

Secondary impact assessment on the
use of *Wolbachia* technology to
suppress *Aedes aegypti* population

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Prepared by Ipsos
for National Environment Agency (NEA)

EXECUTIVE SUMMARY:

Ipsos has conducted a thorough secondary impact analysis (ecological, biological, social and economic impacts) based on interviews with experts, survey with the public and in-depth secondary research. No critical secondary impacts were found with regard to using Wolbachia as a mosquito suppression tool in Singapore.

Two low- to moderate-risk secondary impacts were identified (i.e. rise in number of other mosquito vectors and unexpected dengue cases). However, NEA already has existing monitoring measures in place to minimize the likelihood of these impacts occurring.

Using Wolbachia as a mosquito suppression tool is complementary to personal control measures that everyone should undertake. It is critical for Singapore residents to continue existing practices (e.g. clearing of stagnant water) to effectively reduce the number of dengue cases.

EXECUTIVE SUMMARY:

No major secondary impacts were identified, control measures are already planned / implemented for impacts with mild and above likelihood of happening

FINDINGS	RECOMMENDATIONS (In consultation with NEA)
<ul style="list-style-type: none"> • A sudden rise in <i>Aedes albopictus</i> numbers in Singapore has been identified as a possible secondary impact, although the impact of such a situation is unknown. 	<ul style="list-style-type: none"> ➤ Monitor numbers of other mosquito species after implementation of the <i>Wolbachia</i> strategy • Gravitraps (which are currently already deployed in dengue hotspot areas) will be extremely helpful in spotting any sudden spike in numbers of any mosquito species. • This allows NEA to take a proactive approach to anticipate any unforeseen effects of a sudden rise in other mosquito numbers
<ul style="list-style-type: none"> • The prevention of unintentional release of female <i>Aedes aegypti</i> mosquitoes is critical in minimising the chances of any unforeseen biological secondary impacts. 	<ul style="list-style-type: none"> ➤ A robust sorting method would minimise the chances of any effects that could follow from an unintentional release of female <i>Wolbachia</i>-carrying <i>Aedes aegypti</i> ➤ Utilisation of radiation (to sterilise any females unintentionally released) is a further measure being explored

EXECUTIVE SUMMARY:

Social engagement would be critical to the success of the *Wolbachia* strategy

FINDINGS

- The public generally feels that dengue is a serious situation in Singapore. The perception of the seriousness of the situation is positively correlated with the support level for the *Wolbachia* strategy.
- There is generally a high level of support for the *Wolbachia* strategy, although the public perception survey may not have comprehensively captured a representative sample of the residents' population, or respondents who may not be as IT savvy
- The public could easily have misconceptions about dengue and the *Wolbachia* technology

RECOMMENDATIONS

- Explain the dengue situation in Singapore using case studies and figures. The *Wolbachia* strategy should be presented as a complementary method to existing practices, that is used to combat the dengue situation
- A follow-up survey based on similar questions as in the online survey could be carried out in heartland areas to better gauge the responses towards the *Wolbachia* strategy
- Ensure and publicise a clear channel for members of the public with questions on dengue or *Wolbachia*. Develop a set of Frequently Asked Questions (FAQs) to address common misconceptions based on survey findings

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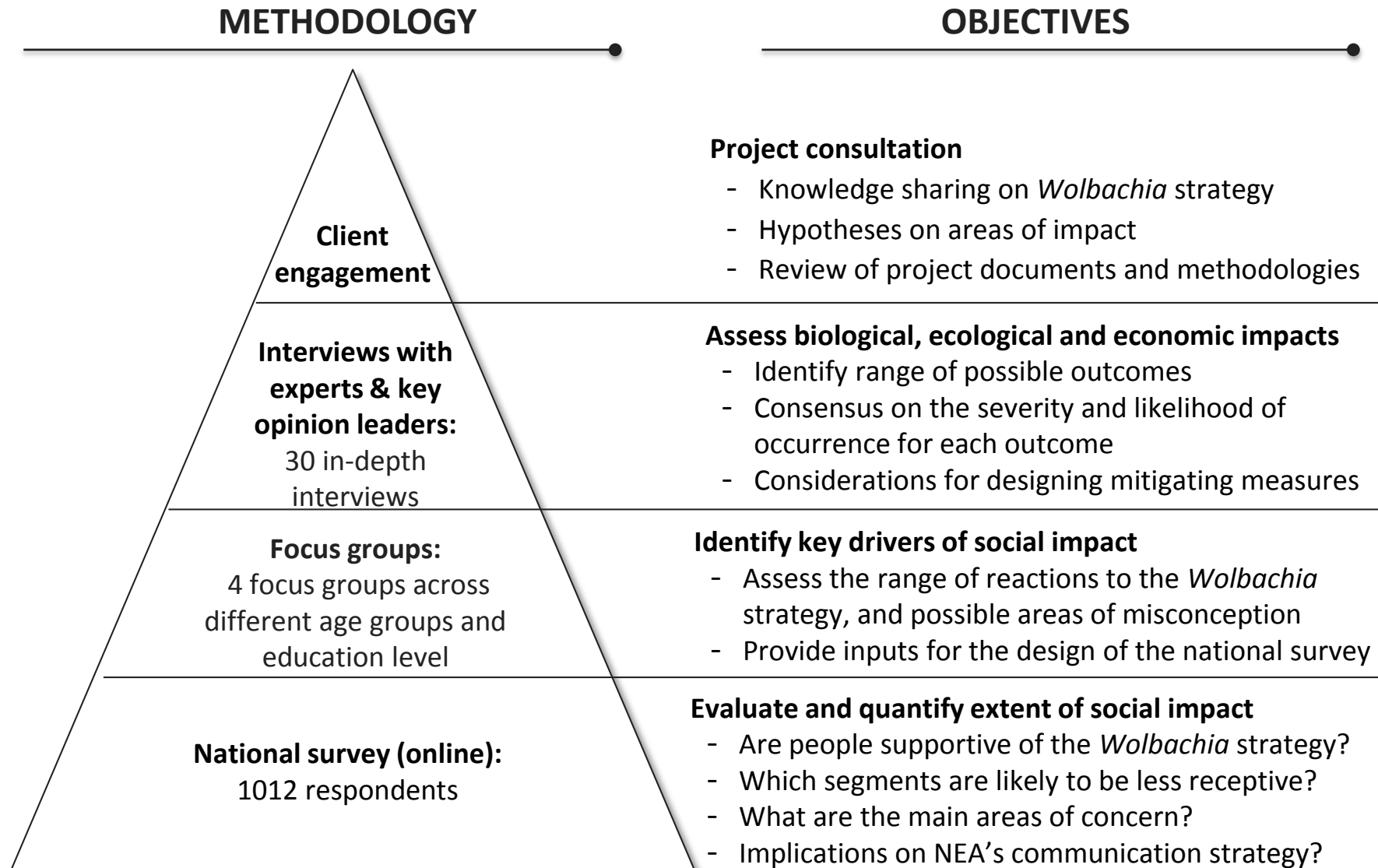
1

