Lymphatic Filariasis in Oceania

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Patricia M. Graves, Peter Wood, and Hervé C. Bossin

Abstract

Lymphatic filariasis caused by the mosquito-transmitted helminth parasite *Wuchereria bancrofti* is an important problem in Oceania. Of the 33 countries and territories included in this review, 24 have been found to be endemic for this disease at some time in the past, and 18 of these were classified as endemic at the start of the Global Programme to Eliminate Lymphatic Filariasis in 2000. After the implementation of large mass drug administration campaigns and (to a lesser extent) vector control over the last 15 years, only ten Oceania countries and territories were still considered to have ongoing transmission of lymphatic filariasis in 2015. Through a systematic literature search and review, we identified 79 individual studies of filariasis in Oceania that were published in 70 papers between 1995 and 2015. Data on mosquito (by species) and human infection prevalence using all currently available diagnostic tests, as well as estimates of acute and chronic filariasis morbidity, were extracted from these publications and tabulated in chronological order by country and outcome measure, noting sampling method and sample size in order to evaluate study quality and precision. No studies were identified from Micronesia; most studies in Melanesia and Polynesia were found from Papua New Guinea (PNG) (30) and French Polynesia (16), respectively. All other countries in Melanesia and Polynesia were represented by 1–7 studies except Wallis and Futuna. The systematic review identified 19 published studies of mosquito infections and 62 of human infections but only 3 on acute morbidity

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(all from PNG in the 1990s) and 11 on chronic morbidity. Since Oceania has a diverse set of mosquito vectors, published reviews of relative efficiencies of different mosquito genera were examined to shed light on their transmission dynamics and hence the potential for elimination of filariasis in Oceania. The review indicates the need for collation of unpublished reports and studies in addition to more geographically representative studies of remaining filariasis infection distribution, as well as quantification of the disability (acute attacks, lymphoedema, elephantiasis and hydrocoele) that will remain once transmission is interrupted, in order to plan for services to alleviate these lifelong effects.

Keywords
Lymphatic filariasis • Wuchereria bancrofti • Pacific • Oceania • Lymphoedema • Hydroceole • Elephantiasis • Anopheles • Culex • Aedes • Mosquito • Vector-borne disease • Melanesia • Polynnesia • Micronesia

Introduction

Lymphatic filariasis is a disease caused by a nematode worm and transmitted by mosquitoes. There are three known species of the parasite, *Wuchereria bancrofti*, *Brugia malayi* and *Brugia timori*, with *W. bancrofti* being the cause of the great majority of infections (WHO 2010). Lymphatic filariasis is transmitted by many species of mosquito in four different genera – *Anopheles*, *Culex*, *Aedes* and *Mansonia* (WHO 2013). In the human body, adult worms (male and female) live in nodules in the lymphatic system and, after mating, produce numerous microfilariae (Mf). The lifespan of adult worms is 4–6 years. Mf migrate from the lymph system to the peripheral blood, often at times of day that coincide with peak-biting activity of local vectors. Female mosquitoes ingest Mf with a blood meal; the Mf then lose their sheath and migrate through the stomach wall to reach the thoracic flight muscles where they develop into first-stage larvae (L1). Over 10–12 days, the larvae grow and moult into second-stage (L2) and third-stage (L3) infective larvae which migrate to the proboscis, ready to infect another human host. The L3 are deposited on the skin and find their way in through the bite wound. The L3 develop into the fourth stage (L4) as they migrate to the lymphatic vessels and lymph nodes, where they develop over a period of about 1 year into adult worms. Infection with the worm and damage to the lymphatic system can cause both acute attacks of adenolymphangitis as well as eventual long-term chronic and irreversible morbidity and disability from lymphoedema, elephantiasis and (in men) hydrocoele.

In 2000, the Global Programme to Eliminate Lymphatic Filariasis (GPELF) was officially launched in response to World Health Assembly resolution 50.29, 1997. The goal is to eliminate the disease as a public health problem with a target year of 2020. The strategy rests on two pillars: (1) interrupt transmission by delivering single annual doses of deworming drug combinations (albendazole plus either diethylcarbamazine (DEC) or ivermectin) to the entire

eligible population where the disease is endemic (defined as prevalence >1 %) and (2) alleviate suffering and disability for those with lymphoedema and hydrocoele. In Oceania, the Pacific Programme to Eliminate Lymphatic Filariasis (PacELF) started working in 1999 even before the GPELF was fully operational. Between 2000 and 2009, approximately 2.8 billion treatments were delivered worldwide through mass drug administration, also known as preventive chemotherapy. PacELF covered 22 Pacific countries and territories (WHO 2006), a subset of the 35 countries and territories of the WHO Western Pacific Region.

At the start of the GPELF, it was estimated that there were 120 million people in 81 countries who were infected with at least one of the parasite species, with 1.34 billion people living in areas where filariasis was endemic. Of those infected, it was estimated that 15 million were affected by lymphoedema and 25 million men had scrotal hydrocoeles. These estimates were based on predictions from relatively sparse mapping studies, at least in Oceania (Michael et al. 1996). Revised global estimates were recently developed (Ramaiah and Ottesen 2014) using a model based on empirical observations of the effects of treatment on infection and clinical manifestations. This estimated that global prevalence of lymphatic filariasis has reduced from 3.6 to 1.5 % through consumption of 4.5 billion treatments between 2000 and 2012 and that in 73 endemic countries there were still an estimated 68 million LF cases that include 36 million Mf carriers, 17 million lymphedema cases and 19 million hydrocoele cases worldwide in 2014. Another recent publication produced a global map of filariasis distribution based on 9033 surveys identified up to 2013 (1322 in the WHO WPRO region), which were used to predict global environmental suitability and prediction of filariasis transmission areas (Cano et al. 2014).

This chapter reviews lymphatic filariasis in Oceania, comprising Micronesia, Melanesia and Polynesia, as geographically defined in the following link and listed in Table 4.1: https://en.wikipedia.org/wiki/List_of_sovereign_states_and_dependent_territories_in_Oceania. All of these countries and territories were included in the PacELF, with the exception of:

1. Australasia, comprising Australia, its outlying islands, and New Zealand (non-endemic at start of PacELF)
2. Hawaii (USA) in Polynesia and Wake Island (USA) in Melanesia (never endemic)
3. Easter Island (Chile) in Polynesia (never endemic)
4. Indonesian provinces of Papua, West Papua and the Maluku Islands (endemic for filariasis in 2000)

The Indonesian provinces of Papua and West Papua (the western half of the island of New Guinea) are included in this review, but the Maluku Islands of Indonesia have been excluded. They are the only area in Oceania that are endemic for *Brugia* filariasis as well as *Wuchereria.* All other areas included in this review have filariasis caused by *W. bancrofti* only (excluding imported cases of *Brugia* in Indonesian Papua).

Table 4.1 Countries included in Oceania showing LF endemicity past and present

	Area, km2	Population (2009)	Pop density/ km2	LF ever endemic	LF endemic 2000	LF ongoing transmission (2015)
Australasia						
Ashmore & Cartier Is (Aus)	199	0		N/A	N/A	N/A
Australia	7,686,850	23,034,879	2.7	YES	NO	NO
Christmas Is (Aus)	135	1,493	3.5	NO	NO	NO
Cocos (Keeling) Is (Aus)	14	628	45.1	NO	NO	NO
Coral Sea Is (Aus)	10	4		NO	NO	NO
New Zealand	268,680	4,465,900	16.5	NO	NO	NO
Norfolk Is (Aus)	35	2,302	61.9	NO	NO	NO
Melanesia						
Fiji	18,270	856,346	46.9	YES	YES	YES
New Caledonia (France)	19,060	240,390	12.6	YES	YES	YES?[b]
Maluku Is (Indonesia)[a]	74,505	1,895,000				
Papua (Indonesia)	319,036	3,486,432	11	YES	YES	YES
West Papua (Indonesia)	140,375	760,855	5.4	YES	YES	YES
Papua New Guinea	462,840	5,172,033	11.2	YES	YES	YES
Solomon Islands	28,450	494,786	17.4	YES	NO	NO
Vanuatu	12,200	240,000	19.7	YES	YES	NO
Micronesia						
Fed States of Micronesia	702	135,869	193.5	YES	YES	YES?
Guam (USA)	549	160,796	292.9	YES	NO	NO
Kiribati	811	96,335	118.8	YES	YES	YES
Marshall Islands	181	73,630	406.8	YES	YES	YES?
Nauru	21	12,329	587.1	YES	NO	NO
Northern Mariana Is (USA)	477	77,311	162.1	YES	NO	NO
Palau	458	19,409	42.4	YES	YES	NO
Wake Island (USA)	2	150		NO	NO	NO
Polynesia						
American Samoa (USA)	199	68,688	345.2	YES	YES	YES
Cook Is (New Zealand)	240	20,811	86.7	YES	YES	YES?
Easter Is (Chile)	164	5,761	31	NO	NO	NO
French Polynesia (France)	4,167	257,847	61.9	YES	YES	YES
Hawaii (USA)	16,636	1,360,301	81.8	NO	NO	NO
Niue (New Zealand)	260	2,134	8.2	YES	YES	NO
Pitcairn Islands (UK)	5	47	10	NO	NO	NO
Samoa	2,944	179,000	63.2	YES	YES	YES
Tokelau (New Zealand)	10	1,431	143.1	YES	NO	NO
Tonga	748	106,137	141.9	YES	YES	YES
Tuvalu	26	11,146	428.7	YES	YES	YES
Wallis & Futuna (France)	274	15,585	56.9	YES	YES	YES?

