

DENGUE CONTROL IN THE STATE OF GOIAS-BRAZIL USING “WMEL WOLBACHIA”: A COST-EFFECTIVENESS STUDY

CONTROLE DA DENGUE NO ESTADO DE GOIÁS-BRASIL USANDO “WMEL WOLBACHIA”: ESTUDO DE CUSTO-EFETIVIDADE

BARBOSA, Aurelio de Melo¹
VERONEZI, Rafaela Júlia Batista²

1. Physiotherapist, PhD student from Medicines and Pharmaceutical Assistance Doctoral Program of Federal University of Minas Gerais, Master of Health and Environmental Science, Public Health diplomate, professor at State University of Goiás, researcher at the Health Technologies Assessment Center from the School of Public Health of the State Health Department of Goiás, aurelio.barbosa@goias.gov.br or aurelio.barbosa@ueg.br.

2. Physiotherapist, PhD in Medical Sciences, Superintendent at the School of Public Health of the State Health Department of Goiás, rafaelajulia@ig.com.br or rafaela.veronezi@goias.gov.br.

ABSTRACT

Context: Dengue and other arboviruses have a considerable economic impact in Brazil. There are vector control strategies for dengue: traditional control with pesticides, Incompatible Insect Technique (IIT) with “wMel Wolbachia”, and Sterile Insect Technique (SIT). **Objective:** To analyze the cost-effectiveness ratio of the IIT/SIT strategy, compared to traditional vector control with pesticides, for dengue prevention from the perspective of the Brazilian Public Health System (BPHS) as the payer and from the societal perspective in the state of Goiás, Brazil. **Methods:** The two strategies were compared using a decision tree model developed in Amua® software. All estimated parameters were derived from published articles or SUS information systems. The willingness-to-pay threshold (WTP), quality-adjusted life years (QALYs), years of life gained, costs, incremental cost-effectiveness ratios (ICERs), and incremental cost-utility ratios (ICURs) were adopted as study outcomes and parameters. We conducted deterministic and probabilistic sensitivity analyses. **Results:** From the BPHS perspective, the IIT-SIT strategy is cost-effective, with an ICUR of R\$ 72,200 per QALY gained, which is lower than the WTP of R\$ 122,064.30/QALY gained. From the societal perspective, the IIT-SIT strategy is dominant (cheaper and more effective than traditional vector control). Sensitivity analyses showed that these results are reliable. **Conclusion:** In the state of Goiás, Brazil, the IIT/SIT strategy is cost-effective from the perspective of BPHS and dominant from the societal perspective, when compared to traditional vector control.

KEYWORDS: Aedes; Wolbachia; Dengue/prevention & control; Cost-Benefit Analysis.

RESUMO

Contexto: A dengue e demais arboviroses têm impacto econômico considerável no Brasil. Há estratégias para controle vetorial da dengue: controle vetorial tradicional com pesticidas; Técnica do Inseto Incompatível (TII) com “wMel Wolbachia” e Técnica do Inseto Estéril (TIE). **Objetivo:** Analisar a razão de custo-efetividade da estratégia de TII/TIE, comparada ao controle vetorial tradicional com pesticidas, para prevenção da dengue, na perspectiva do Sistema Único de Saúde (SUS) como pagador e na perspectiva societal no Estado de Goiás, Brasil. **Métodos:** As duas estratégias foram comparadas usando um modelo de árvore de decisão desenvolvido no *software* Amua®. Todos os parâmetros estimados foram derivados de artigos publicados ou dos sistemas de informação do SUS. Limite de disposição para pagar (LDAP), Anos de vida ajustados pela qualidade (QALYs), anos de vida ganho, custos e razões de custo-efetividade incremental (RCEI) e custo-utilidade incremental (RCUI) foram adotados como desfechos e parâmetros do estudo. Análises de sensibilidade determinísticas e probabilísticas foram conduzidas. **Resultados:** Na perspectiva do SUS como pagador, a estratégia de TII-TIE é custo-efetiva, com RCUI de R\$ 72,2 mil reais por QALY ganho, que é inferior ao LDAP de R\$ 122.064,30/QALY ganho. Na perspectiva societal, a estratégia de TII-TIE é dominante (mais barata e mais efetiva que o controle vetorial tradicional). As análises de sensibilidade mostraram que esses resultados são confiáveis. **Conclusão:** No Estado de Goiás, Brasil, a estratégia de TII/TIE parece ser custo-efetiva na perspectiva do SUS e dominante na perspectiva societal, quando comparada ao controle vetorial tradicional.

PALAVRAS-CHAVE: Aedes; Wolbachia; Dengue/prevenção & controle; Análise Custo-Benefício.

INTRODUCTION

Dengue and other arboviruses have a considerable economic impact in Brazil: in 2016, total costs, which included vector control costs, direct medical costs, and indirect costs, were estimated at R\$2.3 billion, representing 0.04% of Brazil's per capita GDP and 2% of the budget

allocated for health.¹

In 2021, the incidence of dengue in the state of Goiás was 801 cases per 100,000 people, the highest incidence in the Central-West region and the second-highest in Brazil, only lower than that of Acre (1,625 cases/100,000 people).²

By 2022, the situation of dengue in Goiás was alarming: the accumulated incidence in the middle of the year was 2,709 cases/100,000 people, more than tripled.³ This requires that the BPHS (Brazilian Public Health System) carry out more efficient environmental surveillance actions for vector control in order to reduce the incidence of arboviruses.

The traditional vector control strategy uses pesticides and environmental sanitation (removal of mosquito breeding sites) for reducing "*Aedes aegypti*" mosquito population. This is the main strategy used by Brazilian Public Health System (BPHS) for dengue prevention⁴, but it is not the most effective vector control strategy.