Overview of study

OBJECTIVES OF STUDY:

- Identify areas which the implementation of *Wolbachia* technology could have a secondary impact on (i.e. ecological, biological, social and economic)
- Assess the likelihood and severity of the secondary impacts
- Identify the significant secondary impacts
- Work with NEA to develop mitigation measures and identify ways to monitor the effectiveness of these measures

OVERVIEW OF STUDY APPROACH





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Secondary impact assessment

SECONDARY IMPACT ASSESSMENT

The following areas were analysed to identify the secondary risks and benefits to the *Wolbachia* strategy

ECOLOGICAL



Ecological secondary impacts look at the potential effects that a reduced number of *Aedes aegypti* mosquitoes could have on the ecosystem.

The ecosystem includes other species of mosquitoes, preys, predators and other organisms linked to *Aedes aegypti* mosquitoes.

BIOLOGICAL



Biological secondary impacts focus on the potential scenarios of the strategy affecting public health under unforeseen circumstances.

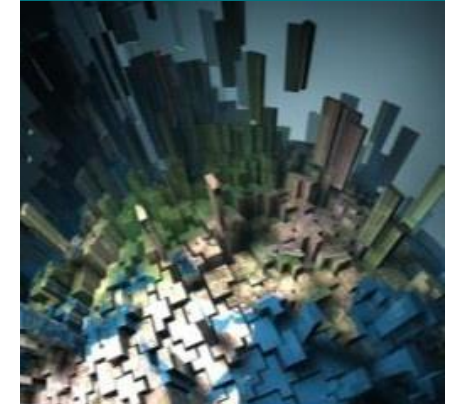
The drivers could include emergence of new dengue strains, evolution of *Wolbachia* bacterium and dengue virus.

SOCIAL



Social secondary impacts focus on the possible reactions or behaviour change by the public that could arise from the implementation of the strategy.

ECONOMIC



Economic secondary impacts look at how the project might cause indirect costs to the nation or the public.

These could include unforeseen medical costs, loss of income and other government expenditure.

SECONDARY IMPACT ASSESSMENT

Key experts/ stakeholders were identified and interviewed to provide their ratings of the relevant biological, ecological and economic secondary impacts based on the below scale:

Likelihood	Severity					
	Ratings	Negligible	Low	Unknown	High	Very High
	Negligible	Negligible Risk	Negligible Risk	Negligible Risk	Negligible Risk	Low Risk
	Low	Negligible Risk	Negligible Risk	Negligible Risk	Low Risk	Low Risk
	Unknown	Negligible Risk	Negligible Risk	Low Risk	Moderate Risk	Moderate risk
	High	Negligible Risk	Low Risk	Moderate Risk	High Risk	High Risk
	Very High	Negligible Risk	Low Risk	Moderate Risk	High Risk	Extreme Risk
<p>Likelihood: Probability of secondary impact occurring based on series of events identified</p> <p>Severity: Extent of impact to the environment/ humans if the secondary impact occurs</p>						

SECONDARY IMPACT ASSESSMENT (SOCIAL)

The results of the public perception survey were used to assess the likelihood of the identified social secondary impacts