[a]Endemic filariasis includes *Brugia malayi*: not considered in this review
[b]YES?: transmission likely interrupted, present only in highly localised areas or not yet certified to be interrupted

The PacELF region comprises a relatively large proportion of the total global number of endemic countries and territories (originally 17 in 2000) but a relatively small proportion of the global population at risk of disease. According to GPELF, by 2009, PacELF had delivered 8.6 million treatments to an estimated 5.8 million population at risk in 14 of the 17 endemic countries and territories (WHO 2010).

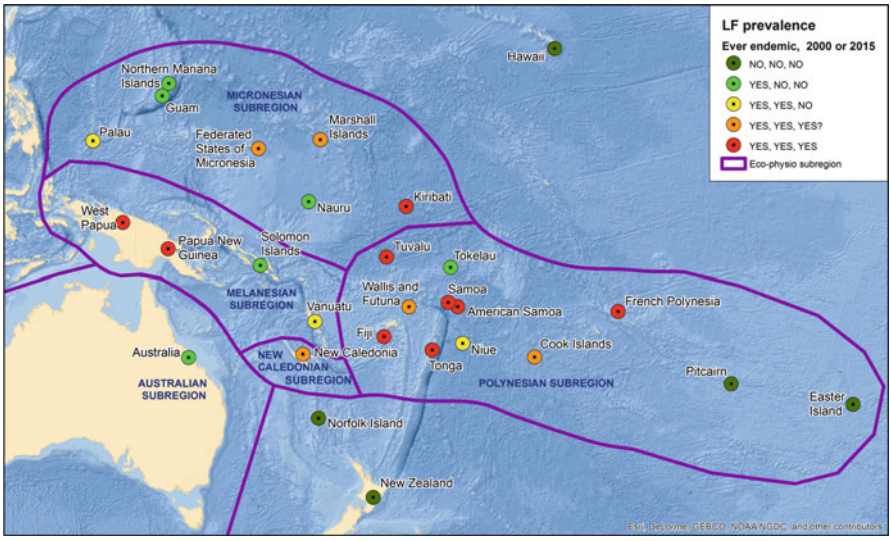

Fig. 4.1 Oceania, showing classification of LF subregions and filariasis endemicity over time (Derived from Sasa (1976), WHO (2006) and WHO (unpublished))

The Pacific Islands have conventionally been divided into three regions – Micronesia, Melanesia and Polynesia – based mostly on human ethnicity and historical migration patterns. Vectors are described as predominantly *Culex* (Micronesia), *Anopheles* (Melanesia) or *Aedes* (Polynesia) (Burkot et al. 2002; Manguin et al. 2010). However, neither the human ethnic divisions nor the mosquito distributions are hard and fast and do not closely align with the different parasite subtypes and transmission patterns of lymphatic filariasis (Fig. 4.1). Following the classification summarised by Sasa (1976), classification for filariasis eco-epidemiological subregion follows the vector type and the periodicity of the parasite. The presence of Mf in the peripheral blood is typically described as nocturnally periodic (Mf appear only during the night) in Micronesia and Melanesia, diurnally subperiodic (Mf are more common in the blood during the daytime but present also at night) in Polynesia or aperiodic (no diurnal pattern) in the New Caledonian subregion. For example, Fiji and New Caledonia are classified as Melanesian countries from the human perspective, but their vectors and *W. bancrofti* subtypes are in the Polynesian and New Caledonian eco-epidemiological subregions of filariasis transmission, respectively. Both have *Aedes* as vectors but very different species – predominantly *Ae. vigilax* in New Caledonia and *Ae. polynesiensis* in Fiji. It is also too simplistic to say that transmission occurs only during the day in Polynesian countries where *Ae. polynesiensis* is the major vector, since there are also night-biting vectors in some areas such as the Samoan Islands (Schmaedick et al. 2014; Hapairai et al. 2015). While there has been limited work on the topic, it appears likely that there is underappreciated genetic diversity in *W. bancrofti* and the possible existence of substrains (Small et al. 2013, 2014; McNulty et al. 2013).

There have been some recent reviews of filariasis or neglected tropical diseases that included Oceania (Kline et al. 2013; Cano et al. 2014; WHO 2006; Chanteau and Roux 2008; Hotez and Ehrenberg 2010) or in specific countries (Graves et al. 2013; Esterre et al. 2005), but no paper has systematically summarised all available empirical data on the prevalence of filariasis infection in mosquitoes as well as in humans, together with the prevalence of both acute and chronic morbidity. Given the push towards filariasis elimination with a target of 2020, it is important to understand the burden of disease in Oceania during the period prior to and during the current elimination campaign that started in 2000. The burden of morbidity is particularly important as the GPELF moves beyond mass drug administration campaigns towards addressing the second pillar of disability prevention.

Mosquito infection rates are of particular interest since it is often stated that the *Aedes* mosquito vectors in the Pacific are highly efficient vectors of filariasis, especially as the prevalence and density of worms in humans decline (Pichon 2002). This phenomenon is examined in the light of studies and meta-analyses of infectivity of people to mosquitoes and dynamics of the transmission in the vector (Snow and Michael 2002; Snow et al. 2006; Stolk et al. 2004). These studies suggest that previously accepted wisdom about facilitation, limitation and proportionality (describing the relationship between human and mosquito infections) in the transmission of filariasis in the Pacific may not be fully valid and requires a more nuanced approach.

Scope of the Review

We conducted a systematic search in PubMed for studies of lymphatic filariasis in the mosquito or human (including acute and chronic morbidity). PubMed was searched in October 2015 using the terms [['filar*' *or* 'Bancroft*'] *and* [Oceania *or* Pacific *or* (each individual country name)]] in the title, abstract or keywords. No date limits were imposed. Published and grey literature lists from an extensive search of literature from PNG (Graves et al. 2013) were added to the document library.

Removal of duplicates and unpublished documents as well as non-Oceania studies or those on non-human filariasis resulted in 571 articles that included information on countries in Oceania or were references on general topics including diagnostics, epidemiology or modelling. An additional 22 articles known to the authors but not found in electronic search were also reviewed for inclusion.

Inclusion criteria were that studies must be in the peer-reviewed literature or published reports/monographs in Oceania countries that reported data on mosquito infection, human infection or human morbidity (acute attacks/adenolymphangitis, lymphoedema/swollen limbs, elephantiasis or hydrocoele) that had a publication date of 1995 or later and included data from no earlier than 1990. Only studies with locally transmitted cases were included (no imported cases). Case reports, reviews, commentaries, diagnostic test evaluations without

population-based empirical data, cohort studies and clinical trials (without empirical population data) were excluded.

Data items extracted included, if relevant and available: date of study (reported if given, if not the year before publication was assigned as year of study); location; type of survey; sampling method; sample size; age group; method of filariasis infection or morbidity detection; prevalence of parasites, disease, antigen or antibody; species of mosquito; and 95 % confidence interval.

If data were part of a community-based trial, the pre- and post-trial data were reported separately. Similarly data from surveys in different years were reported separately where possible. Summary data on human infection over multiple sites were reported if possible and presented appropriately, especially for PNG sites where detailed data up to 2011 has already been published (Graves et al. 2013).

Sampling methods and sample sizes were noted and are included in tables of results as measures of survey quality, representativeness and precision of estimates. Outcomes are presented for mosquito infection by method of detection (dissection or PCR) and by region separately (Melanesia and Polynesia) given the differences in vector species.

Results of the Search Strategy

The publications identified in the initial search ranged in year from 1896 to 2015. There was only one paper pre-1944. Data extraction was restricted to the publication years 1995 onwards. Figure 4.2 shows the flow of study selection. After exclusion at either title/abstract or full text review stage, a total of 70 publications covering 79 distinct surveys in particular countries of Oceania were included. A 'survey' in a particular country can include either mosquito or human assessment or both.

Table 4.2 summarises the number of included studies by region and country. No published studies were identified from any Micronesian country. PNG and French Polynesia had by far the most studies in Melanesia and Polynesia, respectively. Indonesia (Papua/West Papua) had only one small study included. No published studies were identified from Wallis and Futuna; all other countries in Melanesia and Polynesia that were endemic at the start of the GPELF in 2000 had at least one published study since 1995.

The included studies are listed in Table 4.3, which shows the type of outcome recorded in each study (mosquito infection, human infection, human acute morbidity, human chronic morbidity) and sampling method.

