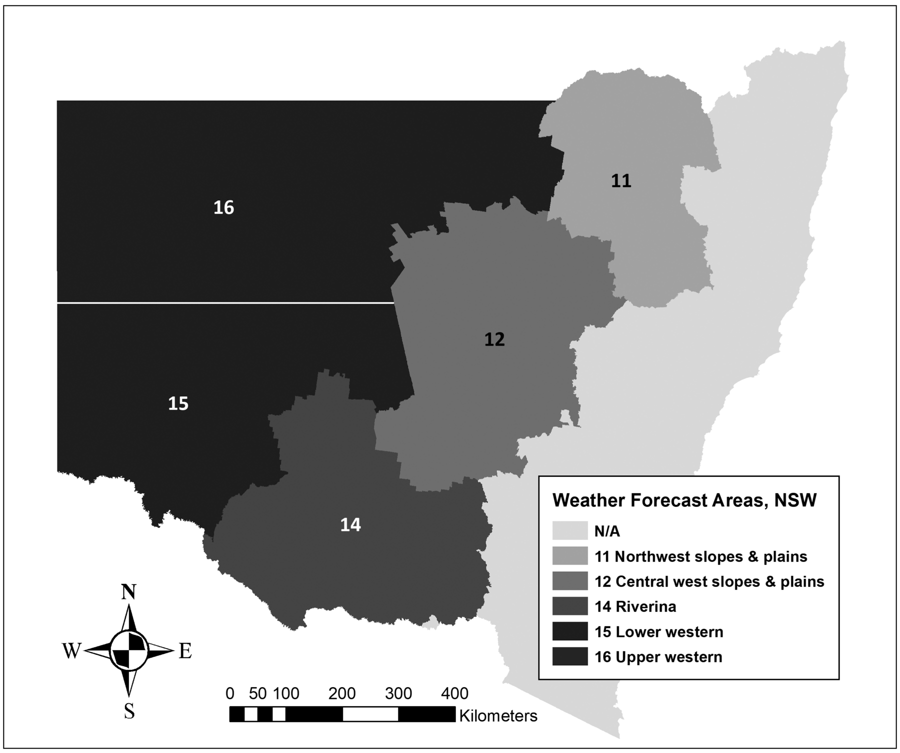

Fig. 1. Weather forecast areas of NSW. N/A denotes not applicable. Shapefile source: DPMC. https://data.gov.au/dataset/nsw-local-government-areas (accessed 3 June 2016).

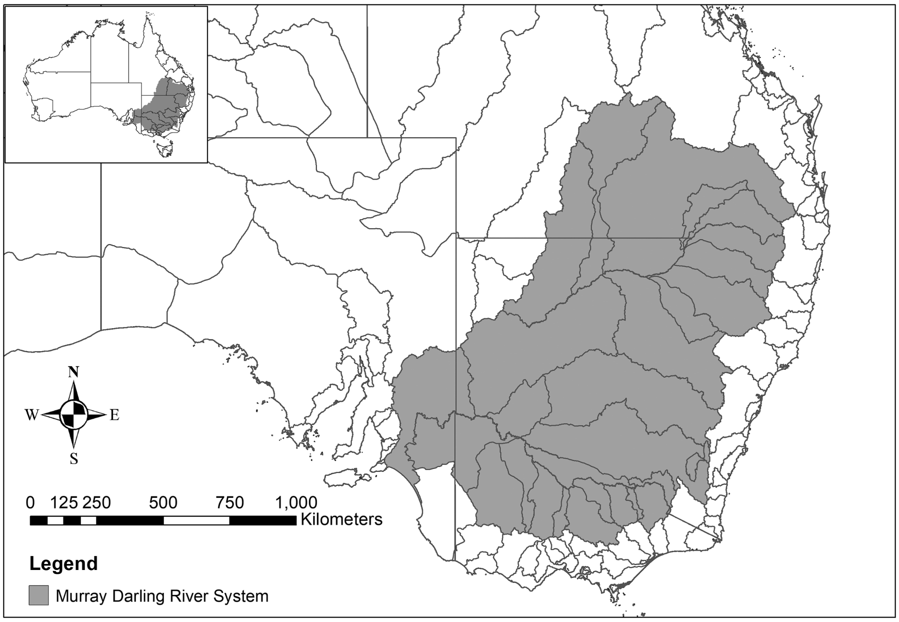

Fig. 2. The Murray-Darling River system, Australia. Shapefile source: DPI. http://www.environment.gov.au/ (accessed 15 October 2018).

and application rate per Statistical Division) were sourced from the Australian Bureau of Statistics (ABS 2005a,b; 2006a; 2008a,b; 2009; 2010; 2011; 2012; 2013a,b).