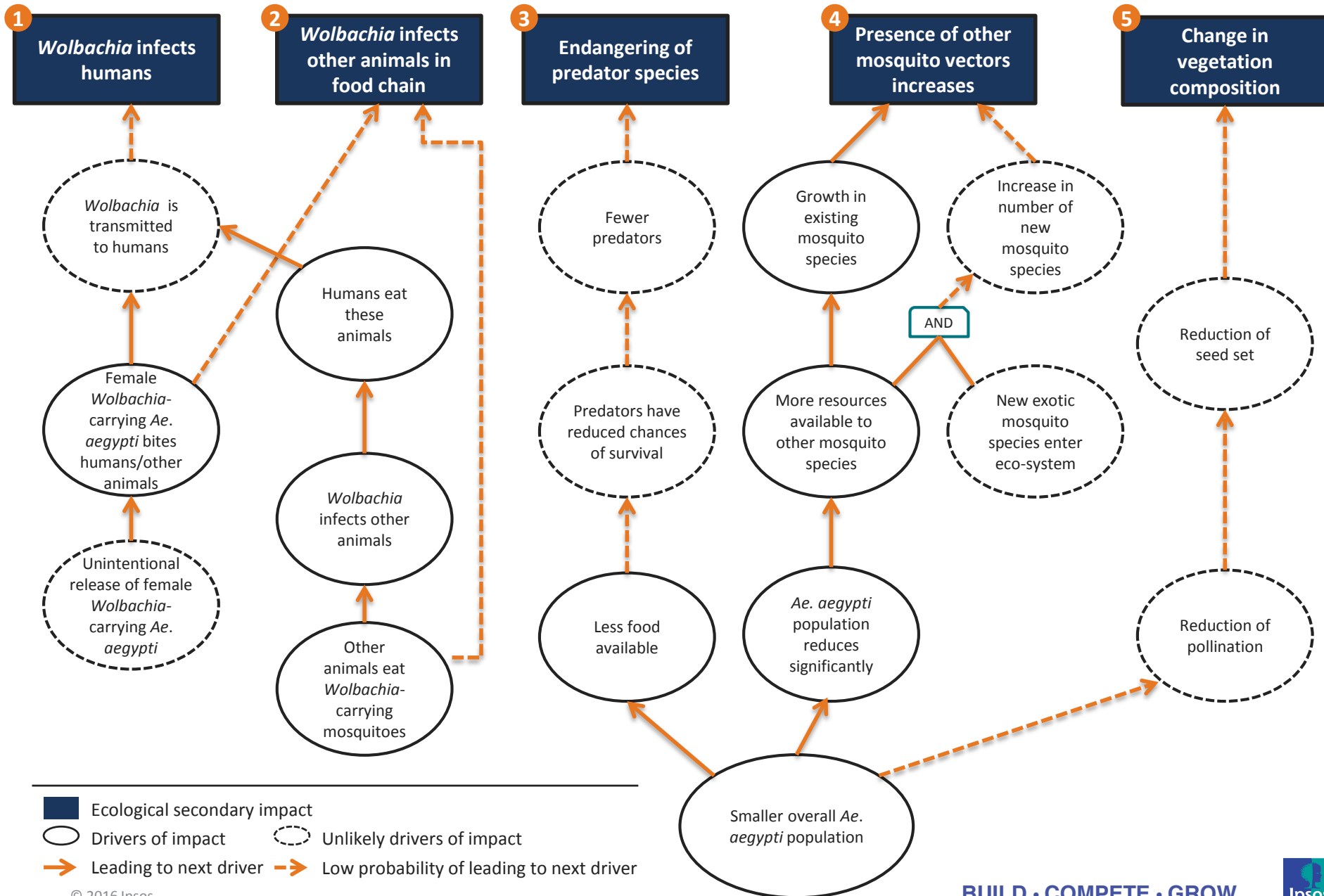
Assessment of likelihood					
Survey Percentage	0-5%	6-25%	26-50%	51-75%	76-100%
Likelihood	Negligible	Low	Moderate	High	Very high
Likelihood: Probability of social secondary impact occurring based on survey results					

3

Ecological secondary impact assessment



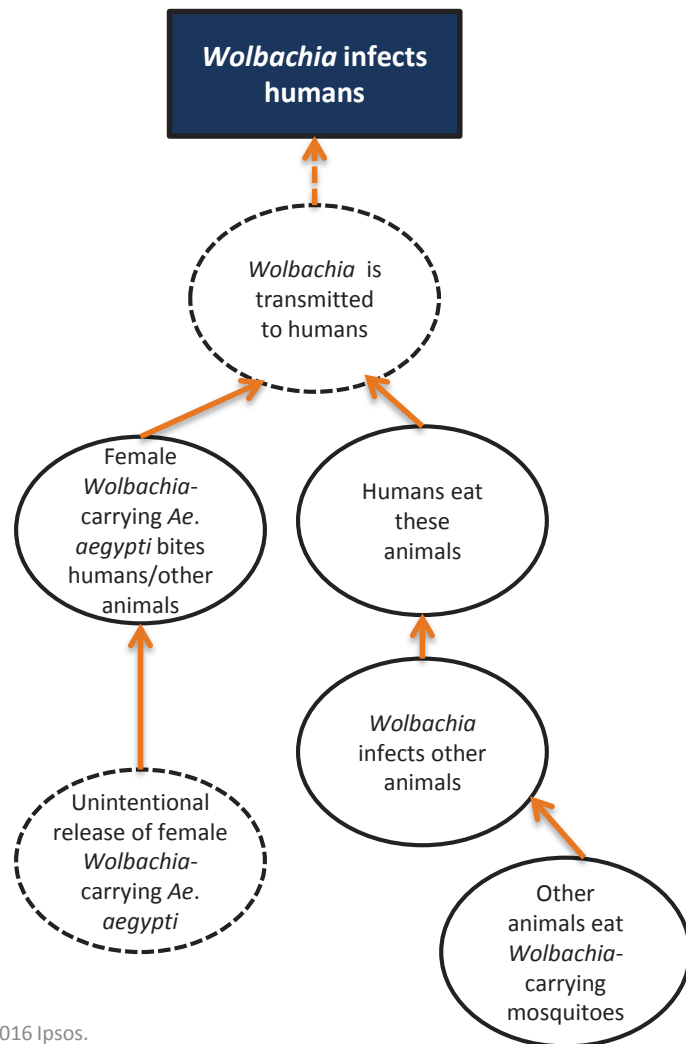
ECOLOGICAL SECONDARY IMPACT (OVERVIEW)



ECOLOGICAL SECONDARY IMPACT (1/5)

Assessing the possibility of *Wolbachia* bacterium infecting humans

FAULT TREE (ECO1)