Filariasis Endemicity by Country in Oceania

The endemicity of filariasis has been assessed at three time periods – firstly 'ever endemic', secondly in 2000 and lastly in 2015 – and the resulting classifications shown in Table 4.1 and Fig. 4.1. Note that Indonesia's Maluku Islands are excluded from this review which is of transmission areas with only *W. bancrofti* filariasis.

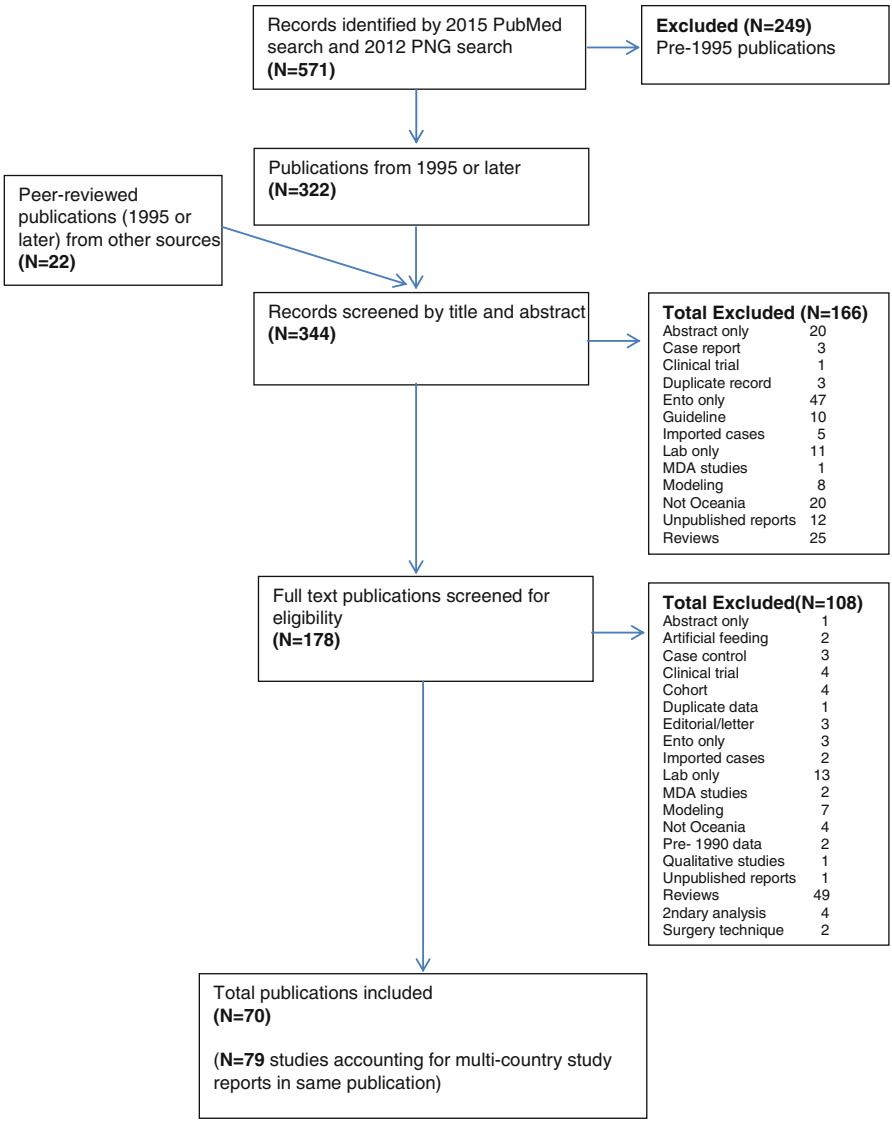

Fig. 4.2 Flow chart of search results

There are 33 countries, territories or provinces listed in Table 4.1, of which 24 have ever been endemic for filariasis. Of these 24, 18 were classified as being endemic in 2000 at the start of GPELF and thus required mass drug administration (MDA). By 2015, only ten countries were still experiencing ongoing transmission. Countries or areas remaining endemic for filariasis in 2015 numbered four

Table 4.2 Summary of included studies published 1995 or later, by region/country

Region	Number of studies
Micronesia	***0***
Melanesia	***40***
Fiji	2
Indonesia	1
New Caledonia	2
PNG	30
Solomon Islands	1
Vanuatu	4
Polynesia	***39***
American Samoa	6
Cook Islands	4
French Polynesia	16
Niue	1
Samoa	7
Tonga	3
Tuvalu	2
Total	***79***

in Melanesia, one in Micronesia and five in Polynesia. A further five countries or territories (New Caledonia, Federated States of Micronesia, Republic of the Marshall Islands, Cook Islands and Wallis and Futuna) were thought to still have transmission only in very localised areas or had interrupted it completely but had not yet been 'validated' as having reached this milestone. Four of these countries had implemented MDA at least in part of the country, with New Caledonia being the exception.

Three countries that were definitely endemic in 2000 had achieved elimination of transmission by 2015: Vanuatu, Palau and Niue. The process of validation involves submission of a 'dossier' for WHO review after completing MDA at high coverage for at least 5 years, followed by three transmission assessment surveys (TAS) in young school-age children to confirm that the number of incident cases is below a defined threshold. Because of the potential for resurgence, several years must then elapse between validation and certification of elimination. During this period, routine surveillance is needed in order to detect potential resurgence.

Filariasis Infection in the Mosquito Population in Oceania

Relatively few studies (19 identified) have been published on mosquito infection rates by either dissection or PCR. The species and numbers of mosquitoes analysed reflected those captured in particular sites. The most effective, efficient and

Table 4.3 Studies included, by region and country

Study name	Reference	Year of study	Location 1	Location 2	Sampling	Study with data on infection in:			
						Mosquito (dissection or PCR)	Human (Mf, Ag, Ab)	Acute Morbidity	Chronic Morbidity
Melanesia									
Fiji									
Mataika (1998)	(Mataika et al. 1998)	1990–1991	Eastern division	Kadavu Is	Convenience		X		
Anon (2012)	(Anon 2012)	2001–2006	Nationwide		Convenience and stratified cluster		X		X
Indonesia									
Bhullar (2010)	(Bhullar and Maikere 2010)	2006–2008	West Papua	Asmat	Patients at clinics		X		
New Caledonia									
Monchy (1999)	(Monchy et al. 1999)	1995–1997	Ouvéa Is		Patients at health facilities		X		
Daures (2015)	(Daures et al. 2015)	2013	Nationwide		Patients at health facilities		X		

PNG									
Bockarie (1996b)	(Bockarie et al. 1996)	1993–1994	East Sepik	Ambunti-Dreikikir	Purposive	X			
Alexander (1999a)	(Alexander et al. 1999)	1993–1994			Purposive			X	
Alexander (2000a)	(Alexander 2000)	1993–1994			Purposive		X	X	X
Kazura (1997a)	(Kazura et al. 1997)	1994			Purposive		X		X
Tisch (2001)	(Tisch et al. 2001)	1994			Purposive		X		
Bockarie (1998)	(Bockarie et al. 1998)	1994–1995			Purposive	X	X		
Bockarie (2000b)	(Bockarie et al. 2000b)	1994–1995			Purposive	X	X		
Tisch (2011)	(Tisch et al. 2011)	1993–1997			Purposive			X	
Bockarie (2002a)	(Bockarie et al. 2002a)	1994–1998			Purposive		X		X
Bockarie (2000c)	(Bockarie et al. 2000c)	1998			Purposive	X			
King (2001a)	(King et al. 2001)	2000(?)			Purposive		X		X
Hise (2003)	(Hise et al. 2003)	2002(?)			Purposive				X
Tisch (2008)	(Tisch et al. 2008)	1994–2003			Purposive		X		
Mehlotra (2010)	(Mehlotra et al. 2010)	2009(?)			Purposive		X		
Reimer (2013)	(Reimer et al. 2013)	2007–2010			Purposive	X			
Bockarie (2000a)	(Bockarie et al. 2000a)	1996	Madang	Middle Ramu	Purposive	X	X		
Alexander (2001)	(Alexander et al. 2001)	1999	Madang	Madang Urban	Convenience	X	X		

(continued)

Table 4.3 (continued)

Study name	Reference	Year of study	Location 1	Location 2	Sampling	Study with data on infection in:			
						Mosquito (dissection or PCR)	Human (Mf, Ag, Ab)	Acute Morbidity	Chronic Morbidity
Bockarie (2002b)	(Bockarie et al. 2002b)	1998	Madang	Sumkar (Bagabag Is)	All households		X		X
Bockarie (2007a)	(Bockarie et al. 2007)	1998–2001			Convenience		X		
Tobian (2003)	(Tobian et al. 2003)	2002(?)	Madang	Usino-Bundi	Convenience				X
Rao (2009)	(Rao et al. 2009)	2001–2003			Purposive	X			
Weil (2008a)	(Weil et al. 2008)	2001–2006			Purposive	X	X		
Sapak (1997)	(Sapak and Williams 1997)	1994	Milne Bay	Alotau	Random households		X		
Sapak (1998)	(Sapak et al. 1998)	1995			Convenience		X		
Sapak (2000)	(Sapak et al. 2000)	1996			Purposive		X		
Selve (2000)	(Selve et al. 2000)	1998–1999	Milne Bay	Samarai-Murua (Misima Is)	Convenience		X		
Hii (2000b)	(Hii et al. 2000)	1993	New Ireland	Namatanai (Lihir Is)	Convenience	X	X		X
Mitja (2011)	(Mitja et al. 2011)	2003–2008			Census		X		
Melrose (2000c)	(Melrose et al. 2000)	1991–1997	Seven provinces	Multiple sites	Convenience		X		
Reeve (2014)	(Reeve and Melrose 2014)	2006	New Ireland and W New Britain		Convenience		X		