Data Processing and Calculations

Each RRV notification was assigned a study month and year according to symptom onset date. Where no symptom onset date was recorded, the study month was assumed to be 7 d prior to report date (i.e., median delay between symptom onset and report date for acute cases with symptom status recorded). A study year commenced 1 June (start of winter) and ended 31 May (end of autumn), and was labeled according to the commencing year. Typically, RRV activity peaks between spring and autumn (Russell 2002) so starting a study year in June allowed the peak transmission season to be captured in 1 yr, rather than being split over two calendar years. The choice to start each study year on 1 June was further justified since analysis of the data showed all outbreaks across the study period were concluded by May.

The direct age-standardized notification rate (ASNR) was calculated for each LGA and study month using the LGA's estimated resident population for the study year and the 2001 Australian residential population (ABS 2006b) as the reference population. An outbreak month occurred if at least four notifications were recorded for the month and the probability of the observed notification number was less than 0.05 based on a Poisson distribution with expected mean calculated using the long-term trimmed-average ASNR for the LGA (Gatton et al. 2004). The long-term trimmed-average ASNR was calculated by averaging the ASNR for each calendar month for each study year, after removing the lowest and highest ASNR. A study month was designated an outbreak event if it recorded the first month of a sequence of outbreak months. See Table 1 for definitions of terms.

A flood month occurred for an LGA if at least one RGS recorded minor flood level (Table 1) at least once during the month. Minor flood level was determined according to the State Emergency Services Flood Sub Plan (2008). 'Flood event' was recorded for a study month if at least one flood month occurred in the preceding 3 mo (Table 1).

A substantial number of LGAs had small estimated residential populations and low RRV case numbers. Accordingly, contiguous LGAs with similar rainfall and temperature, as determined by 30-yr averages for total annual rainfall and daily minimum and maximum temperatures, were aggregated to form climate zones. To ensure sufficient flood and outbreak data for analyses, a climate zone was only included in the analysis if it comprised three or more LGAs. Average annual population density for the study period and for each climate zone was calculated by dividing combined estimated resident populations of LGAs for all study years by the combined land area of LGAs, divided by 22 yr.

An LGA was assigned an irrigation area (total hectares) and water application rate (megalitres per hectare) based on the long-term annual averages for its Statistical Division. The amount of land area irrigated and the water application rate were categorized as described in Table 2. A climate zone was assigned land area and application rate categories based on the predominant categories for its constituent LGAs. Population density for a climate zone was calculated by dividing the combined LGAs' annual average population by the combined LGAs' land area.

Statistical Analyses

Prior to analysis, data entries for the first month of an outbreak event were retained while entries for subsequent outbreak months in the sequence were removed. The relationship between flood event (predictor variable) and outbreak event (outcome variable) within each climate zone was analyzed using generalized estimating equations (GEE) with a logit function in a two-step process. The LGA was considered the repeated measure. For each climate zone, 12 data subsets were produced; one for each calendar month of the outcome variable (outbreak). Each calendar-month subset contained the outcome variable status for the month, plus the predictor variable (flood event) for the nominated month. In the first step, a GEE model was developed for each calendar-month subset, thus initially producing 12 models (January to December) per climate zone. As RRV is a seasonal disease, conducting the analyses month-by-month ensured that high season months were not compared with low season months so

Table 1. Definition of terms

Term	Definition
Study month	Any month of any year for the study period e.g., Jan. 2002
Study year	Any year of the study period commencing 1 June and ending 31 May of the following year, labeled according to the first year
Calendar month	One of the 12 named months of the year e.g., Jan.
Outbreak month for LGA	Any study month for an LGA recording an outbreak
Flood month for an LGA	Any study month with at least one river station gauge recording at least a minor flood level at any time during the study month
Minor flood level	Flooding causing inconvenience such as minor road closures and/or low-level bridge submergence (SES 2008)
Outbreak month for CZ	Any study month with at least one LGA in the climate zone recording outbreak
Outbreak event for LGA	Any unbroken sequence of outbreak months for an LGA with the first month of the sequence deemed the study month of the event
Flood event for LGA	Recorded for a study month if at least one of the preceding 3 mo was designated a flood month
Outbreak event for CZ	An unbroken sequence of outbreak months, even if the outbreak from 1 mo to the next occurred in a different LGA
Flood event for CZ	An unbroken sequence of flood events, even if the flood event from 1 mo to the next occurred in a different LGA
Key outbreak event	The calendar month for which an outbreak event was statistically and significantly predicted by a flood event, with individual outbreak events not necessarily preceded by its key flood event; e.g., if June outbreak events were predicted by Mar.–May flood event, then a June outbreak in 2005 would be considered a 'key outbreak event' regardless of whether it was preceded by a Mar.–May flood event
Key flood event	The calendar month for which a flood event was statistically and significantly predictive of an outbreak event, with individual flood events not necessarily followed by its key outbreak event; e.g., if Mar.–May flood events predicted June outbreak events, then a Mar.–May flood event in 2005 would be considered a 'key flood-event' regardless of whether it was followed by a June outbreak event
Flood-preceded key outbreak event	Any key outbreak event preceded by its key flood event
Rain-adjusted	The result of adjusting the model for 'total monthly rainfall', lagged by 1, 2, or 3 mo
Flood day	Any day on which a river gauging station recorded at least minor flood level

CZ, climate zone.