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SECONDARY IMPACT ASSESSMENT

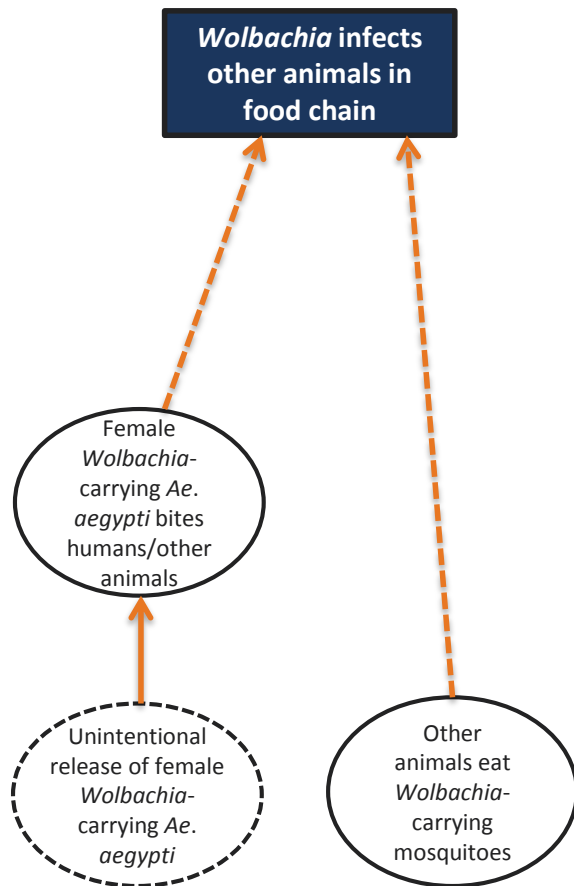
Ratings	
Likelihood	Negligible
Severity	Unknown
Assessment	Negligible risk

- The likelihood of *Wolbachia* being transmitted to or infecting humans is extremely low.
- Based on existing observations, *Wolbachia* has never been found to be transmitted across organisms through the food chain before.
- Many mosquito species that bite humans (e.g. *Ae. albopictus* and *Culex*) naturally carry *Wolbachia* but have not been observed to transmit *Wolbachia* in the biting process.
- There is likely to be a functional constraint as to why *Wolbachia* does not infect vertebrate hosts like humans, although this mechanism has not been explained to date.

ECOLOGICAL SECONDARY IMPACT (2/5)

Assessing the possibility of *Wolbachia* bacterium infecting other animals in the ecosystem

FAULT TREE (ECO2)



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SECONDARY IMPACT ASSESSMENT

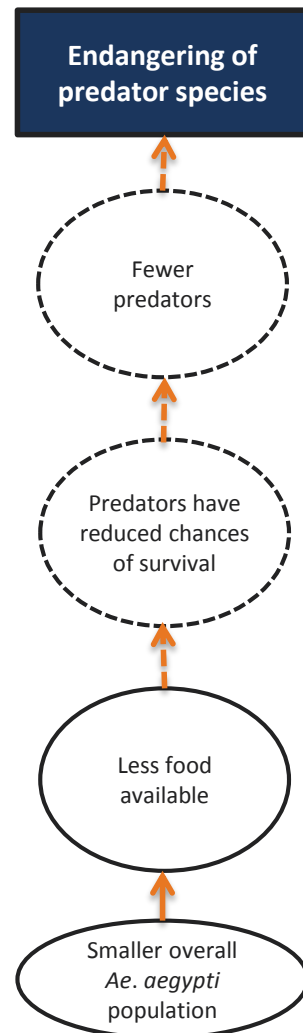
Ratings	
Likelihood	Negligible
Severity	Unknown
Assessment	Negligible risk

- Similar to the impact of *Wolbachia* infecting humans, it is highly unlikely that the horizontal transmission of *Wolbachia* occurs between different species of animals.
- There have been extremely few cases of horizontal transmission of bacterium strain occurring, which suggests that it is a relatively rare event that occurs on an evolutionary timescale.

ECOLOGICAL SECONDARY IMPACT (3/5)

Assessing the possibility of the *Wolbachia* strategy endangering other species in the ecosystem

FAULT TREE (ECO3)



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SECONDARY IMPACT ASSESSMENT

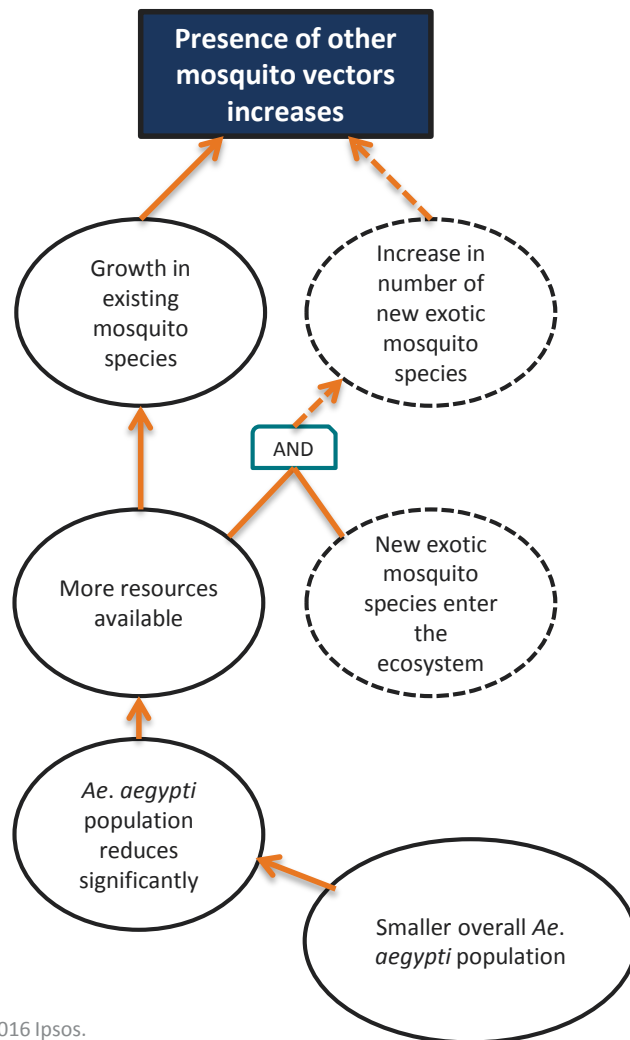
Ratings	
Likelihood	Low
Severity	Low
Assessment	Negligible risk

- There are no birds, fish, mammals or insects that depend solely on *Aedes aegypti* as a source of food.
- It is estimated that mosquitoes typically represent no more than 3% of any predators' (e.g. frogs, lizards, spiders) diet, of which the *Aedes aegypti* accounts for a very small percentage
- It is highly unlikely that the reduction of *Aedes aegypti* population will have a significant impact on the survival of their predators.

