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## Update on Zika virus transmission in the Pacific islands, 2007 to February 2016 and failure of acute flaccid paralysis surveillance to signal Zika emergence in this setting

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## ABSTRACT

**Objective:** *To describe the distribution and magnitude of Zika virus (ZIKV) infections reported in the Pacific islands from 2007 to February 2016; and explore the utility of routine acute flaccid paralysis (AFP) surveillance to detect ZIKV emergence.*

**Method:** *We searched for evidence of ZIKV cases and outbreaks in the Pacific using a PubMed search, reviewed Pacific peer communication channels and through personal communication with relevant WHO staff. Routine acute flaccid paralysis reporting data from 2000 to 2015 was reviewed to determine whether unexpected surveillance exceedances correlated with ZIKV emergence in specific Pacific island countries.*

**Findings:** *We report nine ZIKV outbreaks in eight Pacific islands countries and areas (Yap State, Federal States of Micronesia (2007), French Polynesia (2013-14), Cook Islands (2014), Easter Island (2014), New Caledonia (2014 and 2015), Solomon Islands (2015) Tonga (2016) and American Samoa (2016), and a further three Pacific countries that detected cases (but have not reported domestic transmission): Vanuatu (2015), Fiji (2015), and Samoa (2015). Despite the reported increase in Guillain-Barre syndrome (AFP) in Latin America, review of fluctuations in detection rates in Pacific Islands found no correlation with ZIKV emergence.*

**Conclusion:** *Although no spatial correlation between AFP surveillance data and reported Zika infections was found in the Pacific island context we recommend that the utility of such a surveillance strategy be further tested in countries that are vulnerable to ZIKV outbreak and have large populations under the age of 15 years.*

## INTRODUCTION

In the past weeks, the world has mobilised efforts to tackle Zika virus (ZIKV), the latest threat to global health security, which is currently spreading rapidly in the Americas [1,2]. Worldwide concern in response to increasing evidence that ZIKV infection may be associated with congenital malformations and autoimmune-neurological presentations, including microcephaly, cranial nerve dysfunction, and Guillain-Barré Syndrome (GBS) [1,3–11] has raised alarm among public health authorities resulting on 1 February 2016 in the World Health Organization (WHO) declaring the event a Public Health Emergency of International Concern [10].

The first human outbreak of ZIKV was documented in the Pacific – in Yap State, Federal States of Micronesia (FSM) – in April 2007 [12]. Since this outbreak 10 other Pacific island countries and areas<sup>1</sup> have reported domestic transmission of Zika including: French Polynesia (2013-14), Cook Islands (2014), Easter Island (2014), New Caledonia (2014 and 2015), Solomon Islands (2015), Vanuatu (2015), Fiji (2015), Samoa (2015), and - at the time of writing - the Kingdom of Tonga (2016), and American Samoa (2016) [13–21]. This paper provides an update on ZIKV transmission in the Pacific islands from 2007 to February 2016. The paper adds Pacific-specific detail to the recently published timeline of global Zika transmission by Kindhauser et al (2006) and supplements earlier (mid-epidemic) reports by Roth et al [14] and Musso et al [13,17]. In addition, routinely reported acute flaccid paralysis (AFP) data from 2000 to 2015 was reviewed to determine whether unexpected

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<sup>1</sup> For the purpose of this paper we have adopted the Western Pacific Regional Office of the WHO's grouping of countries and areas that fall within the grouping of 'Pacific islands'. These include: American Samoa, the Cook Islands, the Federal States of Micronesia, Fiji, French Polynesia, Guam, Kiribati, the Marshall Islands, Nauru, New Caledonia, Niue, the Commonwealth of the Northern Marianas Islands, Palau, Samoa, the Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu and Wallis and Futuna. Further, for the purpose of this paper Easter Island (an area of Chile) has been included.

surveillance exceedances correlated with ZIKV emergence in affected Pacific island countries and areas.

## **METHODS**

We sought to identify published and unpublished information on human Zika cases and outbreaks in the Pacific island from 2007 to February 2016 (time of writing). We conducted a literature search using the search terms “Zika” and “ZIKV” in PubMed and reviewed identified papers for their relevance to events in the Pacific island; we reviewed and extracted event-relevant information from PacNet <sup>2</sup> posts (<http://goo.gl/zSOaeO>) and WHO’s Weekly Pacific Surveillance Reports (<http://goo.gl/xrIStN>); and to triangulate and update information on known events, and to identify and collect information on undocumented events we consulted WHO’s Division of Pacific Technical Support in Fiji.

