Economic evaluation of *Wolbachia* deployments in Suva, Fiji and in Port Vila, Vanuatu[*]

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2 June 2020

EXECUTIVE SUMMARY

Introduction

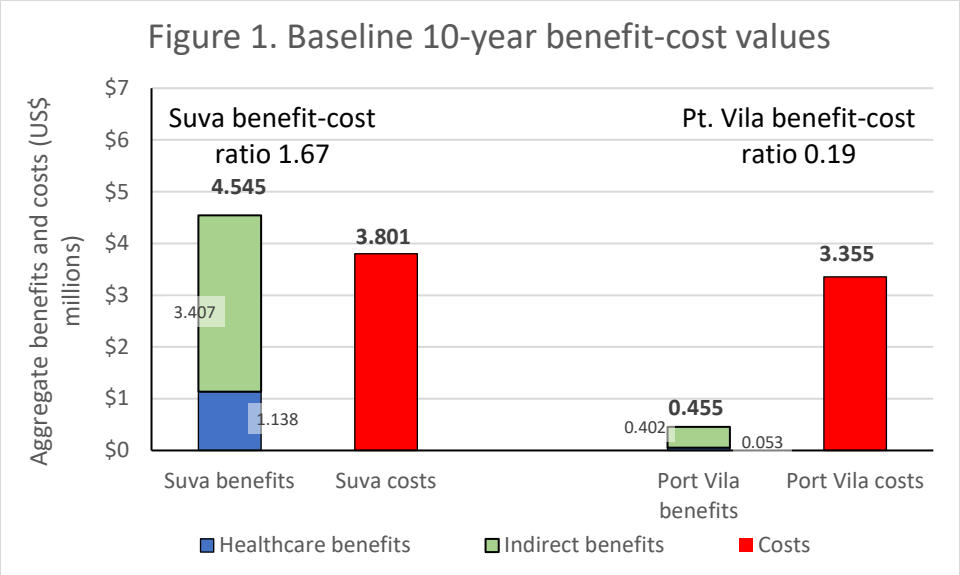
The World Mosquito Program deployed *Wolbachia* mosquitoes in Suva, Fiji and in Port Vila, Vanuatu over 2018-19 as a method for controlling dengue. Observational and modeling studies indicate that this technology appears effective and cost-effective in major cities of large endemic countries, such as Indonesia. However, the technology's cost-effectiveness in smaller countries is not known. We conducted both benefit-cost and cost-effectiveness analyses of *Wolbachia* deployment in the largest cities of two small Pacific Island countries. These countries, Fiji and Vanuatu, had 2018 per capita gross national incomes (GNI) of US$5,860 and US$3,130, respectively. The intervention areas in Suva, Fiji, and Port Vila, Vanuatu, had 225,000 and 54,000 inhabitants, respectively.

Key Results

Economic evaluations using primary and secondary economic and epidemiological data reveal that *Wolbachia* deployments proved economically advantageous and cost-effective in Suva, Fiji but not so in Port Vila, Vanuatu from a societal perspective. Based on a conservative 10-year lifetime of *Wolbachia's* durability and a baseline effectiveness of 75% (derived from the World Mosquito Program's quasi-experimental study in Yogyakarta), the benefit-cost ratio was 1.67 in Suva, meaning that *Wolbachia* deployment returns US$1.67 to the economy of Suva for every dollar spent. The fact that this ratio is greater than 1.00 indicates that the program is favorable. On the other hand, in Port Vila, Vanuatu, the benefit-cost ratio for an expected 10-year lifetime was only 0.19. As this ratio is substantially less than 1.00, *Wolbachia* was not favorable by this measure in Vanuatu (see **Figure 1**).