ECOLOGICAL SECONDARY IMPACT (4/5)

Assessing the possibility of *Wolbachia* strategy resulting in an increase in population of mosquito vectors of various diseases

FAULT TREE (ECO4)



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SECONDARY IMPACT ASSESSMENT

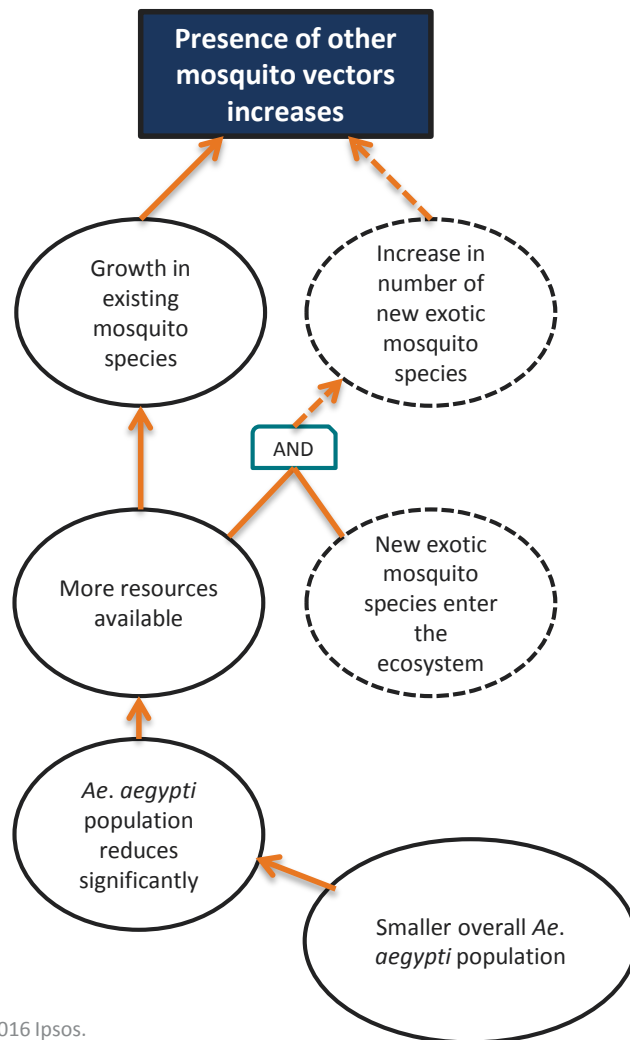
Ratings	
Likelihood	High
Severity	Unknown
Assessment	Moderate risk

- In Singapore's case, *Aedes albopictus* has the highest likelihood to replace the local *Aedes aegypti* population through competition for resources (e.g. larval breeding, living space).
- If the suppression strategy successfully reduces the *Aedes aegypti* population, it is possible that resources freed up could present a vacant niche for *Aedes albopictus* to take over and increase in numbers.
- Almost complete replacement has been observed before in South-East USA, and in some of the outer islands of the Torres Strait.
- However, despite the high likelihood of a replacement occurring, no adverse effects (e.g. increased dengue cases or other vector-borne diseases) were observed in previous cases.
- It is recommended to closely observe the above secondary impact through the monitoring of *Aedes albopictus* levels in areas of release.

ECOLOGICAL SECONDARY IMPACT (4/5)- MITIGATION MEASURES

Assessing the possibility of *Wolbachia* strategy resulting in an increase in population of mosquito vectors of various diseases

FAULT TREE (ECO4)



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SECONDARY IMPACT ASSESSMENT

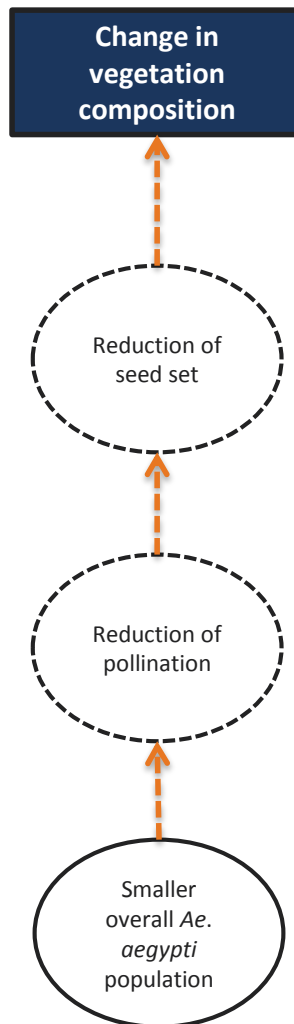
Ratings	
Likelihood	High
Severity	Unknown
Assessment	Moderate risk

- NEA has already deployed Gravitraps in most dengue cluster areas in Singapore that enable the agency to monitor the number and species of mosquitoes
- Gravitraps will be a useful and effective tool that Singapore can utilise to monitor the number of *Aedes albopictus* and other container-breeding mosquito species in the areas of release after the implementation of the suppression strategy

ECOLOGICAL SECONDARY IMPACT (5/5)

Assessing the possibility of *Wolbachia* strategy resulting in a change in the local vegetation composition

FAULT TREE (ECO5)