The "wMel" strain of the "*Wolbachia pipientis*" bacterium has been successfully introduced into *Aedes aegypti* mosquitoes and subsequently demonstrated in laboratory studies (in vitro) to reduce the transmission of a variety of viruses, including dengue, Zika, chikungunya, yellow fever, and Mayaro virus, which cause human diseases, known as arboviruses.⁵

The Incompatible Insect Technique (IIT) consists of releasing "*Aedes aegypti*" mosquitoes infected with *Wolbachia* bacteria into environments where there is a high infestation of these mosquitoes and a higher incidence of arboviruses. These incompatible insects are less likely to become infectious, to disseminate arboviruses, and can suppress or replace the natural population of mosquitoes due to the fatal cytoplasmic incompatibility between the mating pairs of the wild-type mosquito with the incompatible type. *Wolbachia* can, therefore, be used to replace the existing mosquito population with a phenotype of lower competence, by releasing females, or to suppress the existing population by releasing males.⁶

According to community trial⁷, the IIT is the most effective strategy for vector control and dengue prevention compared to the traditional strategy, because the IIT reduces the mosquito

population, it decreases the incidence of dengue and it prevents hospitalization due to dengue.⁷

Thirteen countries have replacement programs in progress at various stages of development, with 12 through the World Mosquito Program (WMP) and one independent program in Malaysia. Meanwhile, China (with *Ae. albopictus*), Singapore, and the US have opted for suppression-based programs due to their perceived greater compatibility with their existing intensive and long-term efforts to suppress mosquito populations.⁶

The Fiocruz Foundation has implemented the Wolbachia Method in Brazil, as part of the World Mosquito Program (WMP), with funding from the Ministry of Health and support from the Bill & Melinda Gates Foundation. The implementation costs of this technique are generally low because Fiocruz itself produces the mosquitoes. The method is also sustainable: from a certain proportion of infected mosquitoes, the transmission of Wolbachia to future generations occurs spontaneously, without the need for further releases of the insect into the environment. Therefore, it is a long-term solution for the control of the dengue vector.^{8,9}

Another method used for the control of *Aedes aegypti* is the Sterile Insect Technique (SIT), which consists of sterilizing the male mosquito by exposing it to ionizing radiation or chemicals. Wild females, when mating with sterile males, produce infertile eggs, reducing the insect's proliferation. The method is used in agricultural pests and is usually combined with IIT for arbovirus vector control. However, sterilized insects must be from the same locality where they will be released, as the release of an exogenous strain could promote resistance to the technique. This also applies to IIT.¹⁰⁻¹²

Thus, the present study was done with the objective of analyzing the cost-effectiveness ratio of the associated IIT/SIT strategy as a vector control and dengue prevention method from the BPHS perspective as payer in the State of Goiás, Brazil, and also from the societal perspective as payer.

METHODS

This is a comprehensive health economic evaluation study with cost-utility and cost-

effectiveness analyses, using a hypothetical-deductive (quantitative) scientific approach. The main hypothesis was that the IIT/SIT strategy, compared to traditional vector control using insecticides and environmental management, is more cost-effective for the health system and society in the state of Goiás.

As this study was a mathematical analysis that did not involve any individual patient data, ethical analysis and approval by a research ethics committee of the proposing institution (State Health Department of Goiás) was not required, and there was no need for informed consent in this context. The study was conducted in accordance with the Helsinki Declaration (revised in 2013), Resolution 466/2012 of the National Health Council, and other Brazilian and international ethical standards.

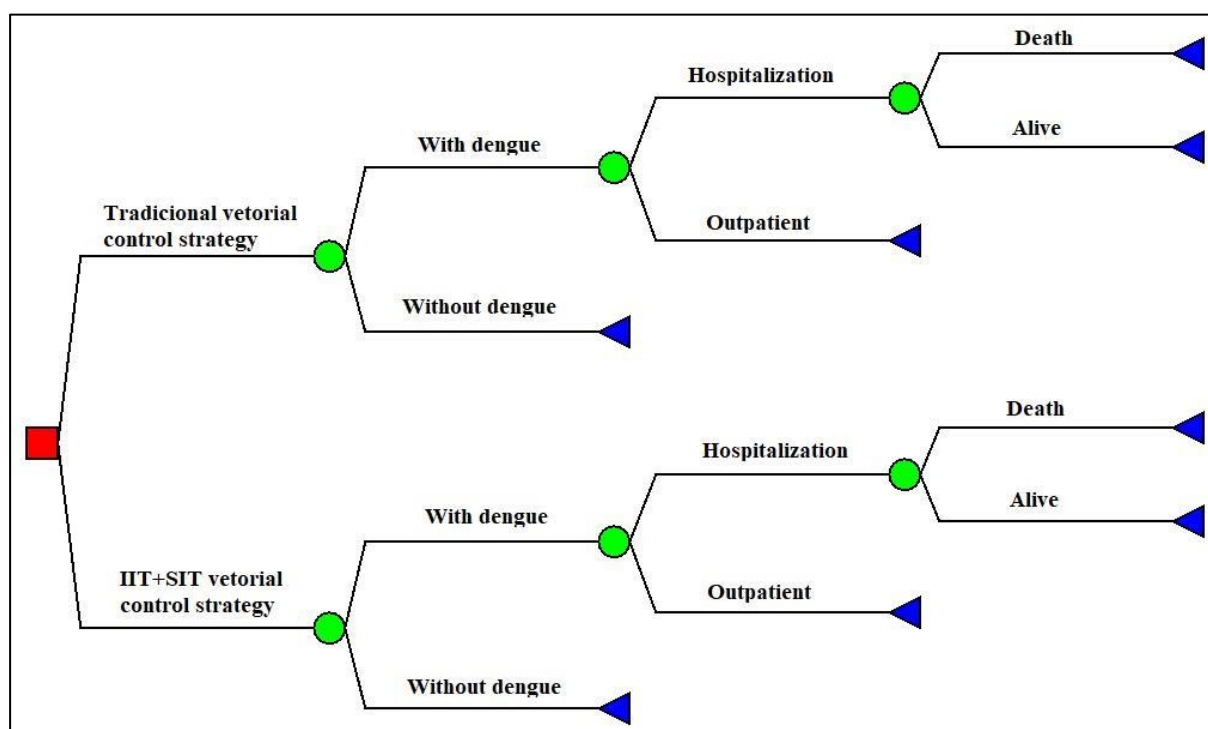
A decision tree model was developed using the Amua® software version 0.3.0, available from <https://github.com/zward/Amua/wiki/Getting-Started>, simulating a hypothetical cohort with the entire population of Goiás. The developed model is showed at **Figure 1** and it is available for free access at https://drive.google.com/drive/folders/1qFnwCt6GX-qNlQI8uwNYSEaJlISbow_e?usp=sharing.