Under another metric, the incremental cost-effectiveness ratio (ICER), lower ratios are better. These ICERs were US$4,980/DALY averted in Suva and US$20,193 in Port Vila. Using criteria suggested by the World Health Organization (WHO) Macroeconomic Commission on Health, these ICERs represent multiples of 0.85 times the per capita GNI in Fiji and 6.45 times in Vanuatu. As the multiple of 0.85 is less than 1.00 but 6.45 exceeds 3.00, *Wolbachia* deployment was highly cost-effective in Fiji, but not cost-effective in Vanuatu.

[*] This work was supported by the Australia Department of Foreign Affairs and Trade (DFAT) through a contract to the World Mosquito Program at Monash University with a subcontract to Brandeis University. All views expressed are those of the authors.



In these middle-income countries, use of *Wolbachia* appears economically viable in Suva, a moderately sized city with a high dengue burden, but not in Port Vila, a small city with a lesser dengue burden. Even if *Wolbachia* in Port Vila remained effective permanently, it would still not be cost-beneficial nor cost-effective.

Interpretation

The best economic metric for policy makers is comparing the ICERs for these *Wolbachia* investments against other public health investments. These are best expressed as multiples of the per capita GNI, where smaller multiples denote better value. Recall that our ICERs for *Wolbachia* were 0.85 times per capita GNI for Fiji and 6.45 times for Vanuatu. Based on the World Bank's classification, Fiji is an upper-middle income country, while Vanuatu is a lower-middle income country. In brief, *Wolbachia* is almost comparable to alternatives in Fiji but substantially inferior in Vanuatu.

COMPLETE REPORT

Summary of approach

This economic analysis incorporated innovative approaches to address several methodologic challenges. To address gaps in secondary data, we incorporated expert opinion. To address incomplete testing of surveillance samples, we used multivariate models to predict dengue positivity. To assess the robustness of our estimations, we conducted sensitivity analyses varying the *Wolbachia* program effectiveness and its duration of expected benefits. Detailed results and data sources are presented in the sections below.

Base-case results

The total cost of program implementation was estimated to be AU$3,801,418 or US$2,724,438 in the Suva region of Fiji and AU$3,355,069 or US$2,404,545 in Port Vila, Vanuatu **(Table A1.1)**.

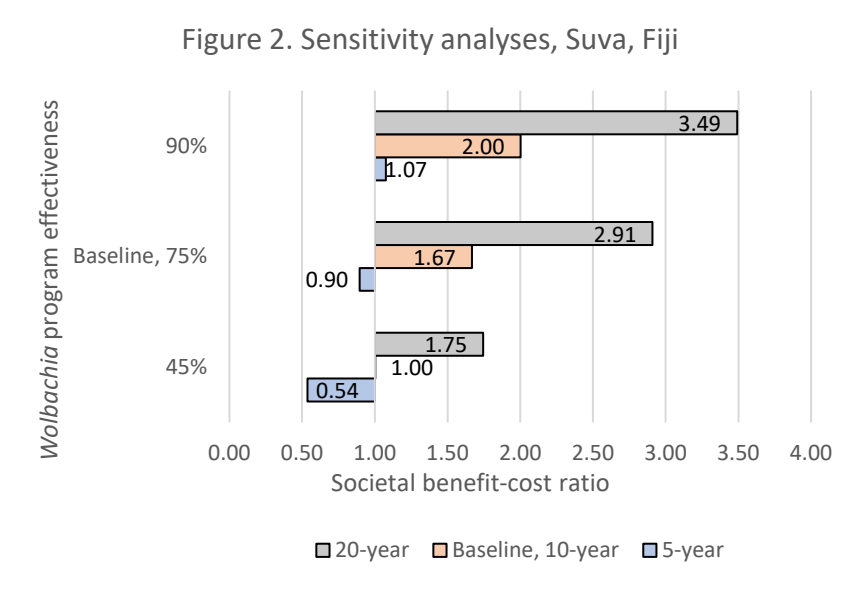
On average, these cities experienced an average of 2,500 and 605 dengue cases (437 and 11 hospitalized, 723 and 150 ambulatory, 1,341 and 445 not-medically attended, including 0.04 and 0.01 fatalities) per year. The fractional fatalities reflect variations and uncertainties among years. The average medical costs were US$177,859 and US$8,303 and aggregate economic costs were US$710,442 and US$71,141 annually, respectively. The *Wolbachia* program was estimated to prevent 1,875 of the 2,500 cases in Suva and 454 of the 605 annual cases in Port Vila. These are reductions of 75%, based on Yogyakarta estimates (see **Tables A1.2 and A1.3**).