We reviewed routinely reported AFP data for Pacific island countries and areas from 2000 to 2015 and compared unexpected surveillance exceedances with ZIKV emergence in the islands to identify any correlation. We conducted a Poisson probability test to calculate p-values at the 5% significance level for years where more cases were reported than expected.

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<sup>2</sup> PacNet is the discussion listserv of the Pacific Public Health Surveillance Network. PacNet’s main function is to serve as an outbreak communication and alert mechanism, and to support outbreak preparedness in the Pacific region [18].

## FINDINGS

Prior to 2007 sporadic human cases of ZIKV had been reported in countries spanning equatorial Africa and Asia but no outbreaks in humans had been documented [2]. Hayes (2009) and Kindhauser et al (2016) provide an account of these cases [22,23].

In 2007, the first outbreak of ZIKV in humans was identified by physicians on Yap Island in Yap State, FSM. The outbreak investigation identified 185 suspected cases of which 49 were confirmed. Investigators estimated the outbreak attack rate to be 73% (95%CI: 68-77%). All cases experienced mild symptoms typically associated with Zika infection – rash (90%), fever (65%), arthralgia (65%), and conjunctivitis (55%). No hospitalisation, haemorrhagic signs or associated deaths were reported [12].

No further Zika cases were detected in the Pacific until October 2013 when an explosive outbreak occurred in French Polynesia [20]. The French Polynesian outbreak – confirmed in 383 cases – lasted six months (October 2013 to March 2014) and is estimated to have infected more than 32,000 cases or 86% (95% CI: 75-93%) of the population [24]. Kucharski and colleagues (2016) estimate the outbreak  $R_e$  at between 1.9 and 3.1 [24]. A number of cases infected with ZIKV during the outbreak developed severe and rare neurological and auto-immune conditions including 42 cases of GBS and 18 foetal or new born cases with unusual and severe neurological conditions. Of the 18 foetal and new born cases ten were diagnosed with microcephaly and severe brain lesions, and eight had anatomical or dysfunctional neurological abnormalities [4,24,25]. Suspicion was raised (and the

hypothesis continues to be tested, although not yet proven) that ZIKV infection was the cause of these sequelae. Phylogenetic analyses demonstrated that the outbreak strain was closely related to the outbreak strain in Yap during 2007 [20].

Given travel pathways and close geographic and cultural ties, the outbreak in French Polynesia is suspected to have been the source of subsequent outbreaks on Easter Island (January to May 2014; 89 suspected cases of which 51 were confirmed) [16], in New Caledonia (January to July 2014, more than 1,385 confirmed cases [21] and January to May 2015, 82 confirmed cases [19]); and on the Cook Islands (February to May 2014; 932 suspected cases of which 54 were confirmed [15]). One case in the 2013 New Caledonian outbreak was reported to have developed GBS [26]; no other severe illness was reported from the outbreaks.

In 2015/16 two Pacific island countries reported autochthonous transmission of ZIKV: Solomon Islands (February to May 2015; 324 suspected cases of which 5 have been confirmed) and Tonga (January 2016 and ongoing; 549 suspected of which 2 have been confirmed). One case in the Solomon Islands outbreak was reported to have developed probable GBS.

Five other Pacific islands reported sporadic (non-autochthonous) Zika cases in 2015/16: Vanuatu (February to March 2015, 1 confirmed case), Fiji (August 2015, 2 confirmed cases), Samoa (September to October 2015, 3 confirmed cases), and American Samoa (February 2016 and ongoing; 99 suspected cases of which 4 are confirmed) [15,18] (**TABLE 1**). A number of imported cases (mainly from the Pacific

islands) have been detected in Australia [27] and New Zealand [28] including one traveller returning to New Zealand from Tonga that developed GBS symptoms [29].

To test a hypothesis that AFP data (routinely collected as a criterion for performance of the Global Polio Eradication Initiative [30,31]) may serve as a useful surveillance strategy for the detection of emergence of ZIKV in previously unaffected countries we compared Pacific islands' data on AFP case from 2000 to 2015 with known Zika transmission. While statically excess AFP cases were notified from aggregated Pacific islands' data in 2000 ( $p<0.004$ ), 2006 ( $p<0.001$ ), 2009 ( $p<0.008$ ) and 2014 ( $p<0.04$ ) statistically significant country level case excesses was only found for the Solomon Islands in 2015 ( $p<0.001$ ) (**FIGURE 1**).

