**Cost Effectiveness Comparison of *Dengvaxia* and *wMel Wolbachia*** **-infected *Aedes aegypti* mosquitoes to control for Dengue in Thailand based on Implementation in Indonesia**

**Abstract:**

 This cost-effectiveness analysis (CEA) compares *wMel Wolbachia* implementation and dengue vaccination as possible programs for the prevention of dengue in Thailand. Two studies on proposed interventions in Indonesia were used as proxies, and adjustments were made considering specific health indicators in Thailand compared to Indonesia. *wMel Wolbachia* strain implementation was found to be more cost effective at averting DALYs attributable to dengue than a dengue vaccination program in Thailand. This conclusion support recent efforts to infect and spread Aedes Aegypti mosquitoes with *wMel Wolbachia* strains for the prevention of dengue and other dangerous arboviruses in the face of increased incidence of neglected tropical diseases and climate change threatening the further rise of arbovirus disease cases.

**Natural History of Dengue:**

 Dengue is a mosquito-borne viral infection which is typically found in regions with tropical and sub-tropical climates where mosquitoes like *Aedes aegypti* and *Aedes albopictus*, the two species that transmit most dengue cases, thrive. The World Health Organization (WHO) estimates that there are 390 million dengue virus infections per year, of which 96 million will manifest clinically. The number of dengue cases reported to the WHO increased over 8-fold in the past 20 years, and while some of these increases can be explained by changes in national reporting practices, the number of dengue cases is expected to continue to rise, with explosive outbreaks in new countries (World Health Organization, 2021).

Dengue manifests with a high fever and symptoms like headache, joint pain, and rash. Because dengue presents similarly to other diseases, including chikungunya, Zika, malaria, and typhoid fever, it can be difficult to diagnose patients with dengue, however, it is possible to perform a blood test to be certain of infection with one of the four dengue serotypes. Unfortunately, there is no present cure for dengue, meaning any work averting dengue cases relies on preventative care.

**Overview of Prevention Methods:**

There are a couple preventative measures that exist to limit incidence of dengue: dengue vaccination in humans and *wMel Wolbachia* infection of *Aedes Aegypti* mosquitoes. The first, and perhaps most used intervention against dengue is the live-attenuated dengue vaccine. Traditional vector control methods, including the use of insecticide-treated bed nets, are largely ineffective, as Aedes mosquitoes typically bite during the day (Hawley, 1998 as cited in Tozan et al, 2014). Thus, intervention measures with bed-nets have generated minimal efficacy research efforts and are thought to have little impact on the spread of dengue disease (Laydon et al, 2021). However, other novel approaches have been proposed to avert DALYs due to dengue, including the use of insecticide treated school uniforms in Thailand, which had an estimated cost effectiveness of $5,248 per DALY averted in 2012 dollars, or $6,234 per DALY averted in 2018 dollars (Tozan et al, 2014). The use of larvicides and adulticide insecticides are also widely used to prevent Aedes-spread arboviruses, however, while they can be effective, these interventions can also impose negative consequences on the surrounding environment.

For these reasons, dengue vaccination programs have been implemented in many countries to target prevention efforts in children, the population that suffers the most from dengue cases. Though several vaccine candidates are in development, currently, the only licensed vaccine is the Sanofi-Pasteur CYD-TDV, also known as *Dengvaxia*. This vaccine protects against all 4 serotypes of DENV as it contains structural proteins genes from each (Laydon et al, 2021). The vaccine is recommended for children ages 9-16 and is administered in 3 doses at months 0, 6, and 12. The dengue vaccine is unique compared to most vaccines in that it is only recommended for those who have already been infected with DENV, as those given the vaccine without previous dengue infection might be at an increased risk of developing severe dengue. This phenomenon was first observed in the Philippines, the first country to introduce *Dengvaxia* on a large scale, and which saw an excess risk of hospitalization for dengue and severe dengue in vaccinees without prior DENV infection and ultimately resulted in the suspension of the *Dengvaxia* program (Wilder-Smith et al, 2019). While vaccination against dengue can provide some protection to children, who usually bear the largest burden of dengue cases, the vaccine is limited in the protection it offers, especially in that it provides no shielding against dengue-naïve individuals. Alternative interventions, therefore, are integral to the success of dengue prevention.