In the model, we simulated the dissemination of wMel Wolbachia mosquitoes in the State of Goiás. The simulation followed the program outlined in a cost-effectiveness study⁶ in the context of Indonesia, with four implementation phases in a particular city (or region), with a total duration of 13 years:

1. Phase 1: Setup, duration of 2 years. Includes the establishment of mosquito colonies in biofactories, laboratories, offices and local regulatory approval, hiring of staff, entomological baseline research (including monitoring of insecticide resistance), program planning and administration, and community engagement campaigns.⁶
2. Phase 1: Setup, duration of 2 years. Includes the establishment of mosquito colonies in biofactories, laboratories, offices and local regulatory approval, hiring of staff, entomological baseline research (including monitoring of insecticide resistance), program planning and administration, and community engagement campaigns.⁶

3. Phase 2: Release, duration of 1 year. Involves the release of Wolbachia mosquitoes over the target areas using the resources established in phase 1.⁶
4. Phase 3: Short-term monitoring, duration of 3 years. Continuous surveillance of the human population and mosquitoes conducted in the release area.⁶
5. Phase 4: Long-term monitoring, duration of 7 years. Reduced entomological monitoring, since the intervention is reliable.⁶

Figure 1. Model (decision tree).



Source: the authors of this paper.

The demographic density of urban areas in Goiás is 2,549.19 people/km², considering that the non-vegetated area (corresponding to the urban area, probably) in Goiás is 2,863.9 km² and the population is 7,300,083 people in 2022. This demographic density in Goiás is similar to the demographic density of a candidate city (Bali) to undergo the intervention in the Indonesian cost-effectiveness study⁶.

It should be noted that the IIT/SIT strategy adopted in Indonesia, in the clinical trial and cost-

effectiveness studies, is adaptable to urban regions of Goiás. However, the logistical, technical, and environmental feasibility of the strategy should be separately researched in a study to be commissioned by the Goiás state government.

The parameters used in the model are specified in **Table 1**. Utility and disutility information related to dengue was obtained from an international literature study¹³. The costs of dengue prevention and dengue treatment were estimated from studies^{4,14} that portray costs for the local reality (Goiás, Goiânia), with inflation updated using the IPCA inflation rate for the period using the citizen calculator¹⁵. The costs of IIT/SIT were estimated from a study in Indonesia. The probabilities of dengue occurrence, hospitalization, and dengue-related deaths in the state of Goiás were estimated from data reported to the Notifiable Diseases Information System (SINAN) and presented in FLINK¹⁶, a public information system of the State of Goiás that consolidates various epidemiological data from the state. The discount rate adopted is 5%, recommended in the economic evaluation guidelines for the BPHS context^{17,18}.

Table 1. Model input parameters related to intervention effectiveness and costs.

Parameter	Average Value	Minimum Value	Maximum Value	Distribution	Source
Probability of contracting dengue (average incidence) in the traditional vector control	0.253898589	0.147437381529852	0.470826153620445	Beta	FLINK‡
Probability of hospitalization for dengue	0.034364782	0.0261280683838269	0.0393803537513405	Beta	FLINK‡
Probability of death from dengue	0.018762528397702	0.0166524338172502	0.0226415094339623	Beta	FLINK‡
Dengue risk ratio in the IIT/SIT intervention	0.2467§§	0.1904§§	0.3195§§	Beta	Utarini <i>et al.</i> ⁷
Cost of traditional vector control per person covered	R\$ 0.254299*	R\$ 0.14*	R\$ 0.48*	Gamma	Santos <i>et al.</i> ⁴
Cost of IIT/SIT intervention per person covered	R\$ 34.550966*	R\$ 16.89*	R\$ 72.83*	Gamma	Brady <i>et al.</i> ⁶
Average cost of hospitalization	R\$ 451.770666*	R\$ 119.17*	R\$ 3,830.20*	Gamma	Martelli <i>et al.</i> ¹⁴
Outpatient care cost	R\$ 0.90493*	R\$ 0.49*	R\$ 1.71*	Gamma	Martelli <i>et al.</i> ¹⁴
Cost by death†	R\$ 118,598.70958*	R\$ 202,343.8‡	R\$ 202,343.83‡	Gamma	Martelli <i>et al.</i> ¹⁴
Cost of absenteeism due to hospitalization	R\$ 349.922431*	R\$ 597.01‡	R\$ 780.32‡	Gamma	Martelli <i>et al.</i> ¹⁴
Cost of absenteeism due to outpatient care	R\$ 149.966756*	R\$ 255.86‡	R\$ 334.42‡	Gamma	Martelli <i>et al.</i> ¹⁴
Discount rate	1.885649142323236	1	3.4522712143931**		Health Ministry ^{17,18}

Continues on the next page...

Table 1. Continuation.

Parameter	Average Value	Minimum Value	Maximum Value	Distribution	Source
Life years gained – LYG	6.894178§	3.765637‡	13‡	Gamma	Suwantika <i>et al.</i> ¹³
Disutility due to hospitalization for dengue (lost QALY)	-0.00013	-0.0000989535634050899	-0.00018	Gamma	Suwantika <i>et al.</i> ¹³
Disutility due to outpatient dengue (lost QALY)	-0.00002.9	-0.0000219896807566866	-0.00004	Gamma	Suwantika <i>et al.</i> ¹³
Utility for the person who dies from dengue (QALY)	3.447089*			Gamma	Suwantika <i>et al.</i> ¹³
Utility for the healthy person (QALY)††	6.894178§	3.765637‡	13‡	Gamma	Suwantika <i>et al.</i> ¹³

Source: the authors of this paper.

Table legend:

*Value discounted.

† Cost of GDP per capita in Goiás multiplied by the number of years lost due to early death from dengue in a 13-year period.