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SECONDARY IMPACT ASSESSMENT

Ratings	
Likelihood	Low
Severity	Negligible
Assessment	Negligible risk

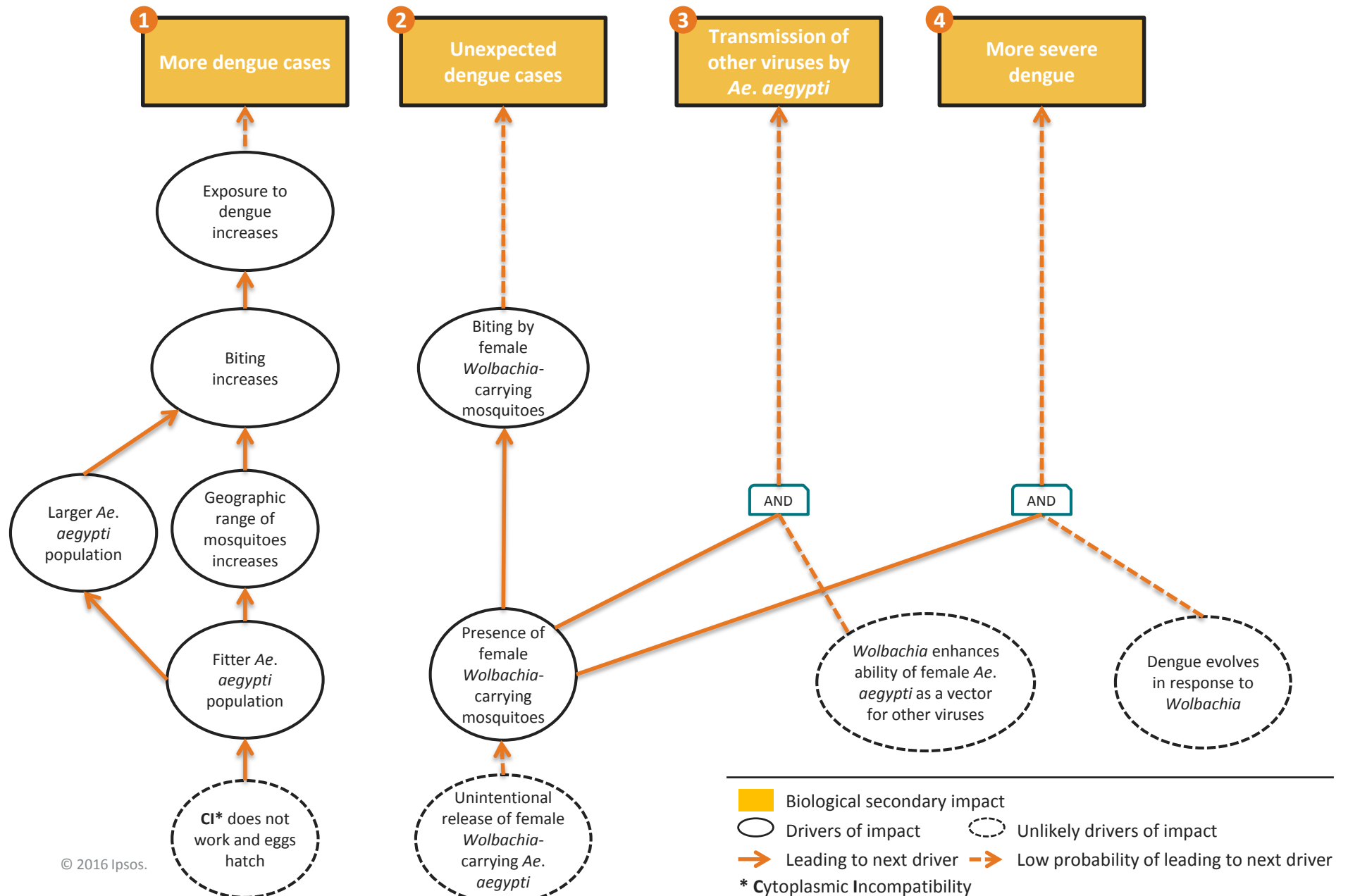
- There are a variety of other insects (e.g. bees, butterflies, moths, beetles) which are better plant pollinators than mosquitoes.
- As *Aedes aegypti* are mainly found indoors around human dwellings, it is unlikely that a decrease in *Aedes aegypti* population will affect plant pollination rates.
- Furthermore, in the case of Singapore, about 80%-90% of the vegetation are managed by humans rather than left to natural pollination.
- This makes it even more unlikely that a reduced *Aedes aegypti* population would result in a significant change in local vegetation composition.