Solomon Is									
Harrington (2013)	(Harrington et al. 2013)	2011	Malaita	Atoifi area	Convenience		X		
Vanuatu									
Fraser (2005)	(Fraser et al. 2005)	2002	Nationwide	Sentinel sites	Purposive		X		
Huppatz (2009)	(Huppatz et al. 2009)	1998–2007	Nationwide	Baseline and sentinel sites	Convenience and stratified cluster		X		
Joseph (2011b)	(Joseph et al. 2011b)	2007	Nationwide	Schools	TAS		X		
Chu (2013)	(Chu et al. 2013)	2010–2012	Penama	Schools	TAS		X		
Polynesia									
American Samoa									
Liang (2008)	(Liang et al. 2008)	2001–2006	Tutuila	Sentinel sites	Convenience and purposive		X		
Chambers (2009)	(Chambers et al. 2009)	2006	Tutuila		Purposive	X			
Mladonicky (2009)	(Mladonicky et al. 2009)	2006	Tutuila		Purposive		X		
Chu (2013)	(Chu et al. 2013)	2011	Tutuila	Schools	TAS		X		
Lau (2014)	(Lau et al. 2014)	2010	Nationwide		Simple random by household		X		
Schmaedick (2014)	(Schmaedick et al. 2014)	2011	Nationwide		Stratified by village	X			

(continued)

Table 4.3 (continued)

Study name	Reference	Year of study	Location 1	Location 2	Sampling	Study with data on infection in:			
						Mosquito (dissection or PCR)	Human (Mf, Ag, Ab)	Acute Morbidity	Chronic Morbidity
Cook Is									
Steel (2001a)	(Steel et al. 2001)	1992	Mauke Is		Census				X
Cuenco (2009)	(Cuenco et al. 2009)	1992	Mauke Is		Census		X		
Steel (2012)	(Steel et al. 2012)	1992	Mauke Is		Census		X		
Huppatz (2009)	(Huppatz et al. 2009)	1999–2005	Nationwide		Convenience and stratified cluster		X		
French Polynesia									
Lardeux (1995)	(Lardeux et al. 1995)	1991	Society Is	Raiatea (Opoa)	Purposive?	X	X		
Nguyen (1996)	(Nguyen et al. 1996)	1991–1994		Raiatea (Opoa)	Convenience		X		
Moulia-Pelat (1995b)	(Moulia-Pelat et al. 1995)	1994	Society Is	Tahaa Is	Census		X		
Nicolas (1997b)	(Nicolas et al. 1997)	1994		Tahaa Is	Convenience		X		
Nicolas (1997d)	(Nicolas 1997)	1994		Tahaa Is	Convenience				X
Nicolas (1999)	(Nicolas et al. 1999)	1994		Tahaa Is	Convenience		X		
Nicolas (1997a)	(Nicolas and Scoles 1997)	1996?		Tahaa Is	Convenience	X			
Esterre (2001)	(Esterre et al. 2001)	1997–1999	Society Is	Maupiti	Census?	X	X		

Nguyen (1999)	(Nguyen et al. 1999)	1997	Leeward Is, Society Is	Incl. Maupiti	Convenience		X		
Russell (2005)	(Russell et al. 2005)	2003–2004	Society Is	Moorea	Convenience	X			
Plichart (2006)	(Plichart et al. 2006)	2003–2004		Moorea	Convenience	X			
Hapairai (2013a)	(Hapairai et al. 2013)	2011		Moorea (Afareaitu)	Purposive	X			
Chanteau (1995)	(Chanteau et al. 1995)	1994?	Australes and Society Is	Rurutu, Moorea, Raiatea	Convenience		X		
Mou (2009)	(Mou et al. 2009)	2008	Nationwide		Stratified cluster		X		X
Gass (2012)	(Gass et al. 2012)	2007–2008	Nationwide	School and community	TAS		X		
Musso (2012)	(Musso and Vialette 2012)	1998 and 2010–2011	Nationwide and Papeete Hosp.		Patients at health facilities		X		
Niue									
Huppatz (2009)	(Huppatz et al. 2009)	2001–2004	Nationwide	Baseline and sentinel sites	Census		X		
Samoa									
Joseph (2010a)	(Joseph and Melrose 2010)	2008?	Upolu	Siufaga village	Purposive		X		
Hapairai (2015)	(Hapairai et al. 2015)	2012	Upolu	Fasito'o Tai village	Purposive	X			
Ichimori (2007)	(Ichimori, 2007)	1993–1998	Nationwide	Upolu and Savai'i	Convenience		X		

(continued)

Table 4.3 (continued)

Study name	Reference	Year of study	Location 1	Location 2	Sampling	Study with data on infection in:			
						Mosquito (dissection or PCR)	Human (Mf, Ag, Ab)	Acute Morbidity	Chronic Morbidity
Huppatz (2009)	(Huppatz et al. 2009)	1999–2004	Nationwide	Baseline and sentinel sites	Convenience and stratified cluster		X		
Joseph (2011b)	(Joseph et al. 2011b)	2007	Nationwide	Upolu and Savai'i	Stratified cluster		X		
Joseph (2011a)	(Joseph et al. 2011a)	2008	Nationwide	Upolu and Savai'i	Convenience		X		
Joseph (2011c)	(Joseph et al. 2011c)	2008	Nationwide	Upolu and Savai'i	Convenience		X		
Tonga									
Huppatz (2009)	(Huppatz et al. 2009)	1999–2006	Nationwide	Baseline and sentinel sites	Convenience and stratified cluster		X		
Joseph (2011b)	(Joseph et al. 2011b)	2007	Nationwide	Schools	TAS		X		
Chu (2014)	(Chu et al. 2014)	2012?	Nationwide	Schools	TAS		X		
Tuvalu									
Joseph (2010a)	(Joseph and Melrose 2010)	2009?	Nationwide		Convenience		X		
Gass (2012)	(Gass et al. 2012)	2007–2008	Nationwide	School and community	TAS		X		

representative trapping and sampling methods for mosquito infection surveys are not well developed; most entomological studies reported here were conducted in areas or villages where human studies were also being done, which obviously has benefits for comparative purposes (Table 4.3). The exceptions were a comprehensive nationwide xeno-monitoring survey in American Samoa, stratified by village (Schmaedick et al. 2014), a smaller study in one village in Samoa (Hapairai et al. 2015) and a well-designed mark–release–recapture study in French Polynesia (Hapairai et al. 2013).

Sample size in mosquito surveys is obviously dependent on the numbers able to be captured and the species distribution. Sampling intensity reflects the relative importance of different vectors in different areas, with numbers varying from less than 10 to over 10,000 dissected for the same species (Table 4.4). The PoolScreen approach which generates confidence intervals around estimates is useful for PCR-detected infection rate estimates and allows the possibility of pooling vectors caught in smaller numbers to generate reasonably precise estimates (Table 4.5). The most important factor for mosquito infection studies is that they reflect the population actually biting humans and that they represent infection rates with human (rather than animal) filariasis species and in competent vectors. Some of these aspects are still under investigation.

In Melanesian countries, the only studies reported have been from PNG, covering three provinces (Table 4.4). *An. punctulatus* infected with L3 (or in one study, any stage larvae) by dissection was found only in East Sepik Province, ranging from 0.0 to 2.1 % infection prevalence. There was a trend of decreasing infection over time in longitudinal studies, demonstrating the likely effect of MDA or long-lasting insecticidal net (LLIN) distribution. Infections were found by dissection in *An. farauti* (0.5 % in Madang Province and 0.6 % in New Ireland), in *An. koliensis* (1.5 % in East Sepik Province) and in *Cx. quinquefasciatus* (1.3 % in an urban area of Madang Province).

PCR detection of infections usually analysed pools of mosquitoes, with estimation of prevalence and 95 % CI using the PoolScreen software. Studies in *An. punctulatus* detected higher infection rates than dissection, ranging from 1.0 to 19.4 % in two provinces. In the Madang study site, decline in PCR-detected prevalence over time in conjunction with MDA was very striking.

There were studies of infection in mosquitoes in three Polynesian countries: American Samoa, French Polynesia and Samoa (Table 4.5). Whether by dissection or PCR, infection was detected in all but two samples of mosquitoes tested. Almost all studies investigated *Ae. polynesiensis*, mostly by PCR; infections were also detected in all other *Aedes* species tested by PCR. Prevalence ranged from 0.1 to 4.7 % in *Ae. polynesiensis* by PCR.

