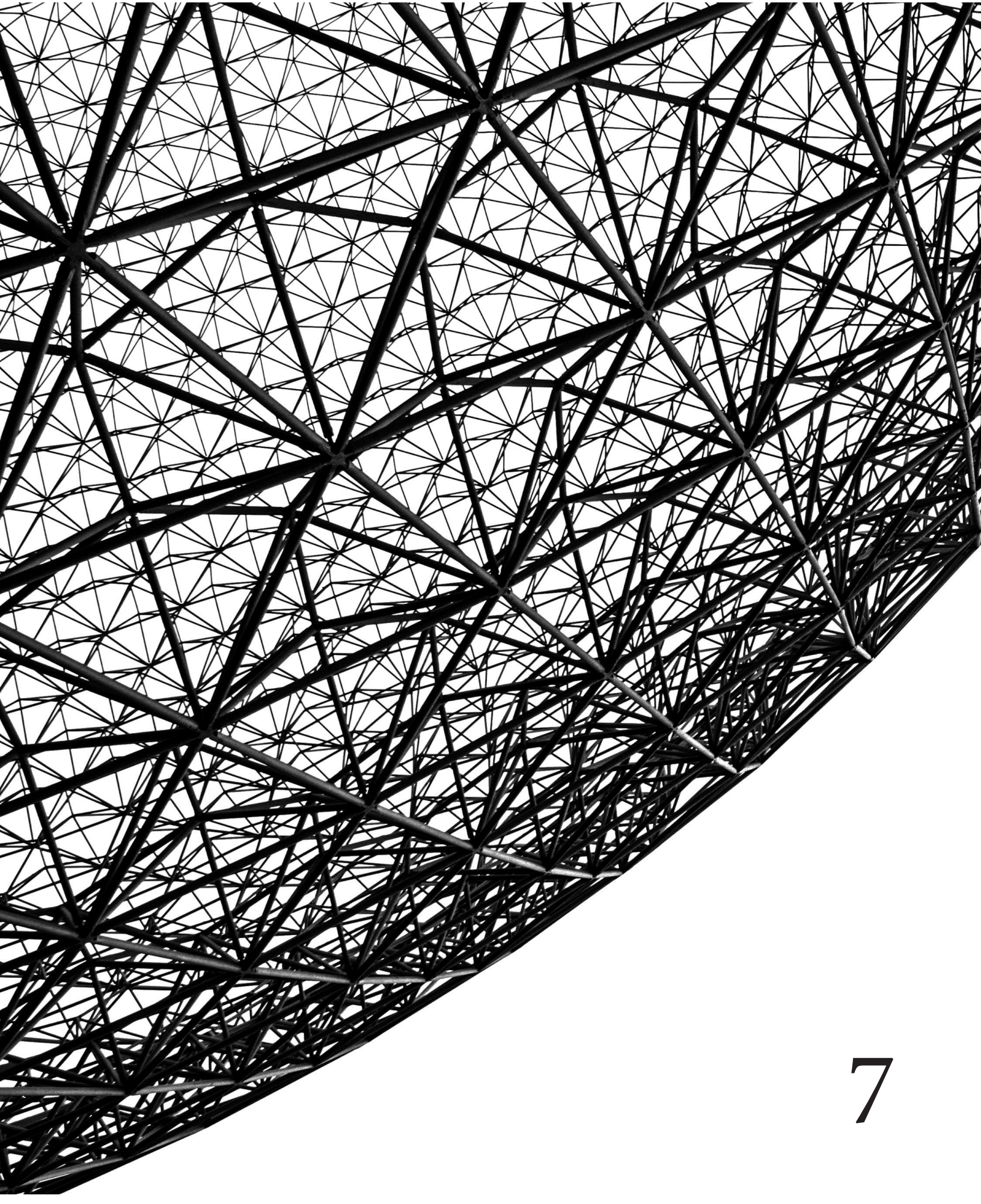

Did Dengvaxia-associated deaths result in an increase in vaccine hesitancy in the Philippines?