Table 2. Categories for area of land irrigated and water application rate

Land area		Application rate	
×100,000 ha	Category	ML/ha	Category
<10	Very small	<3.5	Low
10–100	Small	3.5–4.4	Moderate
101–150	Medium	4.5–5.0	High
>150	Large	>5.0	Very high

ha, hectare; ML, megalitres.

that only unusual RRV activity was detected. This approach also reduced the need to include temperature in the model in the context of only 22 data points. Where flood event was a significant predictor of outbreak event for a given calendar month and climate zone, the model moved onto step two where it was rerun to adjust for 'total monthly rainfall' lagged by 1, 2, and 3 mo (i.e., rerun three times), to determine whether outbreak could be explained by flood beyond any effect due to rainfall alone.

Level of Statistical Significance and Software

Because each monthly analysis utilized only 22 data points (22 yr of notification data), the significance level was set at 0.08 for the first step (i.e., analyses not adjusted for rainfall). This approach allowed for capturing potentially statistically significant results that may have been overlooked in the context of limited data (i.e., low statistical power). For step two (i.e., for the rain-adjusted analyses), the significance level was set to the standard accepted level of 0.05. Also, since the GEE analyses involved multiple testing which increases the risk of a type 1 error, the results of the adjusted analyses were compared to the Bonferroni corrected P-value of 0.002.

Maps were created using ArcMAP version 10.6 (Esri, Redlands California), and statistical analyses were conducted using SPSS version 22.0 (IBM, Armonk, New York).

Ethical Approval

Ethical approval was provided by the Population & Health Services Research Ethics Committee, Cancer Institute, NSW Government; approval numbers: AU RED Reference: HREC/13/CIPHS/43 and Cancer Institute NSW reference number: 2013/09/474; as well as the University Human Research Ethics Committee, Queensland University of Technology; approval number 1300000841. Informed consent was not required due to the large number of notifications.

Results

The study area contained 50 LGAs, of which 36 were eligible for analysis. These 36 LGAs represented 56% of the geographical area of NSW and were divided among eight climate zones (Table 3). Flood events occurred most frequently in climate zones of the North-west Slopes (n = 32), North-west Plains (n = 31) and Far West (n = 29).Outbreak events occurred most frequently for the North-west Slopes (n = 15), Central-west Slopes (n = 15), North Riverina (n = 15) and North-west Plains (n = 16). Population density was highest in North Riverina (6.8 people/sq.km), followed by South

Table 3. Climate zones, LGAs and their characteristics

Climate zone	LGAs (abbreviation)	Rainfall (mm) Tmax; Tmin (°C)	Pop. density (p/sq.km)	OE (*n*); FE (*n*)	Irrigation area; application rate
North-west Slopes	Gunnedah (GUN), Gwydir (GWY), Inverell (INV), Narrabri (NRB), Tamworth (TAM), Warrumbungle (WMB)	600–1000 24–28; 9–12	1.94	15; 32	Medium; moderate
Central-west Slopes	Dubbo (DUB), Forbes (FOR), Narromine (NRM), Parkes (PAR), Wellington (WEL)	400–600 21–24; 9–12	3.38	15; 19	Small; moderate–high
North Riverina	Griffith (GRI), Leeton (LEE), Murrumbidgee (MUM), Narrandera (NRD), Wagga Wagga (WAG)	400–600 21–24; 9–12	6.76	15; 10	Large; high
South Riverina	Berrigan (BER), Corowa (COR), Deniliquin (DEN), Murray (MUY)	400–600 21–24; 9–12	3.52	12; 25	Large; low
Central-west Plains	Bogan (BOG), Carrathool (CAR), Lachlan (LAC), Warren (WAR)	400–600 24–28; 9–12	0.29	9; 21	Small; high
North-west Plains	Coonamble (CNB), Moree Plains (MOR), Walgett (WAL)	400–600 24–28; 12–15	0.58	16; 31	Small; high
West Murray	Balranald (BAL), Conargo (CON), Hay (HAY), Wakool (WAK), Wentworth (WEN)	200–400 24–28; 9–12	0.27	5; 11	Large; low
Far West	Bourke (BOU), Brewarrina (BRE), Central Darling (CEN), Cobar (COB)	200–400 24–28; 12–15	0.09	7; 29	Small; high

appl., application; FE, flood event; mm, millimeters; *n*, number; OE, outbreak event; pop, population; p/sq.km, persons per square kilometer; Tmax, average annual maximum temperature; Tmin, average annual minimum temperature.