Sensitivity analysis for Suva, Fiji

In Suva, Fiji, from a societal perspective that includes both direct and indirect costs averted, the benefits, discounted at a 3% rate, were estimated to be US$4,545,161. Sensitivity analyses for 5-, 10- and 20-year durations gave US$2,440,213, US$4,545,161 and US$7,927,188, respectively. The benefit-cost ratio in Suva, Fiji from a societal perspective was above 1 in the 10- and 20-year time horizon estimates. A 5.63-year time horizon was estimated to be the break-even period; that was the period for which the benefit-cost ratio was 1.00. Similarly, using DALYs discounted at a 3% rate, the gross cost-effectiveness ratio ranged from US$2,856/DALY averted to US$9,277 /DALY averted and translated to 0.49 and 1.58 times the GNI of Fiji, proving to be highly cost-effective (assuming a cost-effectiveness threshold of 3 times the GNI of a country.) On the other hand, from a health care perspective alone, the benefit-cost ratio was under 1 (i.e., unfavorable for all time horizons. The estimated benefits from a health care perspective were US$610,907, US$1,137,881, and US$1,984,571, respectively, for the 5-, 10- and 20-year time horizons.

The sensitivity of the estimates to the effectiveness of *Wolbachia* deployment were tested. The lower (45%) and upper (90%) estimates of effectiveness were derived from studies conducted in Rio de Janeiro, Brazil (45%) and Cairns, Australia (96%, rounded down to 90%), respectively. For the baseline 10-year time frame, the program remained cost-beneficial (benefit-cost ratio of 1.001 slightly exceeded 1.00) even at a 45% program effectiveness from the societal perspective. Similarly, the cost-effectiveness ratios for the best- (20 years and 90% effectiveness) and worst-

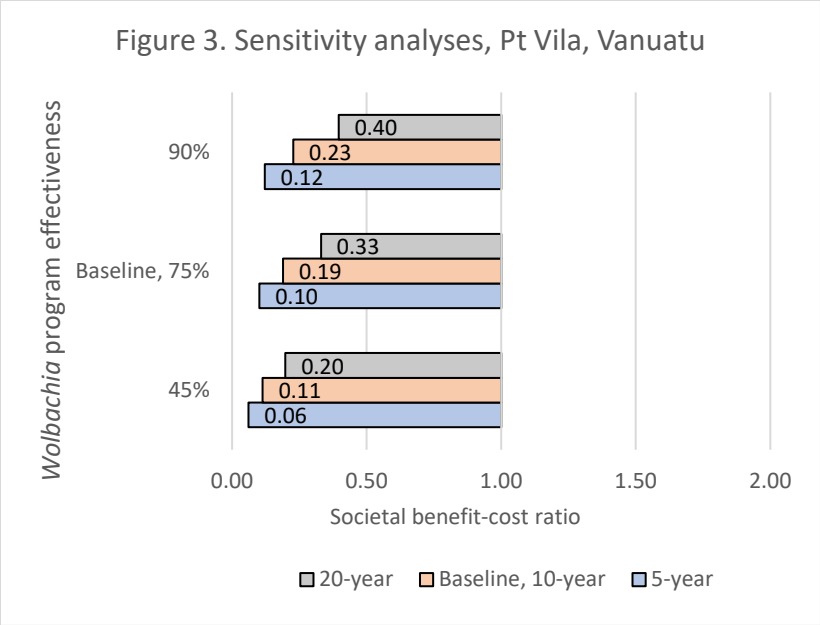
case (5 years and 45% effectiveness) scenarios were estimated to be US$2,380 and US$15,461, respectively. These translate to 0.41 and 2.64 times of Fiji's GNI (below the recommended threshold), making the *Wolbachia* program cost-effective even at the lowest effectiveness rate in Suva, Fiji. The benefit-cost and cost-effectiveness ratios for the sensitivity analyses are given in **Table A1.4** and **Figure 2**.