One such novel approach is to use *wMel Wolbachia* bacteria to infect populations of *Aedes aegypti*. *wMel Wolbachia* infection limits a mosquito’s ability to transmit dengue, chikungunya, Zika, and yellow fever virus, and infected mosquitoes can suppress and replace the natural, non-infected population (Aliota et al, 2016, Van den Hurk, 2012, and Walker et al, 2011, as cited in Brady, 2020). The World Mosquito Program (WMP) is using these features of *wMel Wolbachia* infection to their advantage by implementing mosquito replacement programs in 11 countries around the world, including Brazil, Colombia, and Indonesia (World Mosquito Program, 2021). Wolbachia implementations pose negligible risk to humans and the environment while also reducing disease transmission, and in controlled trials, these implementations have had a protective efficacy of 77% against all dengue serotypes (Utarini et al, 2021). While these mosquito-replacement programs require large initial investments, once established, the replaced mosquito populations are self-sustained and can provide valuable long-term benefits without additional interventions.

**Rational for Indonesia as a Proxy for Thailand:**

Both Indonesia and Thailand experience a relatively high prevalence of dengue, and implementation efforts in Indonesia can be used to guide those in nearby Thailand. Both countries are in Southeast Asia, which experiences most dengue cases worldwide, however Indonesia experiences a greater burden of dengue compared to Thailand (0.84% of total DALYs compared to 0.09% of total DALYs, respectively) (IHME, 2021). The prevalence of dengue in the population, is similar overall between the two countries, with Indonesia having a slightly higher prevalence per 100,000 than Thailand (61.05 compared to 59.88, respectively), as seen in **Table 1**.

**Table 1**: **Dengue Prevalence for both sexes (per 100,000), IHME 2019**

|  |  |  |
| --- | --- | --- |
| **Age-Group**  | **Thailand** | **Indonesia** |
| Under 5 | 47.18 | 38.58 |
| 5-9 | 77.75 | 70.19 |
| 10-14 | 92.94 | 78.21 |
| 15-49 | 63.97 | 60.68 |
| 50-74 | 44.80 | 55.76 |
| All Ages | 59.88 | 61.05 |

Thailand and Indonesia are also similar in other indicators. Thailand has a slightly higher life expectancy compared to Indonesia (77.15 compared to 71.716, respectively) (World Bank, 2019) and experiences a smaller GBD than Indonesia, with 17,539.50 Years of Life Lost (YLL) per 100,000 in 2019 compared to Indonesia’s 19,844.05 YLL (IHME, 2021). Thailand’s Healthcare Access and Quality (HAQ) index is also higher than that of Indonesia (69.5 and 44.5, respectively), according to the 2016 IHME GBD study (Fullman et al, 2018). In terms of dengue-specific indicators, Indonesia lost 249.55 DALYs to dengue per 100,000 in 2019, while Thailand lost only 27.07. Other development indicators from 2019 are included in **Table 2**. These factors combined make Indonesia a useful proxy country for program implementations in Thailand.

**Table 2**: **Comparison of Development indicators for Thailand and Indonesia, 2019**

|  |  |  |
| --- | --- | --- |
| **Development Indicators** | **Thailand** | **Indonesia** |
| Population (World Bank) | 69,625,581 | 270,625,567 |
| Life Expectancy at birth (World Bank) | 77.15 | 71.716 |
| Healthy Life Expectancy at birth (HALE) (Knoema) | 66.80 | 61.70 |
| Fertility rate (World Bank) | 1.514 | 2.288 |
| % Population in largest city (World Bank) | 14.87 | 3.93 |
| % Population aged 10-14 (World Bank) | 16.824 | 26.215 |
| Land Area (sq miles) (World Bank) | 510,890 | 1,877,519 |
| Area of largest city (sq km) (World Bank) | 1,568.7 | 764.48 |
| HAQ Index (2016) (IHME) | 69.5 | 44.5 |
| GBD (YLL/100,000) (IHME) | 17,539.50 | 19,844.05 |
| DALYs lost to dengue (rate) (IHME) | 27.07 | 249.55 |

In this study, I will compare the cost effectiveness of dengue vaccination and *wMel Wolbachia*-infection replacement programs in Thailand using data from proposed interventions in Indonesia. The cost of these interventions was adjusted based on a comparison of proxy cost indicators in both countries. DALYs averted were taken and adjusted from studies proposing dengue vaccination or *wMel Wolbachia* implementation in Indonesia, and then adjusted for Thailand based on target population size, disease prevalence, HAQ index score, and, most importantly loss of DALYs to dengue in each country per 100,000.