4

Biological secondary impact assessment



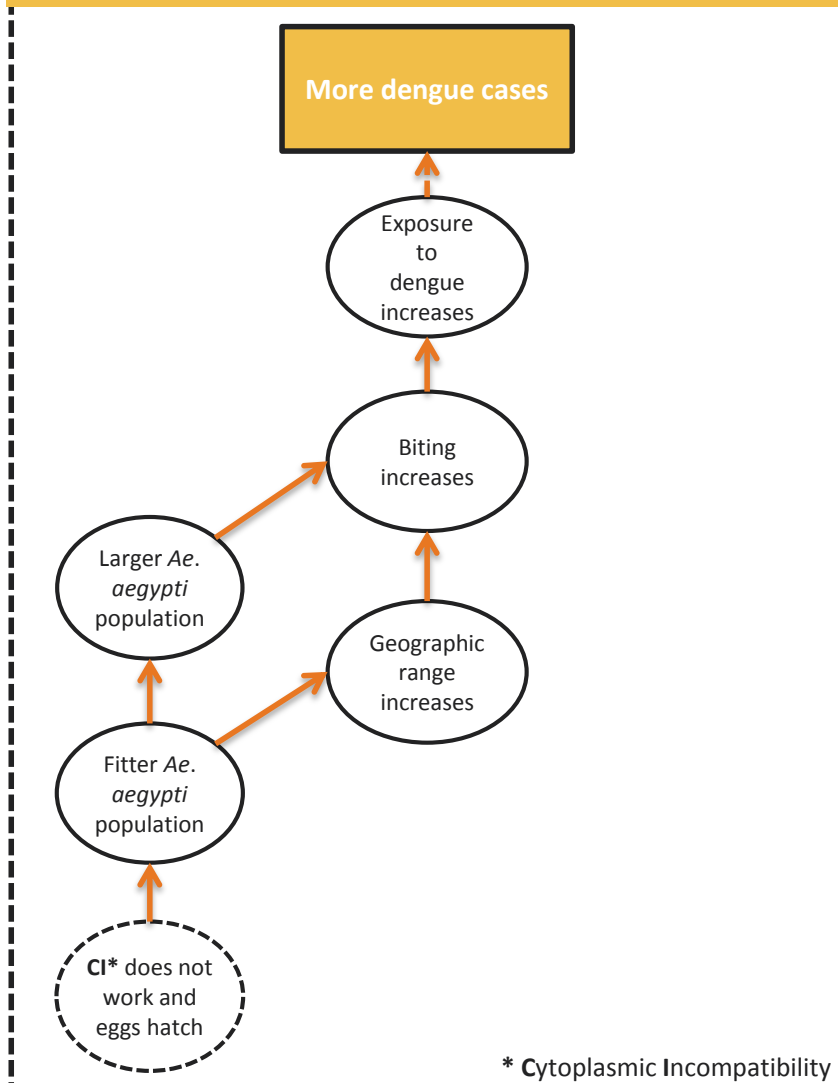
BIOLOGICAL SECONDARY IMPACT (OVERVIEW)



BIOLOGICAL SECONDARY IMPACT (1/4)

Assessing the possibility of *Wolbachia* strategy resulting in an increase in dengue cases (CI Failure)

FAULT TREE (BIO1)



SECONDARY IMPACT ASSESSMENT

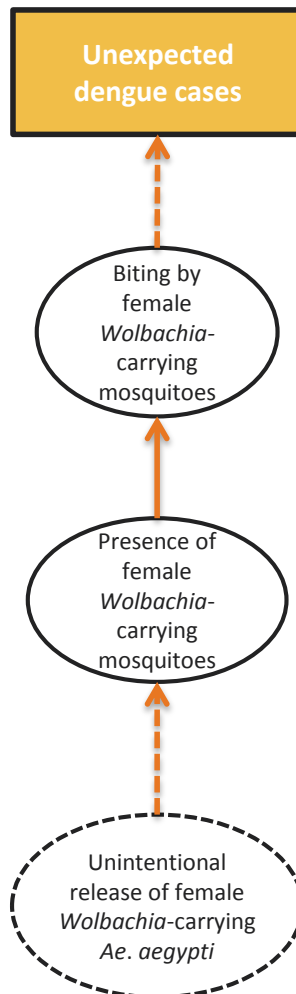
Ratings	
Likelihood	Negligible
Severity	High
Assessment	Negligible risk

- *Aedes aegypti* that have been transinfected with different strains of *Wolbachia* (e.g. *wMel*, *wMelPop*, *wAlbB*) are known to display nearly complete CI (McMeniman *et al.* 2009; McMeniman and O'Neill 2010).
- (Yeap *et al.* 2011) investigated the effectiveness of CI when *Aedes aegypti* mosquitoes are released into the environment. The results showed that CI worked at almost 100% effectiveness in the field
- This is further reinforced by (Axford *et al.* 2016) where complete CI was shown in *wAlbB*-carrying *Aedes aegypti*.
- From the observations so far, CI has been highly effective in the external environment
- However, monitoring of CI levels will still be essential to look out for any early warning signs that could threaten the success of the strategy.

BIOLOGICAL SECONDARY IMPACT (2/4)

Assessing the possibility of *Wolbachia* strategy resulting in the incidence of unexpected dengue cases (Unintentional release of female *Wolbachia*-carrying *Ae. aegypti*)

FAULT TREE (BIO2)



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SECONDARY IMPACT ASSESSMENT

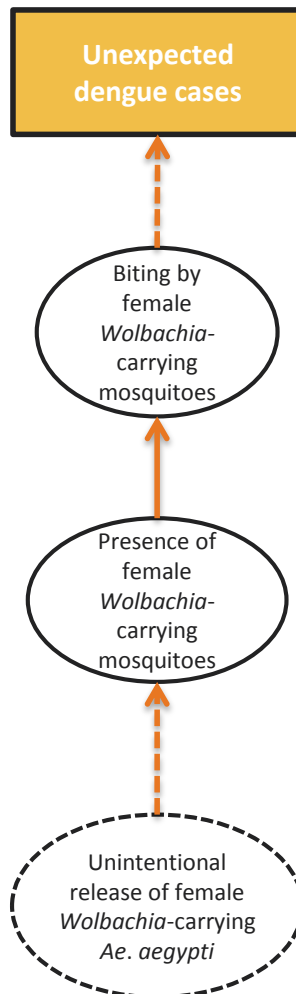
Ratings	
Likelihood	Low
Severity	High
Assessment	Low risk

- The unintentional release of female *Wolbachia*-carrying *Aedes aegypti* mosquitoes could result in an increase in number of female *Aedes aegypti* mosquitoes in the environment
- This could contribute to biting incidence and possibly to the number of dengue cases

BIOLOGICAL SECONDARY IMPACT (2/4)- MITIGATION MEASURES

Assessing the possibility of *Wolbachia* strategy resulting in the incidence of unexpected dengue cases (Unintentional release of female *Wolbachia*-carrying *Ae. aegypti*)

FAULT TREE (BIO2)