Karim Atassi, Nicole Cifelli, Maddie Clark, Adrianna Lemieux, Leen Makki, Janine Xu, Mercedes Yanes Lane

ABSTRACT

The development of the Dengvaxia vaccine and the subsequent vaccination campaign of 2016 in the Philippines proved to be an outstanding failure. This case study focuses on the impact of the vaccination campaign, which had a goal of vaccinating one million schoolchildren, ultimately reaching 830 000 students. Sanofi Pasteur's failure to adequately warn the Filipino public about Dengvaxia's effect on antibody-dependent enhancement (ADE), coupled with rushing the implementation of the program by the Department of Health, ultimately led to the shutdown of the campaign in 2017. Therefore, we predict that the media sensationalization of the campaign, which created a public outrage, led to distrust of the healthcare system and vaccine hesitancy as well as an increase in vaccine-preventable diseases such as measles in the Philippines.

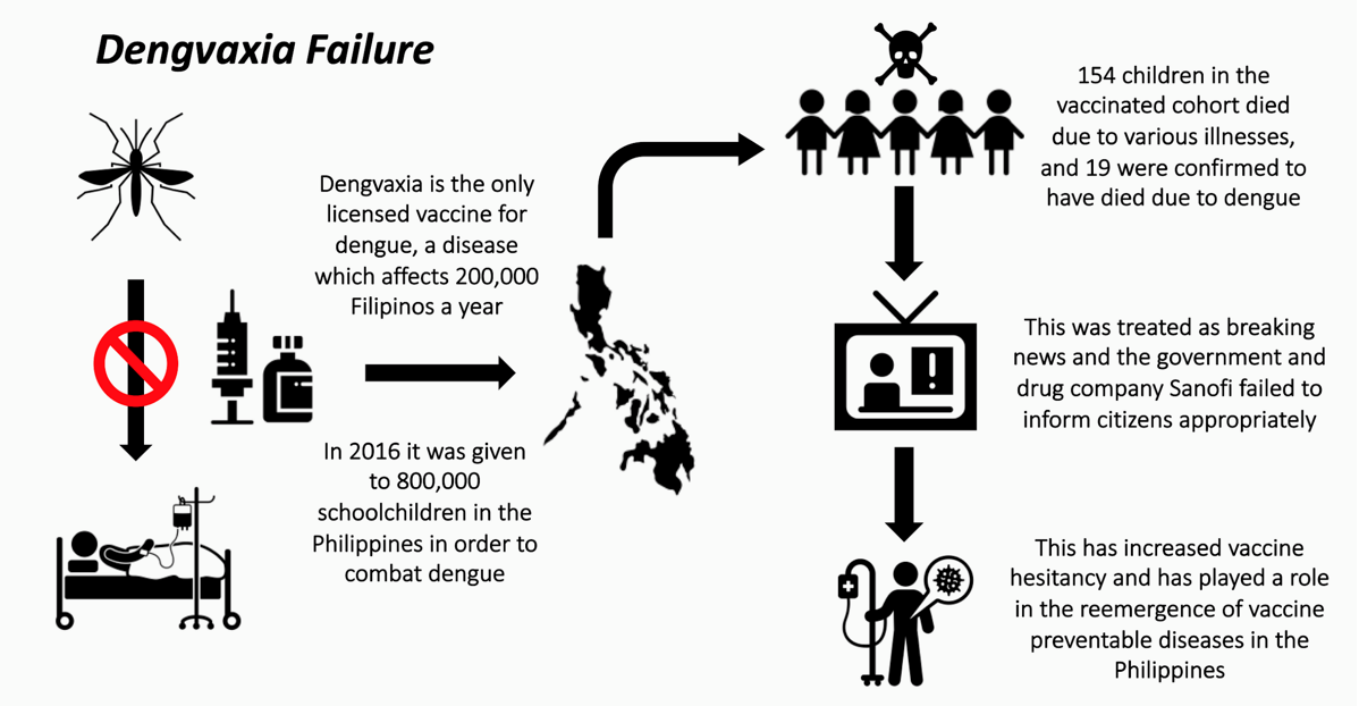

Figure 1: Visual Abstract of the Case Study

Background and Motivation for the Intervention

Dengue (DENV) affects over 100 countries and caused 390 million infections globally in 2013. It is a viral disease transmitted by the Aedes aegypti mosquito which has four different serotypes. While dengue is self-limiting in most cases, a small proportion progress to more severe manifestations, such as dengue hemorrhagic fever (1). In the past 50 years, incidences of dengue have risen 30-fold, but there is still no dengue-specific vaccine (2). The development of vaccines is quite complicated, as an initial infection with DENV can trigger an immune response that can either protect or enhance the disease during the subsequent infection. Although controversial, this theory, proposed by Halstead, is called antibody-dependent enhancement (ADE) and explains why a second encounter with a different dengue serotype might be deadlier than the first. A first infection with DENV-1 prompts B-cells to make antibodies to coat and kill the virus; the B cells become dormant after the infection. A second infection with a different serotype activates these cells to make the exact same antibodies as before. However, antibodies to DENV-1 do not bind well to the other DENV serotypes, making the immune response ineffective and causing a more severe form of dengue. The ADE theory is thought to prove especially true in children who have never had dengue before in regards to vaccination. It is theorized that when uninfected but vaccinated children are first infected with dengue, the vaccination serves to prime the immune system, which then responds dangerously to the first infection following vaccination (3).