**Burden of Dengue in Thailand:**

For this study, DALYs are the best method to quantify the burden of dengue as this will account for both years of life lost (YLL) and years lost to disability (YLD). While symptoms from dengue generally only last 2-7 days, most patients are disabled for at least 4 days following the onset of symptoms, based on a cohort study of patients in Brazil, Puerto Rico, and Thailand (Tiga Loza, 2011). Though dengue is not one of the largest contributors of DALYs in Thailand, the burden of dengue is expected to increase in the coming years because of greater spread and more suitable temperatures for mosquitoes due to climate change (Colón-González, 2013). For these reasons, and the fact that all current healthcare efforts to limit dengue disease burden are preventative, it is imperative to implement cost-effective prevention measures in countries where dengue burden is expected to rise.

 Two studies proposing program implementations in Indonesia were used to compare the cost-effectiveness of the schemes in Thailand in this study: Suwantika et al (2021), which examined the cost-effectiveness of implementing a country-wide dengue vaccination program, and Brady et al (2020), which examined the costs and benefits associated with *wMel Wolbachia* implementation in several cities in Indonesia. Though Suwantika et al (2021) calculated cost-effectiveness in their study with Quality-Adjusted Life Years, or QALYs, for the purpose of this analysis, the number of averted cases and deaths from the findings were converted into DALYs, the same outcome measure used in Brady et al (2020). Both these outcome measures will be further adjusted, however, to account for the difference in prevalence of dengue and the different health system capacities of each country, specifically in terms of DALYs lost to dengue per 100,000.

**Target Populations:**

 There are two differing target populations for this study: children aged 10-14 and the population of the largest city. These different populations result from the different implementations, as dengue vaccination is only recommended for children between the ages of 9-16, and *wMel Wolbachia* implementation is most effective in urban centers where the density of humans and mosquitoes is greatest. Though *Dengvaxia* is recommended for children ages 9-16, estimates of the population between those ages in each of the two countries is not available from the World Bank DataBank. Instead, the population between ages 10-14 will be used as a proxy for the true population of interest for the dengue vaccination program in Thailand.

 In addition to examining children between the ages of 10-14 for the dengue vaccination implementation, this study will separately examine the populations of people living in each country’s largest city for the *wMel Wolbachia* implementation. As *wMel Wolbachia* implementation will disrupt transmission of dengue from all mosquitoes in a given location, all age cohorts in urban centers are expected to benefit from this intervention. *wMel Wolbachia* implementation will also prevent the passage of other arboviruses, however, this additional benefit will only be examined as a supplemental benefit in the discussion, as prevention of DALYs attributable to dengue is the primary outcome measure of this study.

A breakdown of the populations of interest can be seen in **Tables 3 and 4**.

**Table 3**: **Population ages 10-14, World bank 2019**

|  |  |  |
| --- | --- | --- |
|  | **Thailand** | **Indonesia**  |
| Population ages 10-14 | 11,713,808 | 70,944,492 |
| Total Population | 69,625,581 | 270,625,567 |
| % Population ages 10-14 | 16.824 | 26.215 |

**Table 4**: **Population in largest city, World bank 2019**

|  |  |  |
| --- | --- | --- |
|  | **Thailand** | **Indonesia** |
| Population in largest city | 10,350,204 | 10,638,689 |
| Total Population | 69,625,581 | 270,625,567 |
| % Population in largest city | 14.87 | 3.93 |

**Adjusting Total Cost of Implementations:**

 The total costs of dengue vaccination, as proposed by Suwantika et al (2021) and *wMel Wolbachia*-implementation, as described by Brady et al (2020) were adjusted based on key price indicators, seen in **Table 5.**