Sensitivity analyses for Port Vila, Vanuatu

In Port Vila, Vanuatu, the societal benefits in terms of costs averted were US$244,354, US$455,135, and US$793,798 for the 5-, 10- and 20-year time frames, respectively. In each scenario, the benefit-cost ratio in Port Vila, Vanuatu from a societal perspective was below 1. Using discounted DALYs, the cost-effectiveness ratios ranged from US$11,578/DALY averted (i.e. 3.7 times per capita GNI) to US$37,612/DALY averted (i.e. 12.02) and were significantly higher (i.e., worse) than the acceptable GNI-based threshold.

From the health care perspective, the benefit-cost ratios were even lower as the estimated benefits for the 5-, 10- and 20-year time frames were US$28,518, US$53,119 and US$92,644, respectively. In Port Vila, the program does not breakeven even at a 1000-year duration of effectiveness assumption. The benefit-cost ratios obtained by varying the program effectiveness (45% and 90%) did not exceed 1.00 in either scenario. Similarly, the cost-effectiveness ratios for the best- (20 years and 90% effectiveness) and worst-case (5 years and 45% effectiveness) scenarios were estimated to be US$9,648 and US$62,686, respectively. These translate to 3.08 and 20.03 times Vanuatu's GNI (**Table A1.4 and Figure 3**).



Data sources and methods

We obtained costs of *Wolbachia* deployment from the World Mosquito Program's 2016-18 activities, baseline numbers of symptomatic dengue cases by setting and outcome from surveillance and global epidemiological data, direct and indirect cost per dengue case by setting from costing studies and experts, and effectiveness from global quasi-experimental studies.

Using surveillance data from the Fijian Ministry of Health and Medical Service's Centre for Communicable Disease Control (FCCDC) and its Patient Information System (PATIS) (January 2016 – August 2019), the Vanuatu Ministry of Health's Public Health Surveillance System (November 2016 – October 2019) and modeled estimates from the Institute for Health Metrics and Evaluation (IHME), an estimated 2,500 average annual positive dengue cases in Suva and 605 average annual positive cases in Vanuatu were identified. Of these, 46.4% cases in Suva and 26.5% cases in Port Vila were estimated to be medically attended in the inpatient or outpatient settings. Missing data and incomplete testing in surveillance system records were handled using multivariate regression where dengue positivity was predicted based on seasonality and notifying health facility. The proportion of medically treated cases, including hospitalized and ambulatory cases, non-medically attended cases and case fatalities are reported in **Appendix A2 (Tables A2.1-A2.3)**.

Direct medical costs in Suva were extracted from a published costing study[1] whereas unit cost estimates for non-medically treated cases were based on expert opinion. Cost per inpatient case in 2018 dollars was estimated to be FJ$587 or US$270 and was updated from 2010 values using Fiji's 2018/2010 GNI ratio **(Table A3.1)**. Across private and public outpatient settings, the cost of dengue treatment was estimated to be FJ$175 or US$80.5 **(Table A3.2)**. Costs associated with traditional medicine and over the counter (OTC) drugs were based on expert opinion and were approximately FJ$3 or US$1.4 **(Table A3.3)**.