Table 4. Ross River virus outbreaks positively predicted by flooding in inland NSW, 1991–2013

Climate zone	Month of OE	Crude OR (95% CI) P^a	Adjusted[b] OR (95% CI) P^a			FP-OE: OE:FE[c]	Years occurring	No. LGAs with FP-OEs (total LGAs)
			1	2	3			
North-west Slopes	Feb.	10.8[d] (3.2, 36.2) <0.001	10.1 (0.7, 149.5) 0.093	18.3 (2.4, 141.3) 0.005	17.1 (1.4, 205.3) 0.025	4:5:16	1996, 2008, 2010, 2011	5 (6)
North-west Plains	Feb.	3.6 (1.0, 13.1) 0.054	6.3[d] (5.0, 7.8) <0.001	5.1[d] (4.7, 5.5) <0.001	8.1[d] (7.9, 8.4) <0.001	4:5:13	1996, 2004, 2011, 2012	2 (3)
West Murray	Feb.	9.1 (2.5, 61.0) 0.024	11.1 (1.3, 96.9) 0.030	10.5 (1.3, 82.7) 0.025	12.7 (1.4, 118.2) 0.026	3:3:7	1993, 1997, 2011	4 (5)

FE, key flood event; FP, flood preceded; no., number of; OE, key outbreak event; *P*, probability value.
[a]Compared to no flood.
[b]Adjusted for rainfall at 1, 2, and 3 mo prior to outbreak event and with each month analyzed separately.
[c]Ratio of 'flood-preceded outbreak events' to all 'key outbreak events' to all 'key flood events'.
[d]Result satisfied the Bonferroni corrected *P*-value of 0.002.

Riverina (3.5 people/ sq.km) and Central-west Slopes (3.4 people/ sq.km). Irrigation practices varied between climate zones with irrigated land areas ranging from small to large and application rates ranging from low to high.

RRV Notifications, Outbreaks, and Flooding

A total of 5,334 notifications were reported during the 22-yr study period, with 69 (1.3%) excluded from further analysis. Of all notifications included in the study, 48.8% had known symptom status, of which 99.8% were symptomatic. Assuming the same distribution for cases with 'unknown symptom status', only 12 (0.3%) may have been false acute cases.

Of 94 RRV outbreak events, 25.3% occurred each in January and February while 12.1% occurred each in April and November. The remaining 25.3% were spread across all other months except June and July, which recorded no outbreak events. RRV outbreak events that were significantly and positively predicted by flood events occurred in three climate zones (i.e., North-west Slopes, North-west Plains, and West Murray; Table 4; Fig. 3). These key outbreak events (see Table 1 for definition) occurred in February, with their key flood events (Table 1) occurring in November, December and/or January.

In the North-west Slopes, flooding significantly increased the odds of a February outbreak event before and after adjusting for rainfall 2 and 3 mo prior to the outbreak. These results suggest that the effect of flooding on outbreaks was independent of rainfall 2 and 3 mo prior but not for rainfall 1 mo prior. Of a total of five key outbreak events, four (80%) were preceded by key flood events (Table 4).

In the North-west Plains and West Murray, flooding significantly increased the odds of a February outbreak event after adjusting for