**Table 5**: **Comparison of Key Cost Indicators (USD)**

|  |  |  |
| --- | --- | --- |
|  | **Thailand** | **Indonesia** |
| Cost of *Dengvaxia* (unit cost per person), 2018 | $324.90 (Joob and Wiwanitkit, 2018)  | $110.64 (Suwantika et al, 2021; Zeng, 2017)  |
| Average salary for a person in the Health and Medical Field (2021)  | $51,816.56/year (Salary Explorer)  | $15,170.34/year (Salary Explorer)  |
| Minimum wage, 2021 | ~$3,650/year (ASEAN Briefing) | ~$2,400/year (ASEAN Briefing) |
| Price of gas, 2021 | $1.123/liter (Global Petrol Prices) | $0.862/liter (Global Petrol Prices) |
| Area of Largest city | 1,568.7 sq km (World Bank)  | 764.48 sq km (World Bank) |
| CHE as % of GDP, 2018 | 3.793% (World Bank)  | 2.781%. (World Bank) |
| GDP per capita, PPP, 2019 | 19,208.598 (World Bank) | 12,312.598 (World Bank) |

Two key indicators were examined for each of the proposed interventions. The cost of the dengue vaccine intervention was adjusted based on indicators for *Dengvaxia* cost in each country and the annual salary of healthcare workers in each country. Though the cost ratios for the proxy indicators are about three times higher in Thailand and Indonesia, because Thailand spends more on health than Indonesia, and has a greater Gross Domestic Product per capita, PPP, the cost of dengue vaccine implementation in Thailand was calculated as a 20% increase on the cost of implementation in Indonesia.

For the Wolbachia implementation, the cost indicators were slightly different. As the Wolbachia implementation does not specifically require healthcare workers, the minimum wage in each country per year was used as an indicator for cost instead of average salary of someone in the health and medical field. Additionally, because the Wolbachia intervention will likely involve a lot of travel to distribute the infected mosquitoes, price of gas per liter in each country was used as a secondary indicator. The minimum wage is approximately 52% higher, while the price of gas is approximately 30% higher in Thailand compared to Indonesia. Additionally, for the Wolbachia intervention, it is necessary to consider the area of implementation, as mosquito populations will be larger and implementation more costly for cities with greater land cover. Jakarta is the largest city in Indonesia, with an implementation area of 764.48 square kilometers. For Thailand, the largest city is the capital of Bangkok, with an area of 1,568.7 square kilometers, making the implementation in Bangkok about 2 times larger than the implementation in Jakarta. For these reasons, the cost of *wMel Wolbachia* implementation in Thailand was increased by a total of 30%, to account for the differences in indicators while acknowledging the additional amount allocated to health by Thailand.

The calculated costs for vaccination implementation, Wolbachia implementation, and overall cost comparisons can be seen in **Table 6**, **Table 7**, and **Table 8**, respectively. Both Brady et al (2020) and Suwantika (2021) expressed the costs associated with their implementations in terms of 2018 USD, so no adjustments will be made for CPI, as the USD units for both are already equivalent. This means, however, that all program costs in Thailand will also be expressed in 2018 USD. The cost of dengue vaccination was based on an implementation population of 4,710,100 children, which was the size of the cohort in the proposal by Suwantika et al (2021), for both Indonesia and Thailand. The unit costs of the Wolbachia implementations were based on the population in each of the largest cities where the implementation would take place.

**Table 6**: **Cost Comparison for Dengue Vaccination**

|  |  |  |
| --- | --- | --- |
|  | **Thailand** | **Indonesia**  |
| Vaccine Price per dose | $24 | $20 |
| Pre-vaccination screening cost per dose | $12 | $10 |
| Cost of vaccine administration per dose | $4.10 | $3.42 |
| Wastage (10%) | $2.40 | $2.00 |
| Cost to obtain dose (1hr opp. Cost)  | $1.38 | $1.15 |
| Side Effect Cost | $0.37 | $0.31 |
| Total Cost per dose | $44.27 | $36.88 |
| Total Cost per person (3 doses) | $132.77 | $110.64 |
| Total Cost (if administered to 4,710,100 children)  | $625.36 million USD | $521 million USD |
| Source | Calculated | Suwantika et al, 2021; Zeng, 2017 |