Indirect societal costs for hospitalized cases, outpatient cases and non-medically attended cases in Suva were calculated using estimates of days affected due to disease for patients and caregivers obtained from Suaya et al.[2] Indirect costs associated with a hospitalized dengue case in Suva was about US$198. Outpatient and non-medically attended non-fatal cases were estimated to cost US$191 **(Table A3.4)**.

To estimate direct and indirect medical costs in Port Vila, Vanuatu, we applied the Vanuatu/Fiji GNI ratio of 0.53 to all unit costs. Dengue related deaths were extracted from IHME for the year 2017. Indirect costs of fatal cases were obtained from Shepard et al.[3] Cost per non-fatal case by setting and indirect costs per fatal case for both Suva and Port Vila are summarized in **Appendix 3 (Table A3.5)**.

Comparison to alternative interventions

Most directly relevant are recent published cost-effectiveness studies of interventions to control dengue. The test-and-vaccinate strategy (as WHO recommended) for the only licensed dengue vaccine found a median societal ICER under baseline assumptions with 30% dengue seroprevalence at age 9 of 0.16 times per capita GNI (95% certainty interval 0.28 to 0.88).[4]

Camino Verde, a community-based vector control program, had ICERs in its research-based implementation of 3.0 times per capita GNI in Mexico (an upper middle-income country) and 16.9 times in Nicaragua (a lower-middle income country). Incorporating all assumed efficiencies, the ICERs would improve to 0.74 and 1.90 times per capita GNI, respectively.[5]

In Indonesia (a lower-middle income country with per capita GNI of $3,894) and using a societal perspective with offsets from savings in curative care, *Wolbachia* would be highly cost effective in Bali with a multiple of 0.27 (95% certainty interval -0.18 to 1.08) times per capita GDP (similar to GNI). In Jakarta, due to its high population density, *Wolbachia* would be cost saving with a negative multiple of per capita GDP, i.e., -0.22 (95% certainty interval -0.39 to 0.19).[6]

In comparing *Wolbachia* against public health interventions outside of dengue, one of the core vaccines supported by the Global Alliance for Vaccine Independence (GAVI) provides a useful standard. A modeling study found the cost-effectiveness (with 95% confidence interval) of *Haemophilus inuenzae* Type b Conjugate was 0.07 (uncertainty interval 0.02 to 0.13) in lower middle-income countries, where the vaccine price would be very low, and 0.22 (uncertainty interval 0.05 to 0.44) in upper-middle income countries.[7]

Acknowledgments

The authors thank the public health authorities of Fiji and Vanuatu for their assistance in providing relevant data, Clare L. Hurley for editorial assistance, and Cameron Simmons for constructive comments.

Appendix

A1. Cost benefit and cost effectiveness analyses

Table A1.1: Base-case benefit-cost and cost-effectiveness analyses for a 10-year timeframe and program effectiveness of 75%

	Suva, Fiji	Pt Vila, Vanuatu
Healthcare sector benefits (USD)	$1,137,881	$53,119
All Benefits, including indirect (USD)	$4,545,161	$455,135
Costs (USD)[a]	$2,724,438	$2,404,545
Healthcare benefit-cost ratio	***0.42***	***0.02***
Societal (incl. healthcare) benefit-cost ratio	***1.67***	***0.19***
Effectiveness (DALYs averted over 10 years, discounted at 3%)[b]	547.03	119.08
Cost-effectiveness (gross), USD/DALY	**$4,980**	**$20,193**
CE as ratio of GNI (US$5,860)	0.85	6.45
[a]Exchange rate (Dec 31 2018) AUD/USD; source: xrates	0.7167	
[b]Present value multiplier for 10 years = 8.53		

