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Safety and Proven Risk Assessment on the Release of Wolbachia-Inserted Aedes Aegypti: Lesson Learned from the Partial Resistance of the Community

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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ABSTRACT

Aims: to describe the basis of partial rejection from the community regarding the government's plan to expand the range of releases of Aedes aegypti mosquitoes which have been inserted with the endosymbiont bacteria Wolbachia spp. to reduce the incidence of dengue hemorrhagic fever and offers a more rational approach based on community based medicine to educate massively first before expecting community participation.
Discussion: Aedes aegypti which laboratorily inserted with Wolbachia, an endosymbiont bacterium, naturally occurring in insects is actually a great success story in several countries, e.g., Brazil. In Jogjakarta, Indonesia this success story also repeated even though unfortunately when the government tries to expand the programme, some part of the community reject it. Lack of sufficient community education perhaps become the main reason of rejection from those who do not understand yet regarding the benefit.

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Conclusion: Tackling social determinants of Health is necessary in order to make a national programme can be implemented and receive support from the community.

Keywords: Mosquitoes; vector control; social determinants; health education; promotion; safety, Indonesia.

1. INTRODUCTION

Dengue hemorrhagic fever (DHF) is a vector-borne disease transmitted by the blood-feeding anthropods (mosquitoes) named Aedes spp. There are two species responsible for DHF named *Aedes aegypti* and *Ae. albopictus* [1]. According to Zeng et al [2], globally, the total number of dengue cases increased enormously. In 2019, according to the region in the world, the Oceania area had the highest age-standardized incidence rates per 100,000 populations (3173.48 (95% UI 762.33–6161.18)), followed by the South Asia region (1740.79 (95% UI 660.93–4287.12)), and then the Southeast Asia region (1153.57 (95% UI 1049.49–1281.59)) [3].

Following incubation period that usually persist 3-7 days, there is an instantaneous commencement of clinical symptoms - mainly high fever, retro-orbital headache and body pain. Typically, DHF's clinical course follows three phases - febrile, critical and recovery [4]. Without proper management, DHF can develop into severe dengue (SD) which is life threatening [5,6].

As dengue cases increase globally, vector control combined with community engagement are focus to prevent spread of the disease [7]. Many effort has been made in order to eliminate DHF, one of them was via entomologically vector control approach; one of the most advanced techniques currently is population replacement in mosquitoes via the release of *Ae. Aegypti* inserted with endosymbiont *Wolbachia* to the environment. It is expected to slowly replace or at least influence the potentially dangerous wild type *Ae. aegypti* with the sterile one [8]. Success story regarding this method came from all over the world, e.g., Australia [9], Bangladesh [10], Brazil [11], Malaysia [12], Vietnam [13] and also from Jogjakarta, Indonesia [14].

Regarding its safety, several studies has been widely reported. Data revealed by Lee et al [15] showed that transient introgression of Wolbachia into *Ae. aegypti* populations being released in the environment actually does not elicit an antibody response to Wolbachia Surface Protein among community members. That statement suggest that humans are not exposed to the major Wolbachia surface antigen, WSP, or in a simpler sentence human does not affected. The results of study regarding risk assessment on the release of Wolbachia-infected *Ae. aegypti* in Yogyakarta, Indonesia conducted by Buchori et al [16] showed that the release of Wolbachia-infected *Ae. aegypti* led to negligible risk.

Unfortunately, although there are many success stories related to this approach, when the Indonesian government intended to expand coverage to other endemic areas, it was met with some resistance from the community, e.g., It is known that 1650 people in Bali, Indonesia that signed a petition against the release of the mosquito because there was an issue circulating that the virus from the Wolbachia mosquito would create a new pandemic in the future [17]. This partial resistance forced the government to postpone its release in Bali.

The aim of this review is to analyze factors that contribute to the partial resistance from the community medicine perspective and suggestions to overcome this obstacle.