**Table 7**: **Cost Comparison for Wolbachia Implementation**

|  |  |  |
| --- | --- | --- |
|  | **Thailand** | **Indonesia**  |
| Total Cost | $173.29 million USD | $133.30 million USD |
| Cost per person covered, all in largest city | $16.74 USD | $12.50 USD |
| Source | Calculated | Brady et al, 2020 |

**Table 8**: **Cost Comparisons for All Implementations**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | ***wMel Wolbachia* Control,** **Thailand** | **Dengue Vaccination, Thailand** |  ***wMel Wolbachia* Control, Indonesia** | **Dengue Vaccination, Indonesia** |
| Total Cost | $173.29 million USD | $625.36 million USD | $133.3 million USD | $521 million USD |
| Unit Cost per person covered | $16.74 USD | $132.77 USD | $12.50 USD | $110.64 USD |
| Source | Calculated | Calculated | Brady et al, 2020 | Suwantika, 2021; Zeng, 2017 |

**Calculation and Adjustment Outcome Measures**:

 DALYs, or disability-adjusted life years, are a quantification of disease burden and deaths attributable to a certain cause in a population. As dengue results in both disability and death, DALYs will be used to compare the outcomes of each of the interventions. DALYs averted can differ greatly between countries, as they are dependent on the type of intervention used, the disease burden, the resulting health outcomes, and the implementing healthcare system. The DALYs averted for the Dengue vaccination implementation in Thailand will be adjusted from the calculated cases and deaths averted from Suwantika et al (2021). The DALYs averted for *wMel Wolbachia* implementation in Thailand are adjusted from the DALYs averted from the Brady et al (2020) mosquito-replacement proposal in Indonesia.

**Converting DALYs from Suwantika et al, 2020**:

 Suwantika et al (2021) estimate the number of averted cases and deaths due to dengue fever (DF) and dengue hemorrhagic fever (DHF), a more severe form of dengue experienced by some patients. Though Suwantika et al (2021) classified their cost-effectiveness analysis in terms of QALYs gained, knowing the number of averted cases and deaths attributed to dengue, it is possible to calculate the DALYs averted with the formula: DALYs = YLL + YLD, where YLL represents the years of life lost, and YLD represents the number of years lived with disability. YLL is calculated by multiplying the number of deaths attributable to the disease by the standard life expectancy at the age of death. For their proposed implementation in Indonesia, Suwantika et al (2021) estimated a total of 2,283 averted deaths in their cohort of 4,710,100 children. Because this program was proposed for children between the recommended vaccination ages of 9-16, the median age of which is 12.5. The average life expectancy in Indonesia is 71.716 (**Table 2**), meaning the median standard life expectancy in years for this cohort at the time of death is 59.216 years. Overall, then, the YLL averted with dengue vaccination can be calculated as 2,283 $×$ 59.216 = 135,190.

 YLD from dengue can be calculated with the formula YLD = $l$ $×$ DW $×$ L, where $l$ = the number of incident cases, DW = the disability weight of dengue, and L = the average duration of the case until remission or death. In a 2015 paper based on the results of the 2010 Global Burden of Disease study, Salomon et al, estimated the healthy years of life lost as follows:

94.5% of symptomatic dengue cases are assigned a disability weight of 0.051 with a mean duration of six days;

5.5% of symptomatic dengue cases are assigned the disability weight of 0.133 with a mean duration of 14 days;

And 8.5% of dengue cases are assumed to have post-dengue chronic fatigue, with a disability weight of 0.219 and with a mean duration of 6 months.