‡ Undiscounted value for ASD (Deterministic Sensitivity Analysis).

§ Value discounted for a period of 13 years.

Discount rate of 5% per year for a total of 13 years.

** Discount rate of 10% per year for a total of 1 years.

†† Mean value of QALY's over 13 years, considering the accumulated QALY's of each person who dies in each year, a value of 0.5 QALY's was assigned in the year of death, and an average was made.

‡‡ Data obtained from FLINK16, values calculated from incidence data estimated from SINAM, values for Goiás in the last 8 years (2015-2022)

§§ Risk ratio values calculated using the online calculator available at https://www.medcalc.org/calc/relative_risk.php.

Years of Life Adjusted for Quality (QALY), Years of Life Gained (YLG), costs, Incremental Cost-Effectiveness Ratio (ICER), and Incremental Cost-Utility Ratio (ICUR) were adopted as study outcomes^{17,18}. The ICUR and ICER were calculated based on the cost ratio and differences in utility or effectiveness between the IIT/SIT strategy and the traditional vector control strategy. The willingness-to-pay threshold (WTP) adopted is the value for Brazil, which is R\$ 122,064.30/QALY gained, for endemic diseases in low-income populations with few available therapeutic alternatives, representing a value three times Brazil's per capita GDP in 2022. The WTP was used to determine the cost-effectiveness relationship between interventions.

The analysis perspective was for the context of the Health System as the payer (the BPHS) in the base-case. As an additional analysis, values were also calculated for an alternative scenario from the societal perspective (the society of Goiás as the payer), where the costs of absenteeism and premature death (loss of socioeconomic productivity) were included.

A deterministic sensitivity analysis (DSA) and probabilistic sensitivity analysis (PSA) were performed to assess the effect of parameter uncertainty on cost-effectiveness results, both for the base-case and the alternative scenario. One parameter at a time was varied within prescribed limits to perform one-way deterministic sensitivity analyses, and variations in ICUR were recorded. The cost and efficiency parameters varied within a minimum and maximum value range based on data obtained from the literature, as previously explained. To conduct the PSA, all parameters from probability distributions were simultaneously sampled. In the PSA, the cost parameter used the Gamma distribution, and other parameters, such as effectiveness, used the Beta distribution. The mean value in the distribution was the value of the base-case, and the standard deviation parameter, minimum value, and maximum value were derived from the literature. 10,000 Monte Carlo samples were executed for each group.

RESULTS

When analyzing the base-case (BPHS perspective in the **Table 2**), where the costs of absenteeism and premature death (loss of socioeconomic productivity) are not included but only direct healthcare costs, we found that the IIT-SIT strategy is more expensive and more effective

than traditional vector control, but his ICUR is below the WTP from the BPHS. Therefore, the IIT-SIT strategy is cost-effective, when compared to traditional vector control.

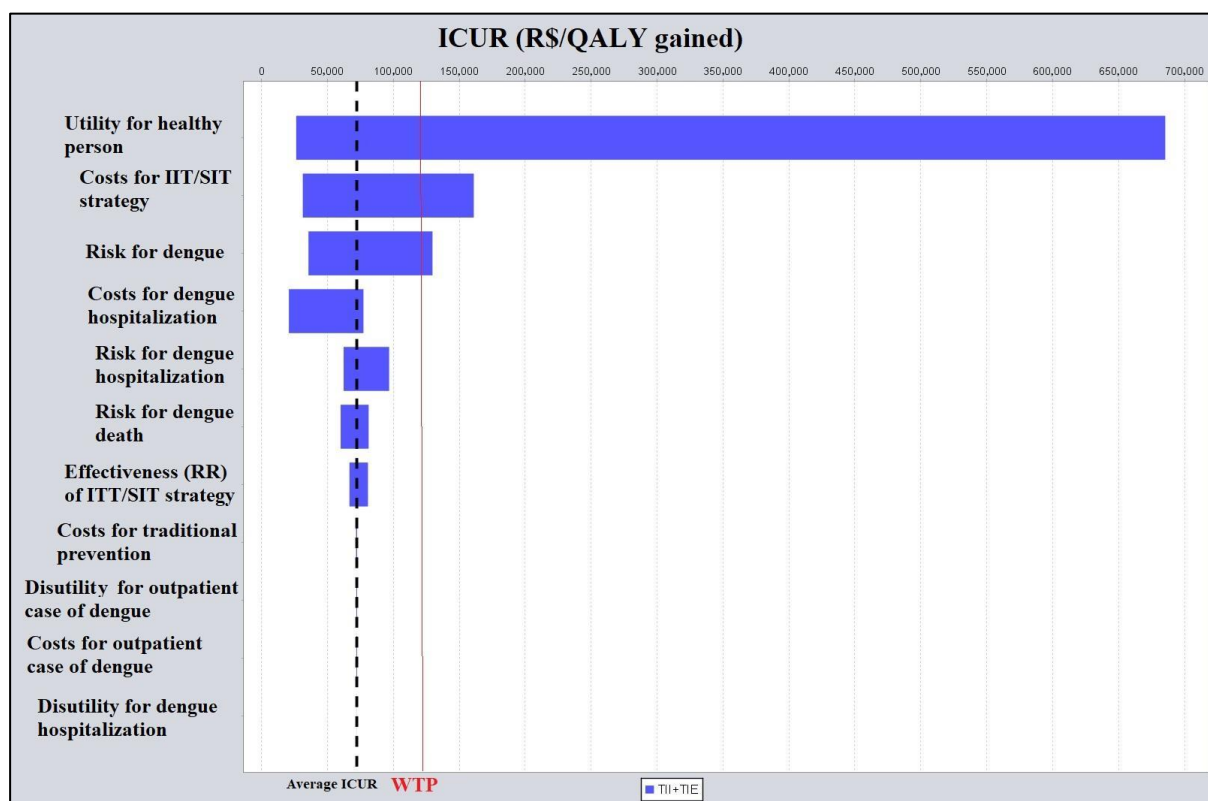
Table 2. Results of the cost-effectiveness analysis.