Over time in Maupiti, French Polynesia, between 1997 and 1999, the prevalence of infection by dissection declined from 1.4 to 0.1 %; similar decline was not seen in villages of Moorea that were assessed by PCR in two consecutive years 2003 and 2004.

Table 4.4 Mosquito infection data – Melanesia

Study name (see Table 4.2 for reference)	Year of study	Location	Dissection: % infected with L3 (*N*)										PCR : predicted % pos (95% CI)
			An. punctulatus sl	*An. farauti*	*An. koliensis*	*An. bancrofti*	*An. karwari*	*Cx. annulirostris*	*Cx. quinquefasciatus*	*Ae. spp*	*Ar. spp*	*Ma. uniformis*	*An. punctulatus sl*
PNG													
Bockarie (1996b)	1993–1994	East Sepik, Ambunti-Dreikikir	2.1 (9551)	0.0 (14)	1.5 (585)	0.0 (7)		0.0 (1371)	0.0 (127)			0.0 (255)	
Bockarie (1998, 2000b)	1994		1.7 (10,237)										
	1995		0.4 (7762)										
Bockarie (2000c)	1998		0.0 (633)										1.8 (0.9–3.1)[a] 1.2 (0.5–2.3)[b]
Reimer (2013)	2007		1.8 (8181)[c]										19.4 (16.7–22.4)
	2010		0.4 (678)										14.9 (10.7–20.0)
Bockarie (2000a)	1996	Madang, Middle Ramu	0.0 (137)	0.0 (38)			0.0 (846)	0.0 (14)	0.0 (7)[d]	0.0 (24)	0.0 (60)		
Alexander (2001)	1999	Madang, Madang urban	0.0 (15)					0.0 (50)	1.3 (80)	0.0 (20)			
Bockarie (2002b)	1998	Madang, Sumkar (Bagabag Is)	0.0 (14)	0.5 (400)				0.0 (4)	0.0 (578)				

Rao (2009)	2001–2003	Madang, Usino-Bundi											4.9 (4.0–6.0)
Weil (2008a)	2001												11.4 (10.9–21.3)
	2003												15.1 (11.7–19.2)
	2004												3.7 (2.2–5.6)
	2005												4.8 (3.3–6.7)
	2006												1.0 (0.4–2.2)
Hii (2000b)	1993	New Ireland, Namatanai (Lihir Is)	0.0 (80)	0.6 (1906)	0.0 (10)			0.0 (18)	0.0 (49)		0.0 (174)		

An Anopheles, *Cx* Culex, *Ae* Aedes, *Ar* Armigeres, *Ma* Mansonia, *spp* species, *sl* sensu lato
[a]ELISA PCR
[b]Standard PCR
[c]Any larval stage
[d]*Culex* any species

Table 4.5 Mosquito infection data – Polynesia

Study name (see Table 4.2 for reference)	Year of study	Location	Dissection: % infected with L3 (*N*)			PCR: predicted % pos (95 % CI)				
			Ae. polynesiensis	*Ae. finlaya* group	*Ae.* spp	*Ae. polynesiensis*	*Ae. finlaya* group	*Ae. aegypti*	*Ae. upolensis*	*Cx. quinquefasciatus*
American Samoa										
Chambers (2009)	2006	Tutuila	0.16 (1894)[a]			0.7 (0.3–1.2)		1.2 (0.02–3.3)	0.4 (0.02–2.0)	
Schmaedick (2014)	2011	Nationwide				0.3 (0.2–0.4)	0.09 (0.003–0.5)	0.9 (0.4–1.8)	0.0 (0.0–0.7)	0.1 (0.03–0.3)
French Polynesia										
Lardeux (1995)	1991	Society Is, Raiatea	2.0 (1740)							
Nicolas (1997a)	1996?					3.0 (1.2–6.0)				
Esterre (2001)	1997	Society Is, Maupiti				1.4 (1.0–2.0)				
	1999					0.1 (0.0–0.3)				
Russell (2005)	2003–2004	Society Is, Moorea	0.4 (853)		0.0 (341)					
Plichart (2006)	2003	Society Is, Moorea: Afareaitu	8.3 (216)[a]			2.5 (1.2–43)				
		Haumi	1.7 (179)[a]			0.8 (0.2–2.0)				
		Maatea	1.3 (478)[a]			0.4 (0.2–1.0)				
		Teavaro	3.0 (67)[a]			3.4 (1.0–8.0)				
		Vaiare	6.2 (81)[a]			1.8 (0.3–5.1)				
	2004	Society Is, Moorea: Afareaitu				3.7 (1.6–7.0)				
		Maatea				0.4 (0.1–1.5)				
		Vaiare				1.4 (0.2–5.0)				

Hapairai (2013a)	2011	Society Is, Moorea: Afareaitu				0.8 (0.2–2.2)				
Samoa										
Hapairai (2015)	2012	Upolu, Fasito'o Tai				4.7 (3.6–6.1)	0.7 (0.2–3.4)			

L3 third-stage larvae, *An* Anopheles, *Cx Culex*, *Ae Aedes*, *spp* species
[a]Any-stage larvae

Filariasis Infection in the Human Population in Oceania

The great majority of the studies included in this review (62 out of 79) reported infection rates in the human population, using either microscopy for Mf, rapid immunochromatographic test (ICT) or the Og4C3 ELISA for adult worm circulating antigen, PCR detection of filarial DNA in blood or the Bm14 antibody test (Table 4.6). A small number of studies reported on the urine antibody test, the Wb123 antibody test or the PanLF test. It is known that infection rate assessed by antigen tests (ICT or Og4C3) results in higher estimates of prevalence than Mf (Gass et al. 2012), since the serological tests detect circulating antigen from adult worms which may or may not be producing Mf. Antibody tests of course measure longer-term exposure but are a measure of ongoing transmission if tested in young children.

Table 4.6 summarises the infection prevalence by test used for the studies included in the time period of review. Studies in Table 4.6 show data reported for all ages, except where noted; some reported data for both all ages and for children (not shown in these cases) which is noted in footnotes. Estimates of less than 1 % prevalence by any measure are shown in bold to indicate where a country is approaching the threshold of elimination.

Sampling for surveys was most often by convenience or purposive methods (Table 4.3) and hence has a high risk of bias, usually towards inflating estimates by sampling areas with most risk of filariasis. The exceptions were surveys that used higher-quality sampling methods such as testing all households or residents of a particular island or area (Bockarie et al. 2002b; Mitja et al. 2011; Steel et al. 2001, 2012; Cuenco et al. 2009; Moulia-Pelat et al. 1995; Esterre et al. 2001; Huppatz et al. 2009-Niue), those that selected a random sample of households (Sapak and Williams 1997; Lau et al. 2014), those that used stratified cluster sampling (Anon 2012-2006 surveys) (Huppatz et al. 2009-some surveys reported in Vanuatu, Cook Is and Tonga) (Mou et al. 2009; Joseph et al. 2011b) and studies that used the transmission assessment survey (TAS) methodology (WHO 2011) for cluster sampling of children in schools or communities (Joseph et al. 2011b; Chu et al. 2013; Gass et al. 2012). Three studies used a passive approach of sampling in patients attending health facilities for any cause. This was done in both a geographically targeted and a nationwide survey in New Caledonia (Monchy et al. 1999; Daures et al. 2015), as well as in the only study identified in Indonesian Papua (Bhullar and Maikere 2010).

Sample size (which influences estimate precision) was crudely classified as small (<300), medium (300–1000) or large (>1000). When sites were combined within studies, most fell into the moderate- or large-size categories, with some exceptions that can be noted in Table 4.6. Future meta-analyses or other follow-up studies in these areas should take into account the precision of these estimates.