 (Salomon et al, 2015 and Stanaway, 2013, as cited in Manh Hung et al, 2018)

Suwantika et al (2021) estimate a total number of 277,289 averted cases of dengue in their cohort of 4,710,100 children. Thus, the averted YLD for the proposed dengue vaccination in Indonesia can be calculated as follows:

$$YLD=l×DW×L$$

$$YLD=\left(.945\right)\left(l\right)\left(0.051\right)\left(\frac{6}{365}\right)+\left(0.055\right)\left(l\right)\left(0.133\right)\left(\frac{14}{365}\right)+\left(0.085\right)\left(l-deaths\right)\left(0.219\right).5$$

$$YLD=219.68+77.80+2,559.62$$

$$YLD=2,857.09$$

This makes the total DALYs averted with dengue vaccination in Indonesia = 135,190 + 2,857 = 138,047 over the course of a 4-year implementation.

**Calculating DALYs for population of interest from Brady et al, 2020**:

 For the *wMel Wolbachia* -replacement program in Indonesia, Brady et al (2020) reported outcome measures for the implementation populations in terms of DALYs. Averted DALYs from the accelerated program, which completes rollout in 3 years, was chosen over the 10-year sequenced introduction to keep implementation periods as similar as possible between the two interventions. In their study, Brady et al (2020) estimate the cost-effectiveness of their proposed implementation in Jakarta at a gross $1566 per DALY averted using an accelerated implementation and estimate total cost of $133.3 million USD. Thus, Brady et al (2020) estimate a total number of 85,121.33 DALYs averted for accelerated *wMel Wolbachia* implementation in Jakarta, Indonesia.

**Adjusting Outcome Measures:**

 Though Dengue prevalence in the 10-14 age group is higher in Thailand compared to Indonesia per 100,000 (**Table 1**), Suwantika et al (2021) uses a population of children ages 9-16 instead of the ages 10-14 used in this study, and therefore, no adjustments based on disease prevalence will be made for the vaccination implementation as it is expected that the overestimation of DALYs from the expanded age group in Suwantika et al (2021) is roughly equivalent to the underestimation of prevalence in Indonesia compared to Thailand. Since the implementation populations for dengue vaccination in Indonesia and Thailand have equal populations, there will be no adjustment based on population size, however, the life expectancy (as reported in 2019) and healthy life expectancy (as reported in 2016) in Thailand are both greater than that of Indonesia (77.15 and 66.80, compared to 71.716 and 61.70, respectively), which would increase the expected number of DALYs averted in Thailand (World Bank, 2019; Knoema, 2016). Specifically, this would increase the YLL averted with dengue vaccination in Thailand to 149,737.45 years from Indonesia’s 135,190 years. The longer lifespan of individuals in Thailand would also impact the *wMel Wolbachia* implementation. Considering the populations living in Bangkok and Jakarta are approximately the same, the DALYs averted by the *wMel Wolbachia* program will be adjusted by a factor of 8% to accommodate the longer lifespan of Thailand’s population.

In addition to the individual program adjustments mentioned, changes must also be made based on Thailand’s healthcare system and current estimates of DALYs lost to dengue per 100,000. Thailand has a much better HAQ index score than Indonesia (69.5 and 44.5, respectively), according to the 2016 IHME GBD study (Fullman et al, 2018). Thailand scored higher than the HAQ global average (54.4) and the HAQ average (47.5) for Southeast Asia, while Indonesia scored lower than both baselines. Additionally, Thailand has about 9 times fewer DALYs attributable to dengue per 100,000 than Indonesia (27.07 and 249.55, respectively). While some of the increased DALYs per 100,000 in Indonesia can be explained by the overall higher prevalence of dengue per 100,000 in Indonesia, some of this can also be attributed to Thailand’s superior healthcare system. This means any implementation in Thailand is likely to have greater health system support and capacity compared to an implementation in Indonesia and therefore more DALYs are expected to be averted in Thailand compared to interventions in Indonesia. For these reasons, the number of DALYs averted will be further increased for both implementations in Thailand by 20%.

**Table 9**: **DALYs Averted by each program in Thailand and Indonesia**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | ***wMel Wolbachia* Control,** **Thailand** | **Dengue Vaccination, Thailand** | ***wMel Wolbachia* Control, Indonesia** | **Dengue Vaccination, Indonesia** |
| DALYs averted | **110,317.89** | **183,113.34** | 85,121.83 | 138,047 |

**Calculation of Cost Effectiveness:**

 To evaluate whether resources are best allocated to dengue vaccination or a *wMel Wolbachia* -infection and replacement program, cost-effectiveness will be calculated for each implementation with the aim of reducing DALYs. The calculation of Cost-Effectiveness uses the following ratio:

$$CER=\frac{total cost of program}{total DALYs averted} $$

Therefore, a more cost-effective program will have a lower CER.