Outcomes	BASE-CASE: BPHS perspective	
	Traditional vector control	IIT-SIT
Costs	R\$ 4.42	R\$ 35.58
cost increment	—	R\$ 58.76
QALY gained	6.89360505	6.89403632
Incremental QALY gained	—	0.00043127
ICUR	—	R\$ 72,251.90/QALY gained
LYG	6.89361325	6.89403834
Incremental LYG	—	0.00042509
ICER	—	R\$ 73,301.78/AVG
Total costs	R\$ 34,703,217.24	R\$ 279,353,047.38
Cost increment	—	R\$ 244,649,830.14
Dengue cases (estimated)	1,993,461 [1,157,591; 3,696,648]	491,787 [220,405; 1,181,079]
Dengue cases avoided	—	1,501,674 [937,186; 2,515,569]
ICER	—	R\$ 162.92/case avoided
Hospitalizations for dengue	68,505 [33,767; 102,142]	16,900 [6,429; 32,634]
Dengue hospitalizations avoided	—	51,605 [27,338; 69,508]
ICER	—	R\$ 4,740.84/hospitalization avoided
Dengue deaths	1,285 [765; 1,888]	317 [146; 603]
Dengue deaths prevented	—	968 [619; 1,284]
ICER	—	R\$ 252,676.14/death avoided
Outcomes	ALTERNATIVE SCENARIO: Societal perspective	
	Traditional vector control	IIT-SIT
Costs	R\$ 63.65	R\$ 50.19
Cost savings	—	R\$ -13.46
QALY gained	6.89360505	6.89403632
Incremental QALY gained	—	0.00043127
ICUR	Strongly dominated (more expensive and less effective)	Dominant (cheaper and more effective than)
LYG	6.89361325	6.89403834
Incremental LYG	—	0.00042509
ICER	Strongly dominated	Dominant
Populational costs	R\$ 499,742,031.07	R\$ 394,062,098.03
Populational cost savings	—	R\$ -105,679,933.04

Source: the authors of this paper.

The deterministic sensitivity analysis (**Figure 2**) showed that the results of the base-case were reliable and the IIT/SIT strategy remained cost-effective under varied conditions. In other words, the analysis confirmed the cost-effectiveness profile of the IIT/SIT strategy compared to traditional vector control. In all evaluated scenarios, ICUR varied from BRL 21,000 to BRL 685,000, approximately. The model was most sensitive to the utility assigned to the healthy state, primarily. However, the cost of the IIT/SIT strategy, the population risk of dengue, and the costs of hospitalization for dengue were also important factors in the sensitivity analysis. The other parameters had less influence on the model.

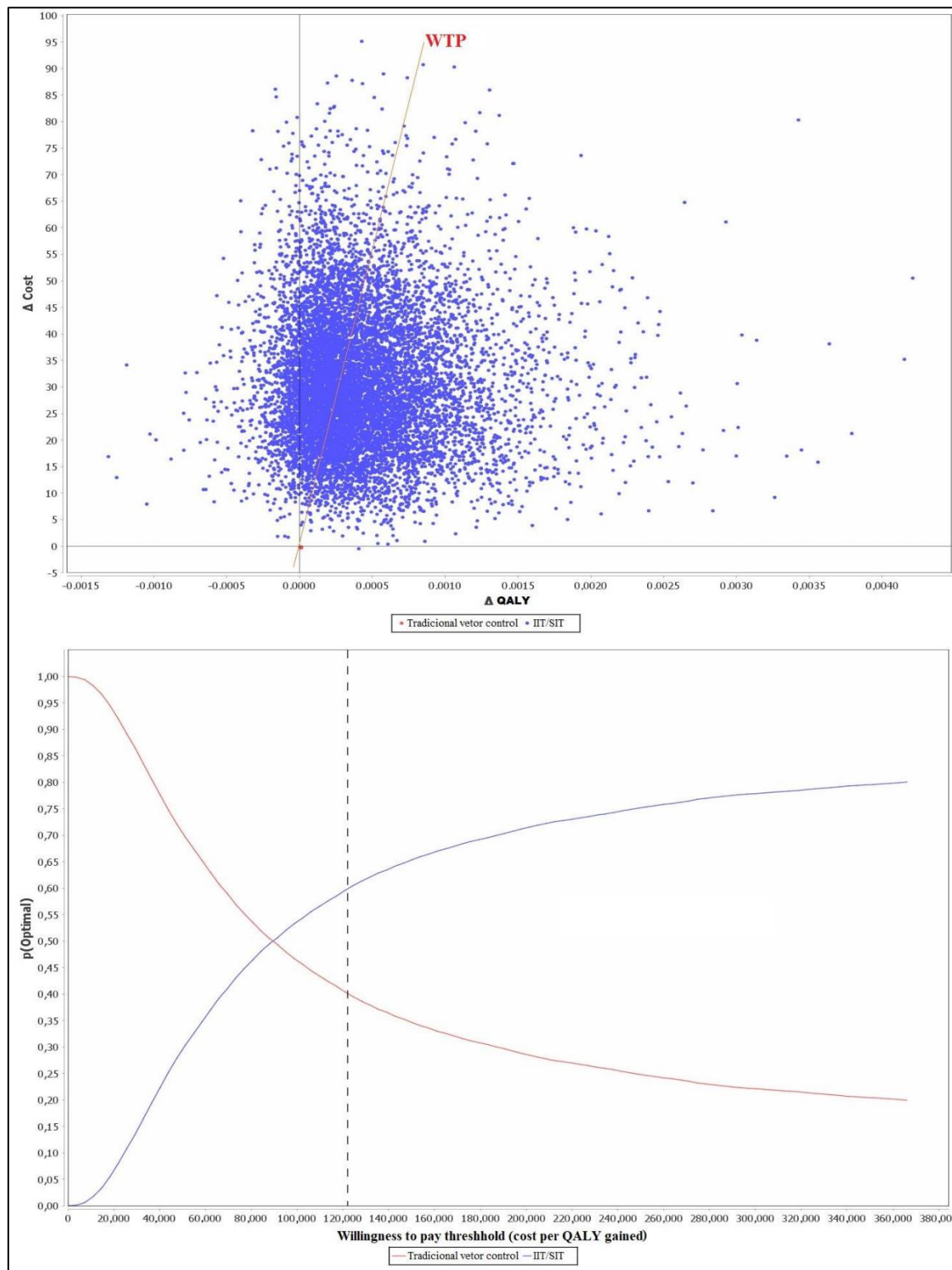
Figure 2. Tornado plot (deterministic sensitivity analysis).