In Melanesia, PNG filariasis studies from 1980 to 2011 have been previously collated and described in detail by district and site (Graves et al. 2013) and thus will not be extensively discussed here, although the current review includes some additional and more recent papers and summarises studies by province. As previously noted, several MDA trials have had impressive impact on filariasis prevalence in

Table 4.6 Human infection data, by diagnostic test

Study name (see Table 4.2 for reference)	Year of study	Location	Mf % pos (*N*)	ICT % pos (*N*)	Og4C3 % pos (*N*)	PCR blood % pos (*N*)	Bm14 Ab % pos (*N*)
Melanesia							
Fiji							
Mataika (1998)	1990–1991	Eastern Div, Kadavu Is	*0.7* (2611)				
Anon 2012	2001 2006	Nationwide	1.4 (6771)	15.2 (5983) 9.6 (6771)			
Indonesia							
Bhullar (2010)	2006–2008	West Papua, Asmat		20.0 (492)			
New Caledonia							
Monchy (1999)	1995–1997	Ouvéa Is	3.7 (376)	33.5 (370)			
Daures (2015)	2013	Nationwide		*0.7* (1035)		*0.0* (7)	

Table 4.6 (continued)

Study name (see Table 4.2 for reference)	Year of study	Location	Mf % pos (*N*)	ICT % pos (*N*)	Og4C3 % pos (*N*)	PCR blood % pos (*N*)	Bm14 Ab % pos (*N*)
PNG							
Alexander (2000a)	1993–1994	East Sepik, Ambunti-Dreikikir	52.3 (2187)				
Kazura (1997a)	1994		66.0 (1666)				
Tisch (2001)	1994		67.0 (1332)		77.2 (1322)		
Bockarie (1998, 2000b)	1994 1995		32.4–88.3 10.7–52.7 *14 villages* (39–343)		60.7–97.2 *7 villages* (60–150)		
Bockarie (2002a) *(14 villages)*	1996 1997 1998		5.7–42.3 (253–802) 1.0–21.8 (257–819) *0.9*–10.9 (165–750)				
King (2001a)	2000(?)		55.7 (97)		77.3 (97)		
Tisch (2008)[a] *(14 villages)*	1994 1998 2003		70.4 (189) 4.0 (189) *0.8* (535)		84.0 (177) 78.0 (177) 16.9 (531)		88.9 (189) 49.0 (189)
Mehlotra (2010)	2009(?)		35.2 (517)			33.9 (517)	
Bockarie (2000a)	1996	Madang, Middle Ramu, 3 villages			50.0 (66) 44.5 (110) 12.8 (86)		
Alexander (2001)	1999	Madang, Madang Urban			2.5 (80)		

Bockarie (2002b)	1998	Madang, Sumkar (Bagabag Is)	28.5 (1026)		53.1 (1030)		
Bockarie (2007a)	1999 2001 2001		27.5 (277) 16.6 (381) 15.6 (348)		52.3 (527)		
Weil (2008a)[b]	2001 2003 2004 2005 2006	Madang, Usino-Bundi	 18.6 (571) 8.3 (696) 3.4 (714) 1.3 (529)	53.3 (627) 47.5 (558) 35.1 (692) 25.2 (695) 17.1 (543)			60.2 (683) 59.3 (560) 39.7 (696) 48.6 (693) 25.1 (550)
Sapak (1997)	1994	Milne Bay, Alotau	24.0 (75)				
Sapak (1998)	1995 *5 villages, daytime*		5.5–50.0 (6–28)				
Sapak (2000)	1996 *4 villages*				36.3–71.0 (? to 434)		
Selve (2000)	1998 1999	Milne Bay, Samarai-Murua (Misima Is)		19.0 (1644) 12.0 (942)			
Hii (2000b)	1993	New Ireland, Namatanai (Lihir Is)		*0.0*–43.3 (36–120)			
Mitja (2011)	2003 East 2003 West 2008 East 2008 West				7.7 (3009) 30.7 (1969) *0.8* (3709) 7.5 (2464)		

(continued)

Table 4.6 (continued)

Study name (see Table 4.2 for reference)	Year of study	Location	Mf % pos (*N*)	ICT % pos (*N*)	Og4C3 % pos (*N*)	PCR blood % pos (*N*)	Bm14 Ab % pos (*N*)
Melrose (2000c)	1990	Western *2 sites*	26.0–51.9 (293–676)		57.0–82.0 (300–676)		
	1993	Western	52.0 (485)		76.1 (485)		
	1993	New Ireland	20.0 (575)		55.0 (575)		
	1994	S Highlands	37.0 (181)		51.9 (181)		
	1994	Gulf	35.1 (222)		64.9 (222)		
	1996	W N Britain	10.1 (69)		37.7 (69)		
	1996	Madang			9.8 (133)		
	1996	Milne Bay *3 sites*	23.1 (212)	52.8 (212)	40.0–66.9		
	1997	Milne Bay *3 sites*		*0.0*–56.3 (61 to 144)	(50–212) 52.8 (144)		
	1998	New Ireland	20.7 (140)	32.1 (140)			
	1998	W Highlands		*0.0* (200)			
	1999	Western *2 sites*			15.0–77.6 (67–247)		
	2000	Western		67.8 (174)	83.2 (262)		
Reeve (2014)	2006	New Ireland, West New Britain	16.3 (808)	31.5 (863)	48.2 (817)		
Solomon Is							
Harrington (2013)	2011	Malaita, East Kwaio *2 sites*			*0.0–0.5* (110–197)		
Vanuatu							
Fraser (2005)	1998	Nationwide	15.0 (660)	27.7 (660)			
	2002	*8 sites*	*0.5* (1171)	6.4 (1171)			
	2002	*2 sites/hosp.*	3.5 (347)	5.9 (769)			

Huppatz (2009)	1998 2005	Nationwide	4.8 (4362) *0.2* (7576)				
Joseph (2011b)	2007	Nationwide[c]	*0.0* (3840)	*0.0* (3840)			
Chu (2013)	2010 2012	Penama[d]		*0.0* (933) *0.2* (954)			
Polynesia							
American Samoa							
Liang (2008)	2001 2003 2006	Tutuila *4 sites* *3 sites* *Schools* [d]	2.7 (1024) 1.0 (917) *0.1* (1371)	11.5 (1024) 13.7 (917) *0.9* (1371)			
Mladonicky (2009)	2006		*0.2* (569)	4.2 (563)			14.1 (538)
Chu (2013)	2011			*0.2* (949)			
Lau (2014)	2010	Nationwide[e]			3.5 (802)		17.9 (806)
Cook Is							
Cuenco (2009)	1992	Mauke Is			15.0 (587)		
Steel (2012)	1992[f]		4.5 (530)		16.0 (550)		
Huppatz (2009)	1999 2005	Nationwide		8.6 (1884) 1.3 (2202)			
French Polynesia							
Lardeux (1995)	1991	Society Is, Raiatea	21.1 (577)				
Nguyen (1996)[g]	1991 1992 1993 1994		21.2 (1161) 21.0 (1179) 12.5 (1182) 6.9 (548)				

(continued)

Table 4.6 (continued)

Study name (see Table 4.2 for reference)	Year of study	Location	Mf % pos (*N*)	ICT % pos (*N*)	Og4C3 % pos (*N*)	PCR blood % pos (*N*)	Bm14 Ab % pos (*N*)
Moulia-Pelat (1995b)	1994 1995	Society Is, Tahaa Is	22.4 (1717) 18.0 (1717)				
Nicolas (1997b)	1994[h]		22.0 (1881)				
Nicolas (1999)	1994[h]				47.4 (1073)		
Esterre (2001)	1997[i]	Society Is, Maupiti	*0.4* (999)		4.6 (997)		21.5 (1055)
Chanteau (1995)	1994	Australes and Society Is, Rurutu, Moorea, Raiatea	1.0–21.5 (5–361)		1.1–41.3 (223–1958)		
Nguyen (1999)	1997	Leeward and Society Is *3 sites*	3.5–12.7 (200–996)	2.4–19.0 (200–996)	4.1–27.1 (200–996)		
Mou (2009)	2008	Nationwide	1.1 (1180)	11.3 (1180)			
Gass (2012)[j]	2007–2008	Nationwide	3.8 (713)	9.0 (1334)	6.3 (1355)	2.2 (1005)	46.0 (1329)
Musso (2012)	2011	Papeete hospital		11.3 (222)	13.5 (1174)		
Niue							
Huppatz (2009)	1999 2001 2004	Nationwide		3.1 (1794) 1.4 (1630) *0.2* (1285)			
Samoa							
Ichimori et al. (2007)[k]	1993 1994 1995 1996 1997 1998	Nationwide *16 health districts*	4.1 (9525) 2.2 (10,112) 1.9 (4551) 2.2 (5997) 1.7 (8305) 1.1 (4054)	4.2 (4054)			

Huppatz (2009)	1999 2004	Nationwide		4.5 (7006) *0.4* (12,719)			
Joseph (2010a)	2009	Upolu, Siufaga village			50.5 (200)		
Joseph (2011b)[c]	2007	Savaii Upolu	*0.3* (2738) 1.2 (2738)	1.7 (2315) 5.7 (2315)			
Joseph (2011a)	2008	Nationwide *4 sites*	*0.0*–3.2 (344–617)	1.6–14.6 (344–617)			34.3–74.9 (344 to 617)
Joseph (2011c)[l]	2008	Nationwide *5 sites*			*0.0*–9.5 (86–167)		7.8–62.0 (126–167)
Tonga							
Huppatz (2009)	2000 2006	Nationwide		2.7 (4002) *0.4* (2927)			
Joseph (2011b)[c]	2007	Nationwide *3 sites*	*0.0* (797)	*0.0* (797)			
Chu (2014)[d]	2007	Nationwide		*0.3* (2434)			
Tuvalu							
Joseph (2010a)	2009?	Nationwide					27.7 (94)
Gass (2012)[m]	2007–2008	Nationwide	*0.1* (1015)	5.0 (1448)	4.9 (1333)	*0.3* (1063)	

[a]Results for some years and tests also given in publication for children 1–6 years old
[b]Results for some years and tests also given in publication for children 2–11 years old
[c]Children 5–6 years old
[d]Children 6–7 years old
[e]Ages 18 years and over, Wb123 antibody prevalence 8.1 % (N = 806)
[f]Results also given in publication for children 1–5 years old, Wb123 antibody prevalence in all ages 60.4 % (N = 553)
[g]Ages 15 years and above
[h]Ages 20 years and above
[i]Results for some tests also given in publication for children <2 years old
[j]PanLF prevalence 14.0 % (N = 1306), urine Ab prevalence 22.5 % (N = 1268)
[k]Results for children <15 years also given
[l]Children <10 years old
[m]PanLF prevalence 24.2 % (N = 1066), urine Ab prevalence 20.1 % (N = 955)

PNG, but these longitudinal studies are concentrated in a few areas (East Sepik, Madang and New Ireland Provinces).