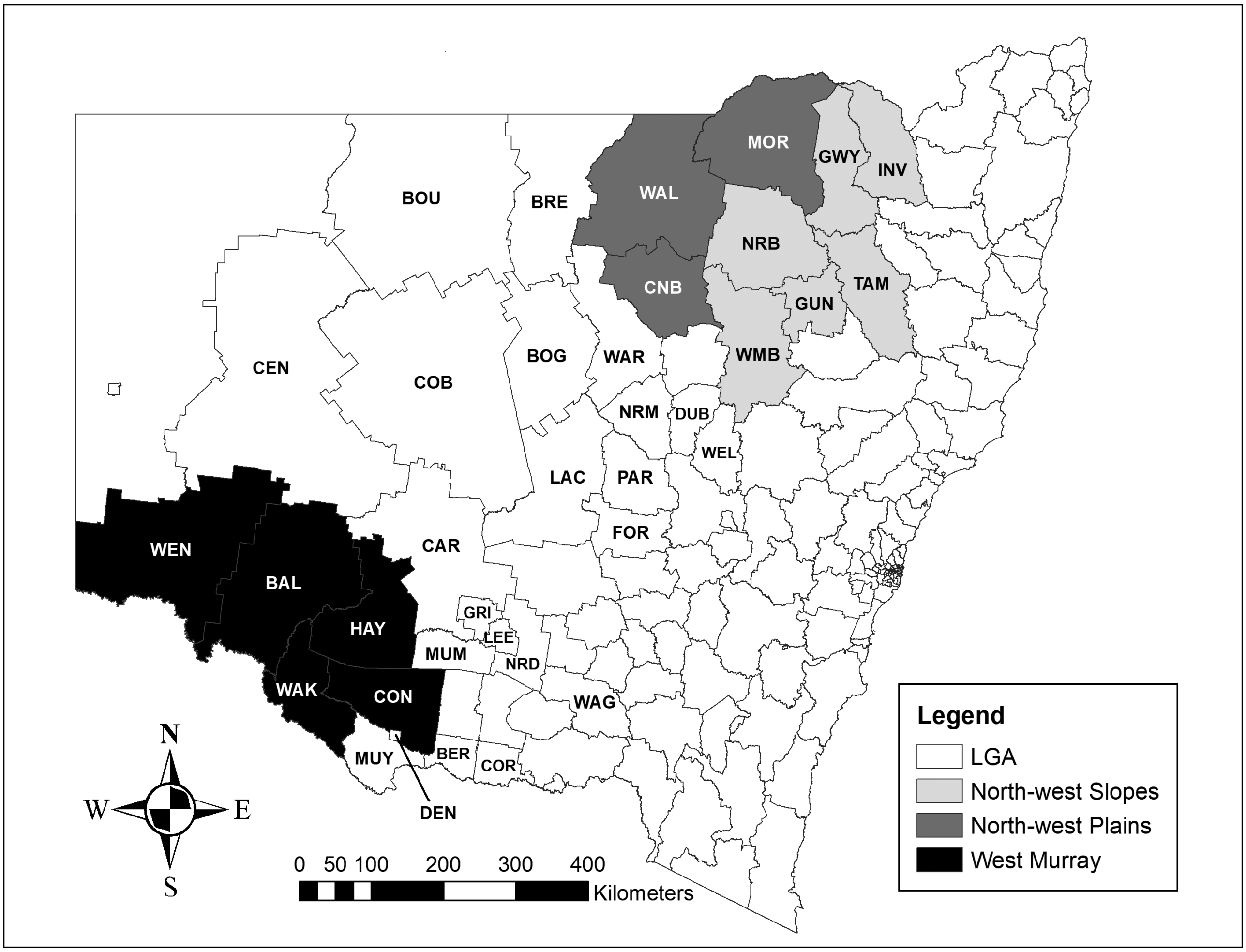

Fig. 3. Climate zones and LGAs with Ross River virus outbreak events positively predicted by flood events in inland NSW, 1991–2013. LGA denotes local government area (see Table 3 for LGA abbreviations). Shapefile source: DPMC. https://data.gov.au/dataset/nsw-local-government-areas (accessed 3 June 2016).

rainfall at 1, 2 and 3 mo prior to the outbreak event (Table 4). These results suggest that the effect of flooding on outbreaks was independent of rainfall at 1, 2, and 3 mo prior to outbreak events. Of all key outbreak events in the North-west Plains and West Murray, 80% (n = 5) and 100% (n = 3) were preceded by key flood events, respectively.

Of all flood-preceded key outbreak events, 82% (n = 9) were preceded by flooding in either January or January and December, with a minimum of seven total flood days (Table 5). Combined with the warm temperatures of January and December, a minimum of 7 d of flood was likely to have sufficiently supported mosquito development among the *Aedes* and *Culex* species (Russell 1993) to promote RRV transmission (Shocket et al. 2018). For West Murray in 1997, although flooding occurred 3 mo prior to the key outbreak event, the duration of flooding was 30 d for at least one RGS. This lengthy flood period in a cooler region of the study area was likely to be supportive of mosquito breeding conditions (Russell 1993) into December and/or January. Therefore, it is plausible that 91% (n = 10) of all flood preceded key outbreak events were attributable to flooding in at least one of the preceding 3 mo.

For the North-west Slopes in 2008, only 3 d of flooding occurred 2 mo prior to the outbreak event, which may be insufficient to support mosquito breeding without follow-up rainfall (Table 5). Therefore, it is unlikely that the 2008 key outbreak event in the North-west Slopes was attributable to the preceding key flood event.

Discussion

This study is the first of its kind to explore the relationship between flooding and RRV outbreaks using riverine overflow data. The results indicate that for inland NSW, flooding in late spring, early summer or mid-summer (i.e., November–January) increases the odds of RRV outbreaks in late summer (i.e., February) in climate zones of the North-west Slopes, North-west Plains and the West Murray.

These results are consistent with that of other studies. Surrogates of flooding, including river height (Bi et al. 2009) and flow (Williams et al. 2009), are associated with RRV activity along the Murray River in South Australia, while observational studies suggest a relationship between riverine flooding and outbreaks. In 1970, a February–April outbreak followed October flooding along the Murray River in NSW (Seglenieks and Moore 1974); while in 1998, a March outbreak followed December overflow of the Katherine River in the Northern Territory (Whelan 1998). Outbreaks also followed flooding associated with heavy rainfall in NSW (Boughton et al. 1984, Hawkes et al. 1985, McDonnell et al. 1994), South Australia (Mudge et al. 1980, Selden and Cameron 1996), Victoria (Marcon 1991), and Queensland (Kelly-Hope et al. 2004). Furthermore, the main lag time of 1 mo between riverine overflow and outbreaks for the current study was consistent with that reported by Bi et al. (2009) of 1–2 mo.