Source: the authors of this paper.

In the probabilistic sensitivity analysis, the IIT/SIT strategy was cost-effective (with RCUI below the LDAP) in 60% of the scenarios, taking into account the LDAP of BRL 122,064.30, as seen in the scatter plots and the curve from LDAP (top and bottom of **Figure 3**). Both sensitivity analyzes demonstrate the robustness of the model.

Figure 3. Graphs of probabilistic sensitivity analysis.



Source: the authors of this paper.

In the analysis of an alternative scenario (societal perspective in the **Table 2**), in which the costs of absenteeism and early death (loss of socio-economic productivity) are incorporated, the IIT-SIT strategy is cheaper and more effective than traditional vector control. Therefore, it is dominant (with lower cost than traditional vector control). This conclusion is confirmed by the probabilistic sensitivity analysis, as the IIT/SIT strategy remained cost-effective in 89% of the scenarios and dominant in 75% of the scenarios, as seen in **Figure 4**. Thus, from society's perspective, it would be mandatory that the IIT-SIT strategy was implemented, as it is more economical, reduces social costs, increases quality of life and reduces morbidity and mortality from dengue.

DISCUSSION

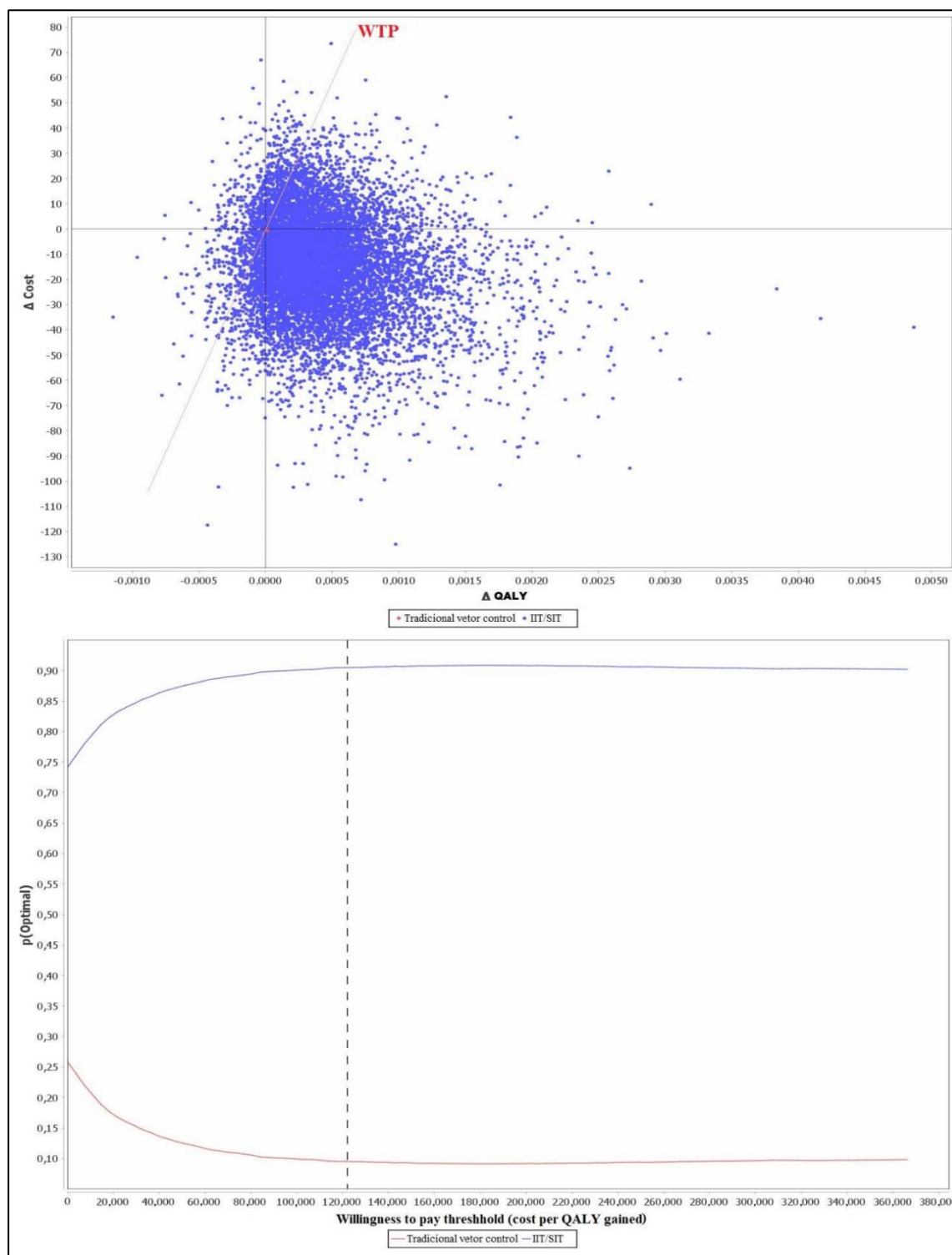
The results demonstrate that the implementation of a program with the IIT/SIT strategy, for the dissemination of mosquitoes with wMel Wolbachia, seems to be cost-effective, from the perspective of the health system (BPHS), and dominant, from the societal perspective: that is, the data suggest that the program should be implemented in the State of Goiás, as it will generate savings for the society of Goiás, for the Government of the State of Goiás and for the BPHS, because it will reduce the costs with vector control of the *Aedes aegypti* mosquito and it will reduce the direct and indirect costs of illness and death from dengue, not to mention other arboviruses.

The cost-effectiveness⁶ study derived from the community trial indicates that, in the Indonesian context, the IIT/EIT strategy is also cost-effective, confirming the data of the present study.