On the other side of the island of New Guinea, only one small study of filariasis in Indonesian Papua has been reported (in contrast to the large number of studies from PNG), showing 20.0 % prevalence in patients attending clinics. The approach of surveying patients attending health facilities was also used in New Caledonia and demonstrated a striking difference in prevalence between Ouvéa Island and a nationwide survey. One study in Solomon Islands (a formerly endemic country) suggested a method for post-elimination surveillance following detection of a suspicious case of filariasis in a relatively young resident. A nationwide survey in Fiji demonstrated extensive ongoing transmission in that country in 2006, with no published surveys since then. Finally for Melanesia, Vanuatu has clear evidence of decline in prevalence leading to its current status of having achieved interruption of transmission.

MDA was not necessary in Solomon Islands and has not been initiated in New Caledonia due to doubt about its necessity. MDA has been conducted nationwide in Fiji and Vanuatu for at least 5 years since 2000. MDA in PNG (outside of research projects or private sector/mining company programmes) has been limited to a few provinces, with only Milne Bay receiving 3 years of MDA of uncertain coverage. Coverage in Indonesian Papua is also unclear. However, all Melanesian countries except Fiji and New Caledonia (where there is no malaria or *Anopheles*) have benefited from large-scale LLIN distributions conducted for malaria prevention and control.

In Polynesia, the country with the most published studies identified is French Polynesia. However, several published studies were also identified from American Samoa, Samoa, Cook Islands, Niue, Tonga and Tuvalu. In most cases, the high prevalence (5 % or higher by ICT) in these countries in the 1990s and early 2000s (before MDA campaigns started) is demonstrated; the exception is Samoa between 1993 and 1998 (Ichimori et al. 2007) during which time MDA was under way with DEC followed by DEC plus ivermectin. However, antigen prevalence was still 4.5 % in Samoa at the start of PacELF. Decline in filariasis prevalence over time is evident in all countries, with most progress achieved in American Samoa, Niue and Tonga as demonstrated by published reports (Table 4.6).

All endemic countries in Polynesia (see list in Table 4.1) have received MDA of at least 5 years (and frequently many more) since 2000 under PacELF. Coverage has generally been adequate (WHO 2006) with the exception of French Polynesia. Vector control strategies such as larval source management are recommended in addition to MDA (Burkot and Ichimori 2002) but are of uncertain efficacy in *Aedes* transmission areas and are not comprehensively implemented or evaluated. Impact of LLIN when vectors are day biting is likely to be limited.

Table 4.7 Human acute and chronic filariasis morbidity

Study name (see Table 4.2 for reference)	Year of study	Location	% with acute morbidity (*N*)	Incidence acute morbidity episodes/ person/year (*N*)	% with enlarged limbs/ elephantiasis (*N*)	% adult men with hydrocoele (physical exam) (*N*)	% with hydrocoele (ultrasound exam) (*N*)	% with any chronic morbidity (*N*)
Melanesia								
PNG								
Alexander (1999a)	1994	East Sepik, Ambunti-Dreikikir		0.31 (3262)				
Alexander (2000a)	1994		16.3 (2187)	0.25–0.45	3.7 (2197)			
Kazura (1997a)	1994				6.2 (1892)	12.3 (907)		
Tisch (2011)	1993 1994 1995 1996 1997			0.39 0.31 0.15 0.19 0.2				
Bockarie (2002a)	1994 1998				5.3 (1273) 3.5 (998)	15.2 (726) 4.8 (563)		
King (2001)	2000? *2 villages*				3.1 (97)			
Hise (2003)	2003				4.2 (906)	1.7 (119)		
Bockarie (2002b)	1998	Madang, Sumkar (Bagabag Is)			2.4 (543)	4.4 (271)		

(continued)

Table 4.7 (continued)

Study name (see Table 4.2 for reference)	Year of study	Location	% with acute morbidity (*N*)	Incidence acute morbidity episodes/ person/year (*N*)	% with enlarged limbs/ elephantiasis (*N*)	% adult men with hydrocoele (physical exam) (*N*)	% with hydrocoele (ultrasound exam) (*N*)	% with any chronic morbidity (*N*)
Tobian (2003)	2002	Madang, Usino-Bundi				9.9 (342)	16.7 (342)	
Hii (2000b)	1993	New Ireland, Namatanai (Lihir Is)			5.7 (527)	1.5 (262)		
Polynesia								
Cook Is								
Steel (2001a)	1992				4.8 (313)	8.0 (313)		
French Polynesia								
Nicolas (1997d)	1994							2.0 (1800)
Mou (2009)	2008							0.5 (1180)

Filariasis Morbidity in the Human Population in Oceania

Morbidity studies were only reported from three countries – PNG, Cook Islands and French Polynesia (Table 4.7). One additional study in Fiji (Anon 2012) reported numbers of cases but no denominator. Sampling was convenience or purposive in all cases, except in Cook Islands where all consenting inhabitants of one island were evaluated (Steel et al. 2001). Sample sizes were moderate (>300) or large (>1000) in the majority of studies.

Acute filariasis morbidity (incidence of acute attacks) was rarely studied in Oceania despite being recommended as a surveillance method (Durrheim et al. 2003). However, several of the studies reported in PNG were large and included rarely available longitudinal information on the impact of MDA on both acute and chronic morbidity (Tisch et al. 2011; Bockarie et al. 2002b). The longitudinal studies from PNG showed the clear impact of MDA between 1993 and 1997 in reducing the incidence from 0.39 attacks per person per year to 0.2 (Tisch et al. 2011). The impact of MDA on chronic morbidity was also seen between 1994 and 1998 (Bockarie et al. 2002b), with prevalence of enlarged limbs reducing from 5.3 to 3.5 % and of hydrocoele in adult men from 15.2 to 4.8 %.

Other cross-sectional studies are useful for quantifying the burden of acute and chronic morbidity to enable alleviation programmes to be put in place in these highly (or formerly highly) endemic areas of Oceania. One study showed that using ultrasound to detect hydrocoeles is more sensitive than clinical examination (Tobian et al. 2003); this study found very high rates of hydrocoele in men residing in a district of Madang Province in PNG. Overall, the prevalence of chronic morbidity was high (>5 % when considering any type of morbidity) in most of these studies, but many are outdated now and new more representative information is needed.

Filariasis Transmission Dynamics in the Mosquito

Given that Oceania is the only area of the world with filariasis transmitted by *Aedes* day-biting (and night-biting) vectors in some areas, it is important to review the topic of the efficiency of different mosquito species. It has long been proposed that certain mosquito genera confer advantages or disadvantages on transmission of filarial worms at particular levels of filariasis prevalence, due perhaps to mosquito anatomical structures that may either destroy worms or assist their passage through the mosquito mouthparts. These phenomena are referred to as facilitation, limitation and proportionality (WHO 2013). For example, 'limitation' is supposed to apply to *Aedes* transmission, where it has been suggested that at low densities of Mf, numbers of L3 stages developing are roughly proportional to numbers of Mf ingested, whereas at high densities of Mf, there is density dependence limiting the numbers of L3 that are able to complete the development in the mosquito. The opposite phenomenon, 'facilitation', has been suggested to apply to *Anopheles*, whereby small numbers of Mf are supposed to be blocked by pharyngeal

armatures in the mosquito, reducing numbers of L3 developing, but large numbers of Mf can overwhelm this putative defence mechanism resulting in greater relative proportion of L3. Thus, *Aedes* mosquitoes are supposedly more efficient transmitters of filariasis than *Anopheles* spp. at lower levels of average Mf in the human population. However, these are all relative efficiencies, since both situations result in transmission that is not equivalent to 'proportionality', i.e. when the number of L3 stages developing in a mosquito is directly and linearly related to the number of Mf ingested earlier.

Recent summary modelling and meta-analysis studies have shed some clear light on this issue and suggest that transmission dynamics cannot be described in such simplistic terms. Transmission from human through mosquito and back again depends on two distinct stages: (1) the uptake of Mf by the mosquito into the midgut and (2) the development of those Mf into L3 stages in the proboscis of the infected mosquito. Both of these transitions can be affected by density dependence or other factors, which may be occurring in different ways in different genera. Two studies (Snow et al. 2006; Snow and Michael 2002) conducted a thorough analysis using empirical data on uptake of Mf and larval development in the mosquito in relation to average Mf density in the human population.