Table 5. Summary of flood days recorded in the 3 mo prior to flood-preceded key outbreak events in North-west Slopes, North-west Plains and West Murray in inland NSW, 1991 to 2013

Climate zone (total number of RGSs)	Month–year of FP-OE	Total number of flood days[a]	RGSs with ≥4 flood days	Maximum number of flood days for at least one RGS		
				Nov.	Dec.	Jan.
North-west Slopes (12)	Feb. 1996	41	5	4	0	9
	Feb. 2008	3	0	0	3	0
	Feb. 2010	14	2	0	0	7
	Feb. 2011	91	6	7	22	6
North-west Plains (10)	Feb. 1996	46	5	4	0	14
	Feb. 2004	25	4	0	0	8
	Feb. 2011	125	6	0	29	18
	Feb. 2012	166	9	5	31	9
West Murray (11)	Feb. 1993	272	7	30	31	18
	Feb. 1997	113	6	30	0	0
	Feb. 2011	231	7	0	30	31

FP-OE, flood-preceded key outbreak event.

[a]Total number of days on which at least minor flood level was recorded, counted across 3 mo and across all RGS in the climate zone.

The current results may be explained by several factors (Fig. 4). Mosquito abundance is an important determinant of RRV transmission. As the life cycle is largely aquatic, floodwaters may boost breeding and abundance (Russell 1986a, 1993, 2002), increasing the risk of disease activity (Russell et al. 1991, Russell 1998, Hu et al. 2010). *Culex annulirostris* (Skuse) and a diverse community of *Aedes* floodwater species (e.g., *Aedes bancroftianus* (Edwards), *Aedes sagax* (Skuse) et al.; Russell 1994) are the most likely species involved in RRV transmission after flooding. Dormant eggs of the floodwater species hatch soon after flood events (Russell 1986b, 1993, 1994), with adults particularly prevalent after flooding in the southeast of the continent (Boughton et al. 1984, Hawkes et al. 1985, Liehne 1988, Russell 1994).

For the current study, flooding was predictive of outbreaks in February only, at a lag of 1–3 mo. This result may be because adult vector abundance or infectivity is not high enough for RRV transmission until temperatures reach certain levels. Adults emerge only when water temperatures measure 20–25°C over several days (Russell 1993), generally not occurring until late spring and early summer for inland NSW (BOM 2016). Furthermore, due to installment hatching (Bader and Williams 2011), floodwater adults only amass several weeks after flooding and *Cx. annulirostris* adult abundance does not peak until January–February (Russell 1986a, 2002). Accordingly, adult mosquito abundance is unlikely to be sufficient for RRV transmission until at least early to mid-summer with outbreaks not appearing until mid- to late summer, allowing for virus incubation, access to medical services and reporting. In addition, adult mosquitoes are not sufficiently infectious until summer when higher temperatures promote virus amplification (Russell 1993, Woodruff and Bambrick 2008).

Reservoir host density and waning immunity are thought to be important factors driving RRV epidemics (Koolhof and Carver 2017) and therefore may explain the link with flooding. Macropods (e.g., kangaroos, wallabies) provide a reservoir for the virus (Harley et al. 2001, Russell 2002) and are considered the most competent hosts for RRV (Russell 2002, Koolhof and Carver 2017) due to their high seroprevalence and high, long-lasting viremia (Stephenson et al. 2018). Flooding promotes clustering of macropods on dryland (Wilson 1957, Wilks et al. 2006) and greater host density may increase vector-host contact and the number of infected mosquitoes, thereby promoting virus transmission to humans. Furthermore, adverse conditions, such as lack of feed due to flooding, can cause physiological stress, thereby diminishing host immunity (Carver et al. 2009). It is estimated that 50% of adult kangaroos and even fewer juveniles possess antibodies for the virus even under standard physiological conditions (Old and Deane 2005, Potter et al. 2014). With waning immunity due to physiological stress from flood conditions, there is significant capacity for viremia among kangaroo populations, potentially promoting the number of infected vectors and leading to more infected humans. Therefore, both increased host density and reduced immunity may enhance RRV transmission and human case numbers. Additionally, multiple transmission cycles of the virus may be necessary before infection prevalence is high enough in the host to spillover to humans (Power and Mitchell 2004), potentially accounting for the time lag between flooding and outbreaks.

The relationship between host and virus may also account for the discrepancy between flood and outbreak frequency. Key flood events were nearly three times as frequent as key outbreak events in North-west Slopes, North-west Plains and West Murray combined, similar to that for Murray Valley encephalitis (Forbes 1978, Russell 1986b). Modeling studies indicate that a single host is insufficient to maintain the virus enzootically, suggesting that virus survival may be dependent upon a multi-host system (Stephenson et al. 2018). Modeling indicates that hosts with short infectious periods, high birth rates and large populations, such as rodents and rabbits, promote virus survival (Glass 2005). Indeed, nearly 20% of *Cx. annulirostris* mosquitoes tested in urban areas had fed on these animals (Jansen et al. 2009). If that is the case, then the presence of several viremic species may be necessary in order for an outbreak to occur after a flood event. Other vertebrate species that may contribute to the multi-host system include horses, possums (Stephenson et al. 2018), and humans themselves (Russell 2002).