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SECONDARY IMPACT ASSESSMENT

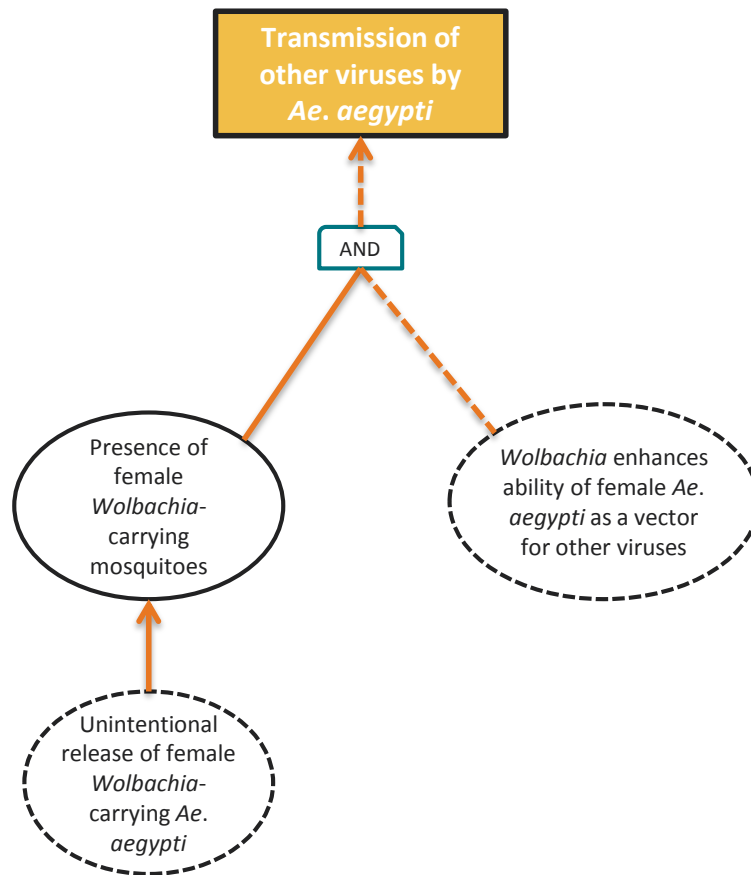
Ratings	
Likelihood	Low
Severity	High
Assessment	Low risk

- The probability of an unintentional release could be greatly reduced by a robust sorting method.
- Utilisation of radiation, that would sterilise any females but would have no fitness effects on males, is a further measure that could be explored.
- Furthermore, if by chance, female *Wolbachia*-carrying *Aedes aegypti* mosquitoes are released, the likelihood that this will contribute to dengue incidence will be greatly reduced by the virus blocking potential of *Wolbachia* (Moreira et al. 2009; Walker et al. 2011; van den Hurk et al. 2012).

BIOLOGICAL SECONDARY IMPACT (3/4)

Assessing the possibility of *Wolbachia* bacterium causing other viruses to be transmitted by *Ae. aegypti*

FAULT TREE (BIO3)



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SECONDARY IMPACT ASSESSMENT

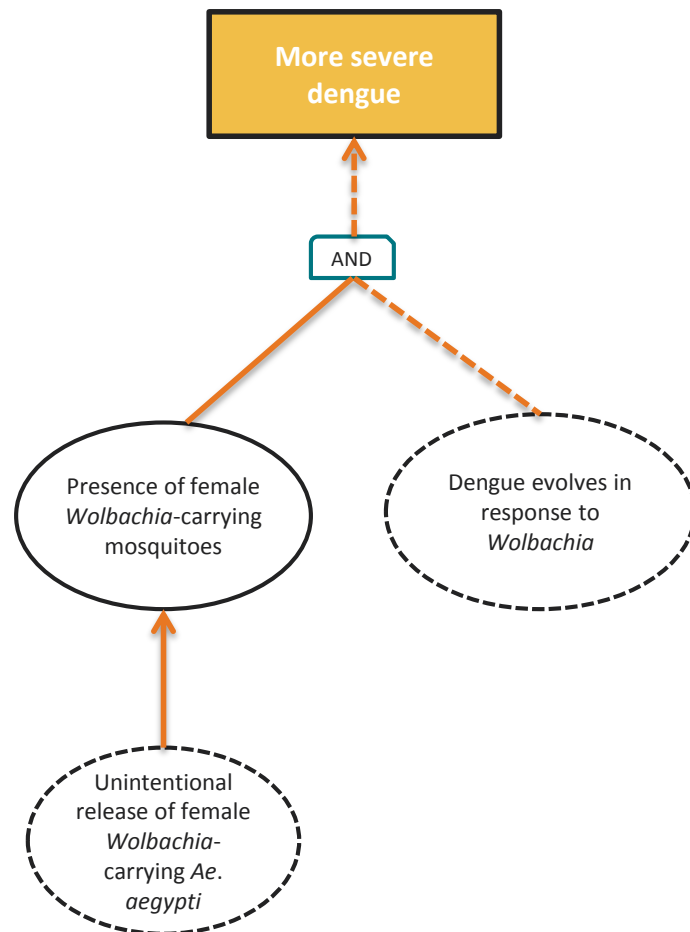
Ratings	
Likelihood	Negligible
Severity	High
Assessment	Negligible risk

- There is currently no evidence that *Wolbachia* will enhance the spread of any other virus, such as West Nile virus, in *Aedes aegypti*.
- However, as it is challenging to predict evolutionary impacts, it should still be monitored for early warning signs.

BIOLOGICAL SECONDARY IMPACT (4/4)

Assessing the possibility of the *Wolbachia* strategy causing more severe dengue

FAULT TREE (BIO4)



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SECONDARY IMPACT ASSESSMENT

Ratings	
Likelihood	Negligible
Severity	High
Assessment	Negligible risk

- Currently there is no evidence that dengue will evolve to counter the *Wolbachia* blocking effects.
- Theoretical studies cannot predict the likelihood of evolution of dengue virulence, but comparative data provide no precedent for *Wolbachia* increasing dengue virulence (*Bull and Turelli, 2013*)