Table A1.2: Suva region, Fiji: cases averted with baseline effectiveness of 75%

Number of cases per year	Number of cases	Numbers of cases averted[a]	Cost per case (US$)		Annual aggregate costs averted (US$)			DALY burden per case	Aggregate annual DALYs averted	% of DALY burden
			Direct	Indirect	Direct	Indirect	Total			
Non-medical cases (all short run)	1,341	1,006	$1.37	$191.05	$1,382	$192,107	$193,488			
Ambulatory cases (all short run)	723	542	$80.45	$191.05	$43,616	$103,583	$147,199			
Hospitalized cases (only short run costs)	437	327	$269.96	$198.05	$88,396	$64,849	$153,246			
Subtotal (short run)					$133,394	$360,539	$493,933	0.0302	56.6	88%
Long run (additional, long run costs of fatal cases)	0.40000	0.30000	$0.00	$129,661	$0	$38,898	$38,898	25	7.5	12%
Total	***2,500***	***1,875***			***$133,394***	***$399,437***	***$532,832***		***64.1***	100%

[a]The quasi-experimental study in Yogyakarta, Indonesia, estimated 75% of dengue cases were averted by *Wolbachia.*

Table A1.3: Port Vila region, Vanuatu: cases averted with baseline effectiveness of 75%

Number of cases per year	Number of cases	Number of cases averted[a]	Cost per case (US$)		Annual aggregate costs averted (USD)			DALY burden per case	Aggregate annual DALYs averted	% of DALY burden
			Direct	Indirect	Direct	Indirect	Total			
Non-medical cases (all short run)	445	334	$0.73	$102.05	$245	$34,050	$34,294			
Ambulatory cases (all short run)	150	112	$42.97	$102.05	$4,829	$11,467	$16,296			
Hospitalized cases (only short run costs)	11	8	$144.19	$105.78	$1,154	$846	$2,000			
Subtotal (short run)					$6,227	$46,363	$52,590	0.0302	13.71	98%
Long run (additional, long run costs of fatal cases)	0.01320	0.00990	$0.00	$77,306.02	$0	$765	$765	25	0.25	2%
Total	***605***	***454***			***$6,227***	***$47,129***	***$53,356***		***13.96***	100%

[a]The quasi-experimental study in Yogyakarta, Indonesia, estimated 75% of dengue cases were averted by *Wolbachia*.

Table A1.4: Sensitivity analyses for benefit-cost and cost-effectiveness analyses[a]

Program effectiveness	Years of benefit - Suva, Fiji			Years of benefit - Pt Vila, Vanuatu		
	Baseline	Worst case	Best case	Baseline	Worst case	Best case
Years of benefit	**10**	**5**	**20**	**10**	**5**	**20**
Healthcare benefit-cost ratio						
Baseline, 75%	**0.42**	0.22	0.73	**0.02**	0.01	0.04
Worst case, 45%	0.25	0.13	0.44	0.01	0.01	0.02
Best case, 90%	0.50	0.27	0.87	0.03	0.01	0.05
Societal (incl. healthcare) benefit-cost ratio						
Baseline, 75%	**1.67**	0.90	2.91	**0.19**	0.10	0.33
Worst case, 45%	1.00	0.54	1.75	0.11	0.06	0.20
Best case, 90%	2.00	1.07	3.49	0.23	0.12	0.40
Cost-effectiveness ratio (gross), US$/DALY averted						
Baseline, 75%	**$4,980**	$9,277	$2,856	**$20,193**	$37,612	$11,578
Worst case, 45%	$8,301	$15,461	$4,759	$33,655	$62,686	$19,297
Best case, 90%	$4,150	$7,730	$2,380	$16,828	$31,343	$9,648

[a]Breakeven number of years for baseline societal benefit-cost ratio was estimated to be 5.63 years for Fiji. The program in Pt Vila, Vanuatu, does not break even ever.