The combination of weather conditions before and after the flood event may also determine outbreak occurrence. In Western Australia, spring–summer rains failed to initiate outbreaks if rainfall in the winter just prior was very low (Mackenzie et al. 2000). In south-eastern inland Australia around the Murray River, large outbreaks followed a combination of low maximum temperatures in late spring, high winter–spring rainfall and low rainfall in the previous spring (Woodruff et al. 2002). Laboratory experiments indicate that RRV transmission is greatest in temperate locations at

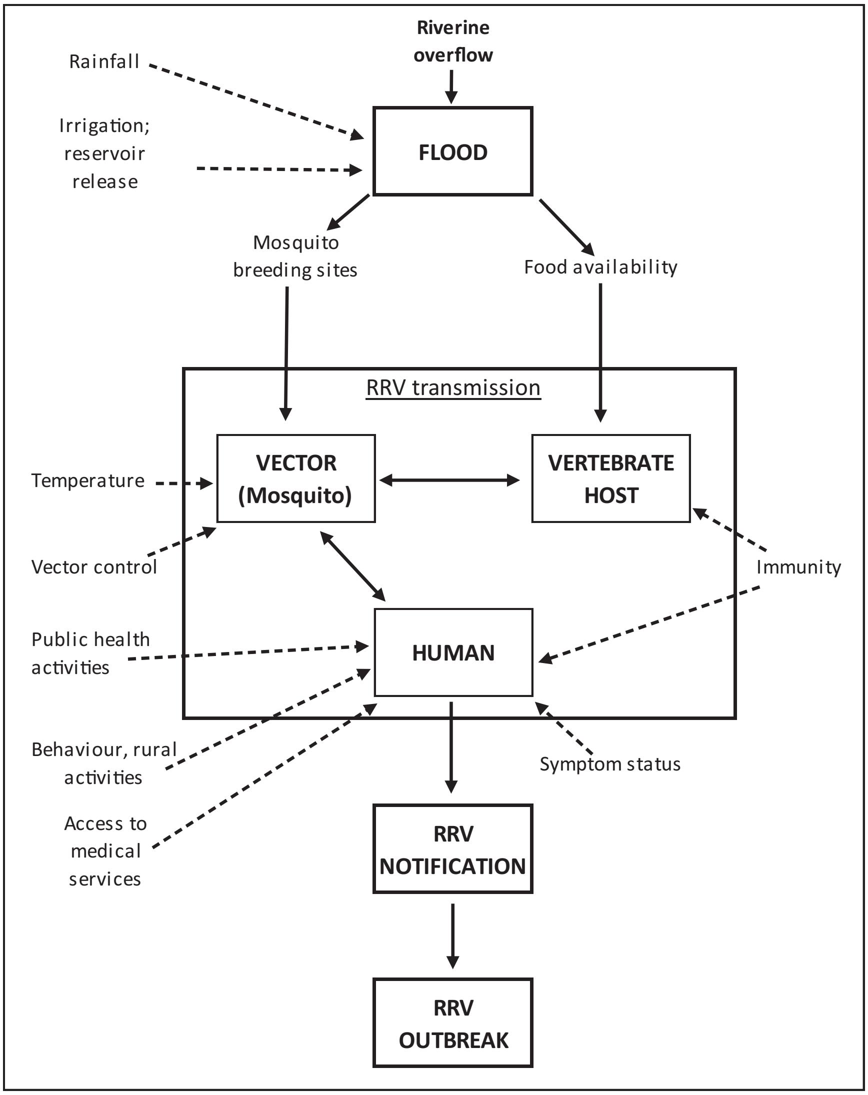

Fig. 4. Framework depicting the factors that impact on flooding, RRV notifications and outbreaks.

26°C (Shocket et al. 2018), indicating that a fairly narrow range of temperatures may be needed for outbreaks to occur. Additionally, post-flood follow-up rainfall may also be important. However, given flooding remained a predictor of outbreaks regardless of the model adjusting for rainfall, post-flood rainfall is unlikely to fully explain why outbreaks followed some years of flood and not others. Nonetheless, post-flood rainfall may determine outbreak severity, a variable not explored in this study. Indeed, Woodruff et al. (2002) found that sustained winter–spring rainfall was associated with summer outbreaks possibly through raising the water table, increasing mosquito breeding sites and mosquito abundance, as well as extending the period of virus amplification. Considering outbreak severity in the context of post-flood rainfall is an opportunity for further research.

The duration, severity, timing, and regularity of flooding may account for the discrepancy between flood and outbreak frequency. For the current study, overflow of 1–2 d duration was given equal flood status to that of 1–2 wk, despite flooding over a few days being less conducive to mosquito breeding and RRV transmission. Furthermore, severe flooding may flush out breeding sites, reducing mosquito abundance and the likelihood of RRV transmission. Indeed, on the Murray River, mosquito numbers are lower after severe flooding than after moderate flooding (McDonald 1979). Severe flooding may also drive people and hosts to relocate (Wilson 1957, Wilks et al. 2006), reducing vector contact between people and hosts (Brown and Murray 2013); while disruption to medical services may reduce case diagnosis and notification (Whelan 1998). Minor flooding, on the other hand, may provide nutritional conditions that attract hosts, making them more abundant (Olsen and Braysher 2000) and closer to residents. Exploring flood severity in future studies may reveal links between host migration, abundance, and outbreak frequency.