For the first part of the process, ten studies (three from Oceania) were included, covering eight different mosquito species in the genera *Aedes*, *Culex* and *Anopheles* (Snow and Michael 2002). Summarised results are shown in Fig. 4.3a and demonstrate that there is indeed density dependence in the relationship between ingested Mf and mean human parasite load (which varied between studies and mosquito species). Models of the relationship indicated that there was saturation of uptake and consequent peak percentage of mosquitoes infected in all three genera, but this saturation varied by genus, occurring at a lower mean Mf density and lower maximum percentage of mosquitoes infected in *Anopheles* than in *Culex* or *Aedes*.

The second stage of the process determines the fate of ingested Mf in mosquitoes after they are taken up (there being overall relatively fewer Mf in *Anopheles*). The second study (Snow et al. 2006) investigated vector-specific density dependence in the development from Mf to L3. This study reviewed 14 empirical studies, of which five were from Oceania, with the same range of mosquito species as before. The study modelled the relationship between L3 numbers and the known or estimated density of Mf taken up, and predicted the number of L3 that would develop, with strikingly different relationships for the three main genera (Fig. 4.3b). The larval infection pattern for *Culex* showed a density-dependent saturation pattern with a peak L3 load flattening at about 5 per mosquito and perhaps declining at the highest Mf ingestion load. The relationships for *Aedes* and *Anopheles* are more characteristic of a positive density-dependent sigmoidal relationship. These two different patterns could be seen to correspond to the previous concepts of 'limitation' in *Culex* with 'facilitation' in both *Aedes* and *Anopheles*. The underlying studies had differing mean Mf uptake ranges by genera, but the shape of the modelled relationship is very similar in the two latter genera at low levels of mean Mf uptake (0–10 per mosquito). However, *Aedes* differs from *Anopheles* in that for the latter, there is no

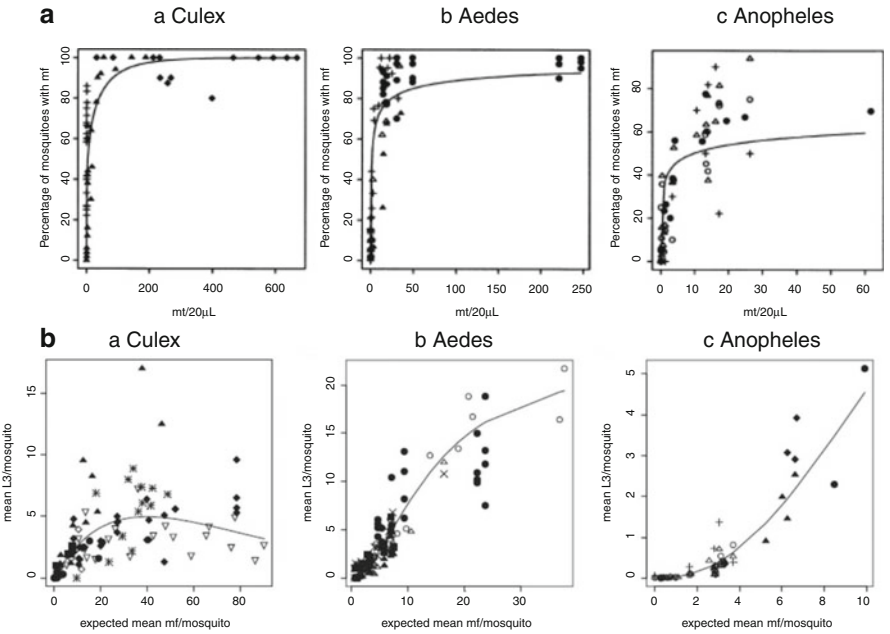

Fig. 4.3 Relative efficiency of different mosquito genera for transmitting filariasis. (**a**) Uptake of Mf to the mosquito blood meal according to mean Mf density in the human population (Snow and Michael 2002). Note different scales by genera resulting from source studies. (**b**) Relationship between mean Mf ingested in the mosquito blood meal and mean infective L3 (Snow et al. 2006). Note different scales by genera resulting from source studies

apparent saturation or 'flattening' of L3 numbers at higher ingested Mf densities, suggesting that 'facilitation' is stronger for *Anopheles* than for *Aedes*.

Overall the two studies together illustrate that usual statements about limitation, facilitation and transmission efficiencies in different mosquito genera are at best too simplistic and at worst potentially wrong. Further modelling based on these reviews and more mosquito infection studies, such as that recently performed in PNG (Erickson et al. 2013), are badly needed in order to predict the likelihood and timing of filariasis elimination in the diverse countries of Oceania.

Discussion and Conclusions

This review has systematically gathered information on infections with lymphatic filariasis caused by *W. bancrofti* in either mosquitoes or humans in Oceania, from available published literature in the last 20 years since 1995 (with data in such studies back to 1990 included). Information on the prevalence of morbidity resulting from infection, both acute and chronic, has also been collated for the same time period. The search identified 79 separate studies in 70 different publications.

Of the 24 countries, territories or areas in Oceania (as defined here, excluding the Indonesian province of Maluku) that have ever been found to be endemic for filariasis, 18 were classified as endemic in 2000, of which only ten had ongoing transmission in 2015. An additional five had probably interrupted transmission but had not been certified as having done so by 2015. The ten remaining endemic areas are Fiji, PNG, Indonesia/Papua and Indonesia/West Papua in Melanesia, Kiribati in Micronesia, and American Samoa, French Polynesia, Samoa, Tonga and Tuvalu in Polynesia. The data presented in this review show clearly the reduction in filariasis in the region over the 15-year period since the start of PacELF and GPELF, while not ignoring the remaining challenges particularly in PNG, Fiji, French Polynesia and Tuvalu where transmission definitely continues at least in some areas. Despite reduction in prevalence of infection in the region overall, few areas have reached a level below 1 %, even in young children with limited years of exposure.

Representativeness of sampling for many surveys was lacking, although has improved over time towards better powered surveys with random individual or cluster sample selection, albeit often in varying age groups and using different diagnostic tests or methods. Given that purposive selection of sites will always be necessary and important for clinical trials and intervention evaluations, it is still urgent that this type of study is counterbalanced by more representative estimates of filariasis prevalence in both humans and mosquitoes with better geographic coverage in neglected countries.

The studies identified here illustrate that the published literature on filariasis in Oceania is very unbalanced, both in terms of the geographic representation and the measured outcome focus (mosquito or human infection, human acute or chronic morbidity). No published studies were identified from anywhere in Micronesia. The most striking example of study bias in Melanesia is the very high number (30) of studies from PNG spanning the whole inclusion period from 1995 to 2015, contrasted with one small study in 2006–2008 from Indonesian Papua on the other side of the same island. Similarly in Polynesia, studies from French Polynesia (16) far outweigh those from any other country, although American Samoa and Samoa had six and seven studies, respectively. One Polynesian territory (Wallis and Futuna) had no publications identified.

There were 19 studies of mosquito infections and 62 of human infections, but only 13 of morbidity, one of which had no denominators given. No individual study included data on all aspects of filariasis infection in the same area, although that comprehensive view was often achieved by separate publications from the same areas, as in PNG/East Sepik Province/Ambunti-Dreikikir District and French Polynesia/Society Islands/Raiatea or Tahaa Islands. Several studies did include both mosquito and human infections, both human infections and morbidity data, or three of the four possible outcomes assessed. It is hoped that this systematic review provides data for future comparative studies of relationships and dependencies between these different outcome variables, as well as for mapping and spatial studies that will assist with prioritising the endgame of the filariasis elimination programme in Oceania.

This review has shown the increasing trend towards xeno-monitoring (PCR detection) rather than dissection for worms in mosquitoes but shows that infection in mosquitoes is often much higher than expected from the human prevalence. Further rollout and improvements in mosquito sampling and testing techniques together with modelling studies using recently revised understanding of transmission dynamics in the human–mosquito–human cycle (reviewed here) are encouraged in order to target and improve current control strategies.

It should be noted that this review did not include the large number of unpublished studies that are reported in PacELF meeting reports and presentation, country elimination dossiers (both completed and in preparation) and other national LF and NTD programme reports. Such information is currently being collected in a Pacific catalogue/repository of published and unpublished documents and database of extracted data through collaboration between WHO/WPRO, James Cook University, Nagasaki University and the Task Force for Global Health in Atlanta, with support from USAID. This catalogue and database will be available to support further systematic reviews, confirm interruption of transmission in more Pacific countries or assist those with remaining challenges to enhance efforts to achieve the goal, to publish 'success stories' and case studies of particular countries for documentation of filariasis elimination and to assist the global programme.

Given the recent high levels of infection in many areas of Oceania prior to PacELF, persisting levels in some areas, lifelong consequences of untreated filariasis infection, difficulty of effective vector control and paucity of available data on both acute attacks and chronic morbidity (lymphoedema, elephantiasis and hydrocoele), it is crucial that more good quality and nationally representative studies are done of the persisting burden of this disabling disease. This will guide intensified intervention and surveillance efforts to ensure that young people of the region are not exposed to ongoing risk of this devastating infection.

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