## DISCUSSION

We present an epidemiological review of ZIKV activity in the Pacific islands from 2007 to February 2016. As infection with ZIKV typically causes mild symptoms that overlap with clinical features of dengue and chikungunya infection (both of which have been circulating in the Pacific in past years [14]), and due to the limited surveillance and diagnostic capacity of most Pacific islands we believe that ongoing and undetected ZIKV transmission in other Pacific island countries and areas is highly probable.

The observation in French Polynesia and the Americas that severe clinical complications are possibly associated with Zika infection highlights the need to strengthen surveillance for this emerging virus, and, in the event of outbreaks

establish rigorous clinical monitoring to detect neurological and other unusual clinical manifestations.

Given the proposed link between ZIKV infection and GBS we hypothesised that AFP surveillance, routinely conducted in all countries for children under the age of 15 years as part of the Global Polio Eradication Program's quality monitoring activity [30], may serve as a useful, convenient and cost-effective surveillance strategy for detecting the emergence of ZIKV in previously unaffected areas. In the Americas (Columbia and Venezuela) it appears that enhanced surveillance after ZIKV introduction is finding an increased rate of GBS cases [32]; this should lead to an increase in AFP reports. While we found this strategy was not effective in Pacific islands countries where populations are small (and hence expected number of AFP cases is low, often <1 per year) and surveillance data quality inadequate, we suggest that the utility of this surveillance strategy be explored in countries vulnerable to Zika transmission and that have large populations under 15 years of age.

The Solomon Islands was the only country where a statistically significant increase in AFP cases correlated with the emergence of Zika virus. This could represent confirmation of the utility of increased AFP detection for signalling the appearance of Zika virus, or reflect more sensitive public health surveillance following a major cyclone, or be a chance finding given that it was the only country where this occurred. This observation reinforces the need to explore AFP surveillance as a strategy for ZIKV detection in other settings.



The transmission of ZIKV in the resource-limited Pacific island context poses unique challenges for public health preparedness and outbreak surveillance. Typically mild symptoms similar to dengue and chikungunya, limited coverage and sensitivity of existing early warning surveillance systems, limited capacity to investigate and verify surveillance signals, widely dispersed populations, poor communication, and inadequately resourced health systems all conspire to make timely and accurate detection of ZIKV incursions problematic. Further investigation is required to determine what factors – in the islands' setting - influence the intensity and speed of ZIKV transmission, and ability of early warning surveillance to detect cases. In this context, it is possible that GBS cases, which remain relatively uncommon, have been missed due to the small case numbers and poor surveillance quality.

WHO recommends that all countries maintain a heightened awareness and build capacity to detect and confirm ZIKV cases; ensure health system preparedness to respond to a possible increased demand for specialised care (for microcephaly and neurological syndromes); strengthen antenatal care; and introduce public health measures to reduce risk of ZIKV spread and infection [9,10].

## **CONCLUSION**

Since the first transmission of ZIKV outside Africa and Asia was documented in an outbreak in Yap State, FSM in 2007, transmission has been reported in 10 other Pacific island countries and areas: French Polynesia (2013-14), Cook Islands (2014), Easter Island (2014), New Caledonia (2014-15), Solomon Islands (2015), Vanuatu (2015), Fiji (2015), Samoa (2015), and - at the time of writing - the Kingdom of Tonga (2016) and American Samoa (2016) causing large outbreaks in some. Infection has been associated with severe clinical complications in French Polynesia. We found no spatial-temporal correlation between routinely collected AFP data and ZIKV emergence in previously unaffected Pacific island countries. We suggest the utility of such a surveillance strategy be further tested in countries that are vulnerable to ZIKV outbreak and have large populations under the age of 15 years.