Appendix A2: Dengue cases

Table A2.1: Derivation of the share of symptomatic dengue cases that are medical

Year	National laboratory dengue samples	Release area laboratory dengue samples	Release area known negative	Release area known positive	Imputed positive medically attended	Total estimated positive medically attended cases	Share of national cases in release area[b]	Total national cases (IHME)	Estimated cases in release area	Share of dengue cases that are medically attended[c]
					Fiji					
2016	8,566	1,749	1,082	189	84	273	20.4%	12,483	2,549	
2017	15,641	3,055	779	1,420	626	2,046	19.5%	12,552	2,452	
Average	12,104	2,402	931	805	355	1,159		12,517	2,500	46.4%
					Vanuatu[d]					
2016								1,351	0	
2017								1,379	0	
Average annual[a]	1,259	418	126	77	83	161	44.3%	1,365	605	26.5%

[a] Average annual (Nov 2016-Oct, 2019); average 2016-2017 for IHME

[b] Fiji share based on share of suspected dengue cases; Vanuatu share based on share of imputed positives

[c] Ratio of surveillance-based to IHME-based estimates of annual dengue positive cases

[d] Some entries are missing for Vanuatu because data were not available by year

Table A2.2: Multi-year distribution of Fiji surveillance data by setting (Jan 2016 thru Aug 2019)

Subgroups[a]	Known positives	Predicted positives	Total positives	%
	Hospitalized			
Secondary inpatient	7	7	14	
CWMH ICU[b]	49	23	72	
CWMH inpatient	1,406	666	2,072	
Subtotal	1,462	696	***2,158***	***38%***
	Ambulatory			
Private primary	17	93	110	
Public primary	1,212	722	1,934	
Secondary outpatient	12	7	19	
CWMH emergency room	993	492	1,485	
CWMH outpatient	16	9	25	
Subtotal	2,250	1,323	***3,573***	***62%***
	Grand total			
All facilities	**3,712**	**2,018**	**5,730**	***100%***

[a] Primary and secondary denote the level of the health care facility.
[b] CWMH ICU: Colonial War Memorial Hospital, Intensive Care Unit (tertiary hospital and national referral center)

Table A2.3: Distribution of average annual dengue cases (2016-2017) by setting

Setting and type of case	Share of total cases (%)	Breakdown of medical cases	Estimated number of cases
	Suva, Fiji		
Total cases	100.0%		2,500
Medically attended	46.4%		1,159
Hospitalized		37.7%	437
Ambulatory		62.3%	723
Not medically attended	53.6%		1,341
	Port Vila, Vanuatu		
Total cases	100.0%		605
Medically attended	26.5%		161
Hospitalized		6.6%	11
Ambulatory		93.4%	150
Not medically attended	73.5%		445

Note: Total cases (which include both fatal and non-fatal cases) are derived from IHME data. Medical percentage uses IHME and surveillance data. Share of medical cases use only surveillance data.

Appendix A3: Costs

Table A3.1: Fiji: direct medical cost per hospitalized dengue case

Item	Amount (FJD)	Amount (USD)[d]
Cost per day, 2010[a]	87.45	
2018/2010 GNI ratio	1.605	
Cost per day, 2018[b]	140.40	64.58
Cost per case, 2018[c]	586.87	**$269.96**

[a] Irava W, Pellny M, Khan I. *Costing Study of Selected Health Facilities in Fiji*. Fiji Ministry of Health; 2012

[b] Updated using 2018/2010 GNI ratio FJ$3,860 / FJ$ 3,650.

[c] Observed length of stay (LOS) in Fiji hospitalization data (4.18 days)

[d] Updated using FJD/USD exchange rate 2018 of 0.46

Table A3.2: Cost per medical ambulatory dengue case, Suva, Fiji

Item	Share of ambulatory medical patients[a]	Visits per dengue episode	Overall visits per episode (product)	Cost per visit (2018 FJD)[b]	Cost per episode (2018 FJD)[c]	Cost per episode (2018 USD)[d]
	Public sector					
Divisional hospital	20%	2.5	0.500			
Subdivisional urban & health center	50%	2.5	1.250			
Subdivisional rural	30%	1.5	0.450			
Subtotal	100%		2.200	74.38	163.64	$75.27
	Private sector					
Private ambulatory	25%	1.5	0.375	30.00	11.25	$5.18
	Overall					
All settings					174.89	**$80.45**

[a] Share of medical patients by type of facility was based on expert judgment. Visits to private providers are in addition to those in public facilities.