Several initiatives for the use of IIT are being implemented in Brazil. The city of Belo Horizonte built, with its own resources, a biofactory for the production of *Aedes aegypti* with Wolbachia. A 250-square-meter structure houses a team responsible for producing 275,000 mosquitoes per week.¹⁹

The State of Minas Gerais signed a commitment term in 2021 for the construction of a mosquito biofactory and implementation of the Wolbachia method for the control of arboviruses, at an estimated cost of R\$ 10.7 million.²⁰

Figure 4. Scatter plot of the cost-utility ratio in the alternative scenario.



Source: the authors of this paper.

The Central Laboratory of Mato Grosso do Sul (LACEN-MS), with the support of WMP Brazil and Fiocruz, received *Wolbachia* mosquito eggs for the implementation of the program in that state. An existing space at LACEN-MS was provided for the project's development, demonstrating that the initial investment does not require new building installations.²¹ In Ceará, Fiocruz plans to build a biofactory, costing R\$ 12 million, which will be a private company with equity participation from Fiocruz and the World Mosquito Program. This unit will be the largest mosquito and *Aedes aegypti* egg production biofactory in the world.²²

According to community trial⁷ data, the introduction of wMel in *Aedes aegypti* mosquitoes in Yogyakarta (Indonesia) reduced the incidence of virologically confirmed symptomatic dengue cases by 77% among residents aged 3 to 45 years. Protective efficacy was observed against all four dengue virus serotypes, especially 2 and 4 (the most prevalent). Protective efficacy in preventing hospitalization due to virologically confirmed dengue was 86%.⁷

Stable wMel transinfection confers a viral resistance state in *Aedes aegypti* mosquitoes that attenuates superinfection by several medically important flaviviruses and alphaviruses. Several mechanisms have been proposed to explain this phenomenon. However, the dengue virus could evolve resistance to wMel. Nevertheless, the need for alternating infection of human hosts and mosquitoes, together with a complex mode of action, may be a restriction on the adaptive emergence of resistant virus populations.^{5-7,12}

The IIT approach is a new class of products for vector control of dengue and other arboviruses. The strategy is quite attractive, as it is maintained in the mosquito population and does not require reapplication. Future studies need to investigate the multivalency of the intervention, as laboratory studies suggest that wMel may also attenuate the transmission of Zika, chikungunya, yellow fever, and Mayaro viruses by *Aedes aegypti*.^{5-7,12}

This cost-effectiveness study has some limitations. Dengue cost data were obtained from the literature, from a cost survey study on dengue prevention in the city of Goiânia, whose data were updated for use in the present investigation. Also, the costs of biofactory implementation and dissemination of the wMel mosquito were estimated from the values reported in the Indonesia study⁶, which in turn estimated costs from other studies in the literature conducted in

several countries in the North (developed) and South (developing), including Colombia. The actual costs of biofactory implementation and dissemination of wMel mosquitoes in the state of Goiás are not known. However, the costs are probably not higher than those of Indonesia or Colombia.⁶

Another limitation is that this cost-effectiveness study used a limited time horizon of only 13 years. However, if the horizon is extended to 100 years, the IIT/SIT strategy becomes predominantly dominant - cheaper and with more benefits than classical vector control - from the perspective of the health system (BPHS).

The IIT/SIT strategy appears to be a safe strategy in terms of impact on biomes. Still, its long-term environmental effects are unknown. The costs of environmental impact, including strategies to mitigate possible environmental disasters, were not considered in this cost-effectiveness study, which is also a methodological limitation.

CONCLUSION

When compared to traditional vector control strategy (use of insecticides and environmental management), the IIT/SIT strategy is cost-effective from the perspective of the BPHS in the state of Goiás and dominant from the perspective of society. Therefore, it is recommended that the state of Goiás implements the TII/TIE strategy for controlling dengue and other arboviruses through the control of the *Aedes aegypti* mosquito.

DECLARATION OF POTENTIAL CONFLICTS OF INTEREST

The authors have no affiliation with pharmaceutical industry or private healthcare service companies. They do not participate in clinical trials of medications. The authors work at the State Health Department of Goiás, which could be a potential source of conflict of interest. The authors had no role in the peer-review process of this article.

This research did not receive any specific funding from public, commercial or nonprofit funding agencies.

The submission and approval by the Research Ethics Committee does not apply to this investigation as it did not directly involve human participants in the research. The research methods used were exclusively documentary, bibliographic and mathematical modeling.

REFERENCES

1. Teich V, Arinelli R, Fahham L. Aedes aegypti e sociedade: o impacto econômico das arboviroses no Brasil. J Bras Econ Saúde [Internet]. 2017 [cited 2022 Sep 30];9(3):267–76. Available from: <https://doi.org/10.21115/JBES.v9.n3.p267-76>.
2. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde, Coordenação-Geral de Vigilância das Arboviroses do Departamento de Imunização e Doenças Transmissíveis. Monitoramento dos casos de arboviroses urbanas causados por vírus transmitidos pelo mosquito Aedes (dengue, chikungunya e zika), semanas epidemiológicas 1 a 52, 2021. Boletim epidemiológico [Internet]. 2022 Jan 7 [cited 2022 Sep 30];1–15. Available from: <https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/edicoes/2022/boletim-epidemiologico-vol-53-no1.pdf/view>.
3. Ministério da Saúde (BR), Secretaria de Vigilância em Saúde, Coordenação-Geral de Vigilância das Arboviroses do Departamento de Imunização e Doenças Transmissíveis. Monitoramento dos casos de arboviroses até a semana epidemiológica 35 de 2022. Boletim epidemiológico. 2022;1–37.
4. Ryan PA, Turley AP, Wilson G, Hurst TP, Retzki K, Brown-Kenyon J, et al. Establishment of wMel Wolbachia in Aedes aegypti mosquitoes and reduction of local dengue transmission in Cairns and surrounding locations in northern Queensland, Australia. Gates Open Res [Internet]. 2020 Apr 8 [cited 2022 Sep 30];3:1547. Available from: <https://doi.org/10.12688/gatesopenres.13061.2>.
5. Brady OJ, Kharisma DD, Wilastonegoro NN, O'reilly KM, Hendrickx E, Bastos LS, et al. The cost-effectiveness of controlling dengue in Indonesia using wMel Wolbachia released at scale: a modelling study. BMC Med [Internet]. 2020 Jul 9 [cited 2022 Sep 30];18(1):1–12. Available from: <https://bmcmmedicine.biomedcentral.com/articles/10.1186/s12916-020-01638-2>.
6. World Mosquito Program. Brazil [Internet]. Monash University. 2022 [cited 2022 Sep 30]. p. 1. Available from: <https://www.worldmosquitoprogram.org/en/global-progress/brazil>.
7. World Mosquito Program. Sobre o Método Wolbachia [Internet]. Monash University. 2022 [cited 2022 Sep 30]. p. 1. Available from: <https://www.worldmosquitoprogram.org/sobre-o-metodo-wolbachia>.