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Table 1. Epidemiological overview of Zika virus transmission in the Pacific islands, 2007 to Feb 2016

Month started	Month ended	Country	Summary	Zika virus infection-associated Guillain-Barré Syndrome reported	Other Zika virus infection-associated neurological conditions reported	Confirmed local transmission	Laboratory confirming pathogen	Reference
Apr-07	Jun-07	Yap State, FSM	185 suspected cases of which 49 were confirmed and 59 were considered probable	No	No	Yes	Hawaii State Laboratory, US CDC	[12]
Oct-13	Mar-14	French Polynesia	383 confirmed cases and an estimated 32,000 consulting cases (75-93% of the population)	42 cases of which 37 (88%) reported an illness comparable with ZIKV infection. Retrospective seroneutralisation test demonstrated that all 42 cases were positive for dengue and Zika virus infection.	At least 18 foetal or new born cases with unusual conditions and severe neurological conditions, including 10 cases with microcephaly and severe brain lesions, and eight cases severe anatomical or dysfunctional neurological abnormalities	Yes	Institut Louis Malardé (ILM), French Polynesia	[20,21,24,33]
Jan-14	Jul-14	New Caledonia	Approximately 1,500 confirmed cases	13 cases from Mar to Jul-14, one of which was ZIKV positive	No	Yes	Institut Pasteur, New Caledonia (IPNC)	[21,26]
Feb-14	May-15	Cook Islands	932 suspected cases including 50 confirmed.	No	No	Yes	ILM, French Polynesia	[15]
Jan-14	May-15	Easter Island	41 suspected with one confirmed case	No	No	Yes	Emergent and Hepatic Virus Laboratory, Chile	[16]
Jan-15	May-15	New Caledonia	82 confirmed cases	No	No	Yes	IPNC	[19]
Feb-15	May-15	Solomon Islands	More than 302 suspected cases with five confirmed	1 probable	No	Yes	ILM, French Polynesia	[15,34]
Feb-15	Mar-15	Vanuatu	1 confirmed case	No	No	No	IPNC	[15,34]

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Aug-15	Aug-15	Fiji	2 confirmed cases	No	Under investigation	No	ILM, French Polynesia	[15]
Sep-15	Oct-15	Samoa	3 confirmed cases	No	No	No	ILM, French Polynesia	[15]
Jan-16	ongoing	Tonga	(As of 7 Feb 2016) 596 suspected cases with 2 confirmed	No	No	Yes	LabPLUS, New Zealand	[15]
Feb-16	ongoing	American Samoa	(As of 12 Feb 2016) 99 suspected cases with 4 confirmed	No	No	Yes	Hawaii State Laboratory, US CDC	[15,18]

Figure 1. Reported Zika virus transmission in the Pacific islands by location and year and acute flaccid paralysis cases reported to the Global Polio Eradication Initiative by country/area and year, 2007-2015

Pacific island countries and areas	North or South Pacific	Zika virus transmission (outbreaks and cases)									AFP cases expected per annum~	Reported <sup>#</sup> cases of acute flaccid paralysis among children <15 years								
		2007	2008	2009	2010	2011	2012	2013	2014	2015		2007	2008	2009	2010	2011	2012	2013	2014	2015
American Samoa	S										<1									
Cook Islands	S									Jan-May	<1									
FSM*	N	Apr-Jun									<1									
Fiji	S									Aug	3	7	4	9	5	6	4	7	8	4
French Polynesia	S							Oct-Dec	Jan-Jul		1	1								
Guam	N										1									
Kiribati	S										<1									
Marshall Islands	N										<1			1						
Nauru	S										<1									
New Caledonia	S								Jan-Jun	Jan-May	1	1	1	3	1					
Niue	S										<1									
CNMI**	N										<1		1							
Palau	N										<1									
Samoa	S									Sep-Oct	1	1		1						
Solomon Islands	S									Feb-May	2	3	3	3	7	3		1	6	9
Tokelau	S										<1									
Tonga	S										<1			1						
Tuvalu	S										<1									
Vanuatu	S									Feb-Mar	1		1						1	1
Wallis and Futuna	S										<1									
<b>Total</b>											<b>10</b>	<b>13</b>	<b>10</b>	<b>18</b>	<b>13</b>	<b>9</b>	<b>4</b>	<b>8</b>	<b>15</b>	<b>14</b>

~ Based on 2015 predictions of GPEI. Expected cases correct for all preceding years except Fiji: 2014 & 2015 expected # cases was 4; Guam: 2000-2002 expected # cases was 0; Solomon Is: 2000-2002 expected # cases was 0; \* Federated States of Micronesia; \*\* Commonwealth of the Northern Marianas Islands; <sup>#</sup> Reported to WHO as part of the Global Polio Eradication Initiative  
Shaded cells indicate corresponding years. Data for Easter Island is not included.