2. A GLANCE AT THE AEDES MOSQUITO WHICH IS INSERTED BY THE ENDOSYMBIONT WOLBACHIA

The *Ae. aegypti* mosquito is actually the main transmitter of dengue, Zika, chikungunya and yellow fever viruses [1]. In the context of dengue, the number of people affected is intensely growing [2,3]. In recent decades, due to (1) population growth, (2) the rapid movement of people due to improvement in transportation, (3) expanding international travel and also (4) climate change have all increased the spread of *Ae. aegypti* mosquitoes and of course subsequently, the number of people affected by Dengue fever has also increased rapidly [2-5]. Dengue fever nowadays, is considered the most critical mosquito-borne viral disease in the world, according to the World Health Organization. It's also the most rapidly spreading, with a 30-fold increase in global incidence over the past 50 years.

The Wolbachia mosquito is basically the *Ae. aegypti* mosquito that have the abilities to transmit the dengue hemorrhagic fever virus; in which it is then inserted with an endosymbiont Wolbachia bacteria [8-17]. Basically, Wolbachia lives inside insect cells and is passed from one generation to the next through an insect's eggs [8,9]. The *Ae. aegypti* mosquitoes do not normally carry Wolbachia, however many other mosquitoes do. So in order to introduce Wolbachia into *Ae. aegypti*, researchers injected the bacterium into its eggs. This eventually produced adult *Ae. aegypti* that carried Wolbachia. Wolbachia blocks viruses like dengue, chikungunya and Zika from growing in the bodies of Aedes aegypti mosquitoes. This means that Wolbachia mosquitoes have a reduced ability to transmit viruses to people. When Wolbachia is established in a mosquito population it results in a decreasing incidence of dengue, Zika, chikungunya. This bacterium will weaken the dengue virus that resides in the mosquito's body and reduce its infectivity. In this way, cases of dengue fever will decrease [8-10].

3. REASONS WHY PUBLIC RESISTANCE EMERGED: LESSON LEARNED

The paradox of why some public health programs do not achieve their potential impact, while other programs succeed in improving health outcomes drastically [18]. Restricted and unreliable funding, lack of automatic means to track and improve performance, workforce limitations, and insufficient political commitment can all cause public health programs to fail [19]. Implementation can succeed and be sustained if organizations and coalitions effectively address important key areas in order to avoid failure and resistance.

Public health policies often face resistance due to various factors. These include concerns about personal freedoms and autonomy, misinformation, distrust in government or healthcare institutions, economic interests, and cultural or ideological differences. People may also fear potential unintended consequences of policies.

3.1 Concern Regarding Personal Freedoms and Autonomy

Policies are often cynically described as unfairly restricting freedom and displacing personal responsibility [20]. The causes of ill health are complex and multifactorial, yet the answers offered mostly by mainstream global culture are strikingly precarious: "bad personal choices are the primary cause of the condition of ill or health, and more personal responsibility is the ultimate solution". Constant exposure to certain narrative *adagium*, especially in the era of social media use, may actually be harming health and well-being [20]. Now is the era of infodemics and misinformation that easily affect people's negative health behaviors [21].

Rather than intelligibly reinforcing people to choose better options/choices in the context of substantial practical, social, and physical/material barriers, it is frequently more effective to direct upstream factors- upstream healthcare is any approach to disrupt these structural barriers and to transform a person's quality of life and health outcomes- [22]; e.g., to modify the environment in ways that facilitate healthy behaviors and making unhealthy behaviors become more difficult to do. Examples of such policies include Covid vaccine incentive [23] prohibitions on smoking in public area [24], reductions in the sodium content of foods [25], or taxes on tobacco, alcohol, and sugary beverages [26]. Such policies are recommended by major health organizations and have been effective—and popularly accepted—in other countries.

Positive ideas like free choice and personal responsibility unfortunately may harm health and well-being [27]. Certainly, such statements can be positive and empowering 28]. Individual choice combined with responsibility can provide strong motivation and encouragement to take action regarding improvement of their health, even for those who are already in illness or disorders [29]. Unfortunately, too focus on choice and personal responsibility only partially paints an incomplete picture of the drivers of health [20]. It diverts focus from the role of social and environmental items in tailoring health condition, e.g., items that each individual commonly cannot affect alone by himself/herself, such as public safety, pollution, inequality, occupational hazards, and affordability of healthy foods and quality health care [30].