[b] Cost per visit in public facilities in 2010 based on Irava et al (2012). Fiji Costing Study; Cost in private facility based on expert judgment

[c] Cost per public sector visit updated from 2010 to 2018 using a GNI factor (2018/2010) = 1.61

[d] Exchange rate, USD/FJD = 0.46 from x-rates.com

Table A3.3: Costs per dengue case that was not medically attended, Fiji[a]

Component	Economic cost per user, FJD[de]	Economic cost per user, USD[de]	Share using among non-medical cases	Economic cost, USD[e]	Comment
Over the counter medicines[b]	2.00	0.92	100%	$0.92	2 cards of paracetamol (Panadol) or similar for 5 FJD
Local medicines (e.g. papaya leaves)[c]	1.41	0.65	70%	$0.45	1-2 doses
Total direct				**$1.37**	

[a] Traditional healers generally do not accept payments for their services. Hence, the associated costs were assumed to be $0. The share of cases seeking care from traditional healers was unknown. All non-medical cases were assumed to require over the counter or local medicines

[b] Two cards of paracetamol (Panadol) (assumed based on expert advice)

[c] Local medicines (1-2 doses) needed 0.5 hours to be gathered, crushed or boiled. Each hour was valued at 2.82 FJD

[d] Exchange rate: FJ$1 equals US$0.46

[e] Economic value per hour = $2.82 calculated using Fiji GNI per capita 2018 equals US$5,860 and assuming a 52-week year and a 40-hour work week.

Table A3.4: Indirect cost per non-fatal dengue case in Fiji by setting using Suaya et.al [a]

Item	Value
Hospitalized	
Days affected	12.3
Fraction of year[b]	0.03380
Estimated indirect cost per hospitalized non-fatal case[c]	***$198.05***
Ambulatory	
Days affected	11.9
Fraction of year[a]	0.03260
Estimated indirect cost per hospitalized non-fatal case[c]	***$191.05***
Non-medical	
Assumed to be the same as ambulatory	***$191.05***

[a] Suaya JA, Shepard DS, Siqueira JB, et al. Cost of dengue cases in eight countries in the Americas and Asia: a prospective study. *Am J Trop Med Hyg.* 2009;80(5):846-855.

[b] Year = 365 days

c Based on 2018 GNI per capita = USD5,860

Table A3.5: Aggregate cost of dengue illness (2018 USD)

	Best estimate[a]	Number of cases	Aggregate dengue cost	Best estimate[b]	Number of cases	Aggregate dengue cost
		Suva, Fiji			Pt Vila, Vanuatu	
Direct medical costs						
Hospital costs	$269.96	437	$117,862	$144.19	11	$1,538
Ambulatory costs	$80.45	723	$58,155	$42.97	150	$6,438
Non-medical costs	$1.37	1,341	$1,842	$0.73	445	$327
Average direct (weighted)	$71.14	2,500	$177,859	$13.71	605	$8,303
Indirect costs (non-fatal cases)						
Hospital costs	$198.05	437	$86,466	$105.78	11	$1,128
Ambulatory costs	$191.05	723	$138,110	$102.05	150	$15,290
Non-medical costs	$191.05	1,341	$256,142	$102.05	445	$45,399
Average indirect costs per non-fatal case (weighted)	$192.27	2,500	$480,719	$102.11	605	$61,818
Indirect costs of fatal cases	$129,661.17	0.4000	$51,864	$77,306	0.0132	$1,020

[a] Values for fatal cases from Shepard et at. (2016); all other data are from the country

[b] Derived from Fiji unit costs using Vanuatu/Fiji GNI ratio of 0.53413; value for fatal cases from Shepard et al. (2016)

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