 The CER for Dengue vaccination in Thailand is calculated to be $3,415.15 per DALY averted.

$$CER=\frac{\$625,360,000}{183,113.34}$$

 The CER for *wMel Wolbachia* infection and mosquito replacement in Thailand is calculated to be $1,570.82 per DALY averted.

$$CER=\frac{\$173,290,000}{110,317.89}$$

**Table 10**: **CEA comparisons between Thailand and Indonesia**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | ***wMel Wolbachia* Control,** **Thailand** | **Dengue Vaccination, Thailand** | ***wMel Wolbachia* Control, Indonesia** | **Dengue Vaccination, Indonesia** |
| Cost per DALY averted | $1,570.82 | $3,415.15 | $1,566 | $3,774.07 |

**Discussion:**

 In Thailand, both the *wMel Wolbachia* -infection implementation and the dengue vaccination implementation were less cost-effective than the estimated implementations in Indonesia. However, based on the CER calculations, *wMel Wolbachia* implementation in the largest city was more cost effective at reducing DALYs attributable to dengue in both countries than a *Dengvaxia* implementation. Vaccination of 4,710,100 children in Thailand would cost $3,415.15 per DALY averted, while implementing a *wMel Wolbachia* replacement program for the *Aedes aegypti* population would cost $1,570.82 per DALY averted. This also makes both implementations more cost-effective than the 2014 proposal to use insecticide-treated school uniforms to prevent dengue in schoolchildren, which had a cost-effectiveness of $6,234 per DALY averted in 2018 dollars (Tozan et al, 2014).

 Though *wMel Wolbachia* implementation has already been shown to be more cost-effective than dengue vaccination in Thailand, this protection against dengue isn’t the only benefit of a *wMel Wolbachia* implementation. For one, the implementation period for accelerated *wMel Wolbachia* implementation is a year shorter than the *Dengvaxia* implementation. Additionally, *wMel Wolbachia* infection of Aedes Aegypti mosquitoes can also prevent cases of other arboviruses, including chikungunya, Zika, and malaria (Aliota et al, 2016, Van den Hurk, 2012, and Walker et al, 2011, as cited in Brady, 2020)). By preventing cases from these other viruses that are also transmitted by Aedes Aegypti mosquitoes, the *wMel Wolbachia* implementations in both Indonesia and Thailand will be even more cost-effective than they initially appear.

 While there are many benefits to the *wMel Wolbachia* implementation, it is necessary to point out the differing priorities of each of the program. Dengue vaccination, available for only children between the ages of 9 and 16, prioritizes the age cohort with the largest prevalence and burden of dengue. *Dengvaxia*, however, can only be given to children who have already had dengue, as those who have the vaccine prior to dengue infection are at an increased risk for contracting a more severe form of dengue. Thus, while *wMel Wolbachia* implementation conversely prioritizes the health of those living in urban centers, it provides protection to all individuals, dengue-naïve and otherwise, in that city. When it comes to implementation, while it is important to examine the cost-effectiveness of an intervention, it is also necessary, in this case, to balance the priorities of serving differing target populations.

**Conclusion**:

This CEA compared *wMel Wolbachia* implementation and dengue vaccination as possible programs for the prevention of dengue in Thailand from proposed implementations in Indonesia. After adjustments for healthcare system quality and health indicators in Thailand compared to Indonesia, a cost-effectiveness ratio in terms of DALYs averted was calculated for both programs. Both *wMel Wolbachia* strain implementation and dengue vaccination were less cost-effective in Thailand than Indonesia, however, *wMel Wolbachia* implementation in both countries was more cost-effective at averting DALYs attributable to dengue than a *Dengvaxia* implementation in both countries. These conclusions support recent efforts to infect and spread *Aedes aegypti* mosquitoes with *wMel Wolbachia* strains for the prevention of dengue and other dangerous arboviruses on the rise.

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