The current study found that flooding positively predicted outbreaks in three of eight climate zones (i.e., North-west Slopes, North-west Plains, West Murray). Why flood-predicted outbreaks occurred in only these three climate zones is uncertain. Rainfall, irrigation and population density were variable across all three and therefore are unlikely to explain the results. The average annual maximum temperature was 24–28°C for all three, but that was also the case for Central-west Plains and Far West which did not experience flood-predicted outbreaks. Climatic conditions across the remaining five climate zones were variable and therefore cannot explain the lack of flood-predicted outbreaks in those climate zones. Flood proximity to population centers may have influenced the results. For some LGAs, RGSs were distant to population centers, thereby recording flood events in non-populated areas where outbreaks were unlikely to occur. Landscape features may also explain outbreak variability between climate zones, the most important being the balance between water availability in the soil and water requirements of local vegetation (i.e., water–soil balance) (Walsh and Webb 2018). On a spectrum of low water–soil balance (most arid conditions) to high water–soil balance (least arid conditions), RRV risk rises sharply to threshold by mid-spectrum. One landscape identified as being at the higher end of the spectrum for water–soil balance was the Murray River Valley (Walsh and Webb 2018), a finding consistent with the flood-predicted outbreaks in the West Murray climate zone of the current study. The North-west Slopes and Plains also appear to have landscapes suited to RRV epidemics more so than other inland areas of NSW (Walsh and Webb 2018).

While the study did not explore alternative sources of water as potential confounders, that is irrigation and reservoir release, these are unlikely to impact on the results. Irrigation is a persistent activity, and reservoir release is conducted regularly to manage the ecological health of the MDR's wetlands (MDBA 2002). Both are therefore likely to contribute more to baseline levels of RRV activity than unusual levels. Indeed, if irrigation is reduced during times of flood then it would have no impact on study results. Similarly, reservoir release is done to avoid risk to townships (MDBA 2002), thereby potentially avoiding RRV outbreaks. Furthermore, if water release does cause riverine overflow, then data recorded by RGSs would have been included in the analyses.

A limitation of this study was the lack of inclusion of mosquito data in the analyses. Modeling studies indicate that including mosquito abundance data improves the predictive capacity of models (Woodruff et al. 2006, Jacups et al. 2008), while other studies show that the increasing abundance of different mosquito species significantly increases the risk of RRV notifications (Ryan et al. 1999, Tong et al. 2005, Hu et al. 2006, Hu et al. 2010). In inland south-east Australia, mean trap counts of *Cx. annulirostris* greater than or equal to 1,000 were significantly associated with a sevenfold increase in RRV notification rate at a lag of 1 mo (Cutcher et al. 2017), and for the South Australian Murray Valley, mosquito abundance was the only variable in the model that significantly predicted RRV activity (Williams et al. 2009). Therefore, understanding the relationship between vector abundance, vector species and RRV activity in inland south-eastern Australia may assist with predicting outbreak status following flood events, providing a better decision support tool for more effective and efficient mosquito control. Future studies modeling flood and RRV outbreak status could incorporate mosquito data as a means of improving predictive ability.

In conclusion, this study found that late spring to mid-summer flooding increased the odds of late summer RRV outbreaks on the North-west Slopes, North-west Plains, and West Murray. To better understand the relationship between flooding and RRV outbreaks in the context of limited data, future studies could incorporate data over a longer time frame (i.e., 1991 to date) as well as from adjacent regions with similar climatic conditions (i.e., Victoria and Queensland). Future studies could also model disease incidence, incorporate the duration of riverine overflow, determine the impact of flood frequency on RRV activity, incorporate mosquito data and determine if residents living close to flood-prone waterways are at greater risk of disease than those living further away.

Flood events are the most commonly occurring natural disaster across the globe and with climate change, are expected to occur more frequently into the future (Few 2006, Poiani 2006). Understanding the interaction between flood and arboviral disease can help minimize disease risk and ensure better use of limited resources. Using flood events to predict location and timing of disease activity has the potential to improve public health outcomes by prompting more timely health alerts and more targeted mosquito spraying programs, thereby reducing environmental pollution, the impact on nontargeted species (Lawler 2017, Muzinic and Zeljezic 2018, Tang et al. 2018) and the potential for insecticide resistance (Russell 1993, Weinstein 1997). If flooding is not predictive of arboviral disease, limited resources can be redirected to other flood mitigation activities. The current results may have implications for other mosquito-borne diseases under flood conditions, such as WNV disease, dengue, and malaria.

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