3.2 Misinformation

The present-day communication situation is characterized by the dynamic and promptly evolving technologies in routine daily life, including health [31,32]. Communication in any form has evolved and now includes popular social media such as Facebook, Twitter, and

Instagram to disseminate massively facts and ideas via content exposure [33]. Communicating and consuming information has shifted from the more traditional methods to the better forms which marked by connectivity, interactivity and real time [34] as part of this communication evolution [31].

The increasing caress of social media platforms by its users with a health agenda and within the health-policy or health-care condition transmits the intended message unlimitedly [35]. Social media nowadays already become an important tool for disseminating and consuming information (which unfortunately is not only always good information, but also bad information with bad intentions from the spreader- the latter usually called misinformation) [36]. In a positive way, social media commonly used to promote public awareness and influencing policy making about health [31].

The spread of misinformation in social media has become a severe threat to public interests [36]. For example, several incidents of public health concerns arose out of social media misinformation during the COVID-19 pandemic [37] and now it is happening again through several videos on social media by public figures in the context of rejection due to the release of *Ae. aegypti* mosquitoes containing endosymbiont bacteria Wolbachia (here are some content that can be found in YouTube™ https://www.youtube.com/watch?v=LM0SmV-zz IQ,https://www.youtube.com/watch?v=xqINFXQJluQ&t=2183s,https://www.youtube.com/watch?v=zKnJIWBhBKc). What many social media users or viewers are rarely informing of is that platforms reserve every right to police user-generated content through a clause in their Terms of Service, usually by incorporating their Community Guidelines by reference [38].

Due to that condition, content moderation is needed, because it is an active and continuous process of reviewing and monitoring user-generated content on online platforms to ensure that it meets certain standards and guidelines [38]. This includes withdrawing inappropriate or offensive content and enforcing community engagement guidelines and as well as conditions that, even though they have not yet occurred, have been regulated in the terms of service [38,39]. Content moderation is the process of reviewing and monitoring user-generated content on online platforms to ensure that it meets certain standards and guidelines. This includes removing inappropriate or offensive content and enforcing community guidelines and terms of service [39]. Content moderation is used in a variety of contexts as a 'governance mechanism' to structure community participation in order to facilitate cooperation combined with civility; or in other words balancing independence with responsibility [40].

On social media, content moderation is ordinarily an automated process based on machinery learning and computational algorithms delineated by bounded human interaction [41]. From this potentially reckless freedom, awareness begins to emerge regarding the importance to examines how activists leverage the technical properties of social media to develop a joint narrative and a collective identity [42]. In the beginning, social media provider has refused the act of arbitrating in public discourse, perceiving of their service to their users/readers as nonpartisan channels for conversations rather than guardians of content [41,43,44]. In recent years, social media providers have been blamed for not accepting their responsibilities on public discourse seriously enough with regard to sensitive topics such as hate-speech [45], injustice with discrimination [46], antisocial aggressive behavior expresses in violence [47], and even to imbalance political interference [48]. Once again, while the platform providers legally bear no responsibility for the content its users generate, many people believe that it is the failure of social media provide to control fake content [49].

In the context of partially rejection in Bali, the array of misinformation is very wide. Some accuse these mosquitoes are harmful due to its genetic engineering properties with various negative potentials related to changes in strains and mutations. There are also fears among community members that Wolbachia can infect the human body. Some even believe Wolbachia bacteria can play a part in spreading homosexual activity in people who get bitten by the mosquito, citing a study reporting that a Wolbachia strain can induce the feminization of genetic males.

3.3 Distrust

Over the last decades, health systems worldwide have encountered a sharp decline in public trust due to several reasons [50-52]. For those unfortunate and marginalized minority populations, who commonly suffer from inequity, poverty and political exclusion, the roots of this tendency terribly sink, chartering a state of two-

ways distrust between these poor people and health provider [53]. Paradoxically, in a much smaller scope compared to trust, distrust does hinder health initiatives, such as effective health care [54]. Wherever distrust reigns, even trust building actions, e.g., prioritizing “the greater good of common interests”, outlining rights and obligations, and expanding transparency capacity, are vulnerable to collapse.