8. Florêncio V, Dourado P, Santos P, Vieira L. Estratégias Exitosas para o Controle da Dengue [Internet]. Goiânia; 2022. Available from: <https://docs.bvsalud.org/biblioref/2022/06/1371259/estrategias-exitosas-para-o-controle-da-dengue-1.pdf>.
9. Pagendam DE, Trewin BJ, Snoad N, Ritchie SA, Hoffmann AA, Staunton KM, et al. Modelling the Wolbachia incompatible insect technique: strategies for effective mosquito population elimination. BMC Biol [Internet]. 2020 Dec 1 [cited 2022 Sep 30];18(1):1–13. Available from: <https://bmcbiol.biomedcentral.com/articles/10.1186/s12915-020-00887-0>.
10. Garcia G de A, Sylvestre G, Aguiar R, da Costa GB, Martins AJ, Lima JBP, et al. Matching the genetics of released and local Aedes aegypti populations is critical to assure Wolbachia invasion. PLoS Negl Trop Dis [Internet]. 2019 [cited 2022 Sep 30];13(1):e0007023. Available from: <https://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0007023>.
11. Suwantika AA, Supadmi W, Ali M, Abdulah R. Cost-effectiveness and budget impact analyses of dengue vaccination in Indonesia. PLoS Negl Trop Dis [Internet]. 2021 Aug;15(8):e0009664. Available from: <https://doi.org/10.1371/journal.pntd.0009664>.
12. Santos SM, Amorim F, Ferreira I de A, Coelho GE, Itria A, Siqueira Junior JB, et al. Estimativa de custos diretos do Programa Municipal de Controle da Dengue de Goiânia-GO. Epidemiol e Serviços Saúde [Internet]. 2015;24(4):661–70. Available from: <https://doi.org/10.5123/S1679-49742015000400008>.
13. Martelli CMT, Siqueira Junior JB, Parente MPPD, Zara AL de SA, Oliveira CS, Braga C, et al. Economic Impact of Dengue: Multicenter Study across Four Brazilian Regions. PLoS Negl Trop Dis [Internet]. 2015 Sep 24;9(9):e0004042. Available from: <https://doi.org/10.1371/journal.pntd.0004042>.
14. Banco Central do Brasil. Calculadora do cidadão [Internet]. 2023. p. 1. Available from: <https://www3.bcb.gov.br/CALCIDADA0/publico/exibirFormCorrecaoValores.do?method=exibirFormCorrecaoValores>.
15. Utarini A, Indriani C, Ahmad RA, Tantowijoyo W, Arguni E, Ansari MR, et al. Efficacy of Wolbachia-Infected Mosquito Deployments for the Control of Dengue. N Engl J Med [Internet]. 2021 Jun 10 [cited 2022 Sep 30];384(23):2177–86. Available from: <https://www.nejm.org/doi/full/10.1056/NEJMoa2030243>.
16. Secretaria de Estado da Saúde (GO). Indicadores de Saúde: Dengue [Internet]. 2022. p. 1–10. Available from: <https://indicadores.saude.go.gov.br/public/dengue.html>.
17. Ministério da Saúde (BR). Diretrizes metodológicas: diretriz de avaliação econômica [Internet]. Brasília: Ministério da Saúde (BR); 2014 [cited 2021 Aug 21]. 1–135 p. Available from:

https://bvsms.saude.gov.br/bvs/publicacoes/diretrizes_metodologicas_diretriz_avaliacao_economica.pdf.

18. Ministério da Saúde (BR). Avaliação Econômica em Saúde: desafios para gestão no Sistema Único de Saúde. Brasília: Ministério da Saúde (BR); 2008. 1–104 p.
19. Fiocruz Minas. Método Wolbachia contra arboviroses chega a Belo Horizonte [Internet]. Fiocruz. 2020 [cited 2022 Sep 30]. p. 1. Available from: <https://portal.fiocruz.br/noticia/metodo-wolbachia-contra-arboviroses-chega-belo-horizonte>.
20. Instituto René Rachou Fiocruz Minas. MG assina termo de compromisso para construir biofábrica da bactéria Wolbachia no estado [Internet]. Fiocruz. 2021 [cited 2022 Sep 30]. p. 1. Available from: <https://www.cpqrr.fiocruz.br/pg/mg-assina-termo-de-compromisso-para-construir-biofabrica-da-bacteria-wolbachia-no-estado/>.
21. Bio-Manguinhos. Biofábrica do Método Wolbachia é inaugurada em Campo Grande (MS) [Internet]. Fiocruz. 2020 [cited 2022 Sep 30]. Available from: <https://www.bio.fiocruz.br/index.php/br/noticias/2112-biofabrica-do-metodo-wolbachia-e-inaugurada-em-campo-grande-ms>.
22. Siqueira L. Fiocruz Ceará utilizará Método Wolbachia para diminuir a transmissão de arboviroses no Estado [Internet]. LARIISA Saúde Digital. 2022 [cited 2022 Sep 30]. p. 1. Available from: <https://lariisasaudedigital.com/news/fiocruz-ceara-utilizara-metodo-wolbachia-para-diminuir-a-transmissao-de-arboviroses-no-estado/>.