Lesson learned from similar rejection in Puerto (USA) is that lack of trust on strangers was an important challenge due to criminal activity involving violence and drug use in some community areas [55].

3.4 Social and Economy Interests

There was widespread controversy and rejection in society. There are various reasons, including that this method is accused of being full of business interests. The Wolbachia mosquito is suspected of being able to induce the disease Japanese encephalitis with the consequence of having to buy and use a vaccine to treat it. Some speculate that these mosquitoes were created to spread other diseases to reduce the human population [56].

Bali is one area that rejects this method. Some residents in Bali opposed a pilot project on the release of 200 million eggs of mosquitoes carrying Wolbachia in Buleleng and Denpasar to reduce the impact of dengue on communities there. The possibility of Wolbachia bacteria being transferred to other insects and the potential impacts of such a host shift on the tourisms related economy and shifted in the micro-fauna composition which is feared will change the environment; these two are among the biggest concerns behind the resistance. Therefore, the spread of millions of Wolbachia mosquito eggs in several areas in Bali has been postponed [56].

4. SUGGESTIONS TO OVERCOME THIS OBSTACLE

Formerly, the initiative, involving *Ae. aegypti* mosquitoes carrying the Wolbachia bacteria, was set to launch in mid-November in Bali. However, Indonesia’s Ministry of Health has decided to indefinitely postpone the program and currently discussing with the Bali Provincial Government to temporarily delay the release of Aedes containing Wolbachia mosquitoes and conduct further public dissemination until the community is prepared.

Effective communication [57], transparency [58], and involving the community engagement initiatives [59] in policy development can help mitigate resistance against innovative change [60]. Equilibrating public health policy goals with individual rights [61] and managing people's concerns [62] are prerequisite for prospering policy implementation.

Main element in the introduction of technological innovations for *Ae. aegypti* management is to break with experience of community based health education, e.g., specifically regarding Aedes life cycle [63,64] and information campaigns, e.g., mosquito awareness week in the Carribean [65] and social participation schemes that have encouraged changes [66] (whether it is effective or not) up to the level of individual or community practices [67] in order to eliminate, protect, or control the variety of vector breeding sites found in the domestic and surrounding environment [68,69].

The effort to Convince constituents of the community regarding how virtuous and advance releasing Aedes mosquitoes that contain endosymbiont Wolbachia to replace wild type *Ae. aegypti* when some of them have antecedently incorporated the opposite view, clearly requisites an exceptional step, starting with (1) community awareness-arousing [70] and (2) intense bi-direction communication to turn initially opposite community members into participants and even partners [71]. The information and awareness campaign should explain the features of the innovations [72], including strengths [73] and its weaknesses [74,75], the release procedures (areas, dates, etc.) which intended to suppress or to replace initial mosquito population [76], the potential risks [16] and, especially, the activities in which the community should intervene or participate [66,71].

This community awareness-arousing campaign must start with teaching and deconditioning potential numerous actors at diverse levels, e.g., national or federal, state or provincial, municipal and local) and the health spokesmen/women in charge of reassembling the strategy and the documents of specific educational subjects that must be to accommodate all the beneficiary effects of the new vector control approach [67]. This is a fundamental step, especially if the innovations are introduced as Interventions for *Ae. aegypti* control strategies intended to complement the activities of traditional vector control programs (initially restricted only to

chemical based fumigation and elimination). It is also a mandatory that the population should always be given spaces to boost concerns and at the same time allowing them to achieve good and fast responses. This approach basically is a fundamental step in avoiding the spread of hoax and misinformation [21, 36, 41, 77].

5. CONCLUSION

In the days of state of the art in health technology and also in information technology, every stakeholder need to continue to be an open mind to every new positive initiative. While at the same time, every stakeholder also has the right to have concerns about the consequences of health policy and must willing to take any responsibilities, whenever necessary, especially regarding to social media usage.

Specifically, the government should not hesitate to take firm action against misinformation and fake news regarding the new technology to fight dengue, simply because they only spread confusion, and even fear among society that in the end will produce distrust to the authority and predictable become resistant to any health programs that actually they need the most.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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