Severe dengue was first recognized in the 1950s during epidemics in the Philippines and Thailand (4). About 170,503 symptomatic Dengue infections and 750 deaths were recorded annually from 2010 to 2014, with a reported case fatality rate of approximately 0.44% (5) Dengue remains a serious public health issue in the Philippines, with recurring epidemics every 2-3 years (6). Tackling dengue is one of the country's top priorities for infectious diseases. Dengue outbreaks are viewed as a political issue; the public often blame their government for not doing enough to prevent the disease as it's seen as a governmental responsibility to prevent the disease. A leading Filipino pediatrician summarizes the situation quite well, stating that: "Any politician who brought a dengue vaccine to the Philippines through the national immunization program could become President" (7).

According to the WHO, if an intervention in a country costs less than its GDP per capita to avert one DALY then it is considered highly cost-effective. If the regimen costs up to three times the GDP per capita then it is considered merely cost effective. Anything higher than three times

the GDP per capita will be deemed cost ineffective (8).

In 2015, the Filipino GDP per capita was $2867 USD (9). The Dengvaxia program was expected to average a value of US$5,101/DALY averted in the Philippines, making it merely cost-effective from a healthcare perspective, which incorporates costs of the vaccine compared to the number of cases treated. From a societal perspective, which incorporates the indirect social costs of illness (ex. unemployment) and the opportunity cost of time required to obtain each vaccine dose , the Dengvaxia program was expected to average a value of US$ 3063/DALY averted, making it even almost highly cost-effective (10).

This shows that the Dengvaxia program was thought to be more cost-effective when the time to carry out the vaccination campaign is taken into consideration, evidence of the indirect social costs Dengue has on productivity(10). This reinforces a social and economic argument for the need of a more effective Dengue vaccine, especially in countries where the incidence is high, as in the example of the Philippines.

In 2015, the Filipino government acquired the only licensed dengue vaccine at the time from Sanofi Pasteur, Dengvaxia. The vaccine was studied in 26 clinical trials including more than 41,000 volunteers, notably CYD23 in Thailand, CYD14 in Asia and CYD15 in Latin America. (11). It is registered in 20 dengue-endemic countries, but immunization implementation has been

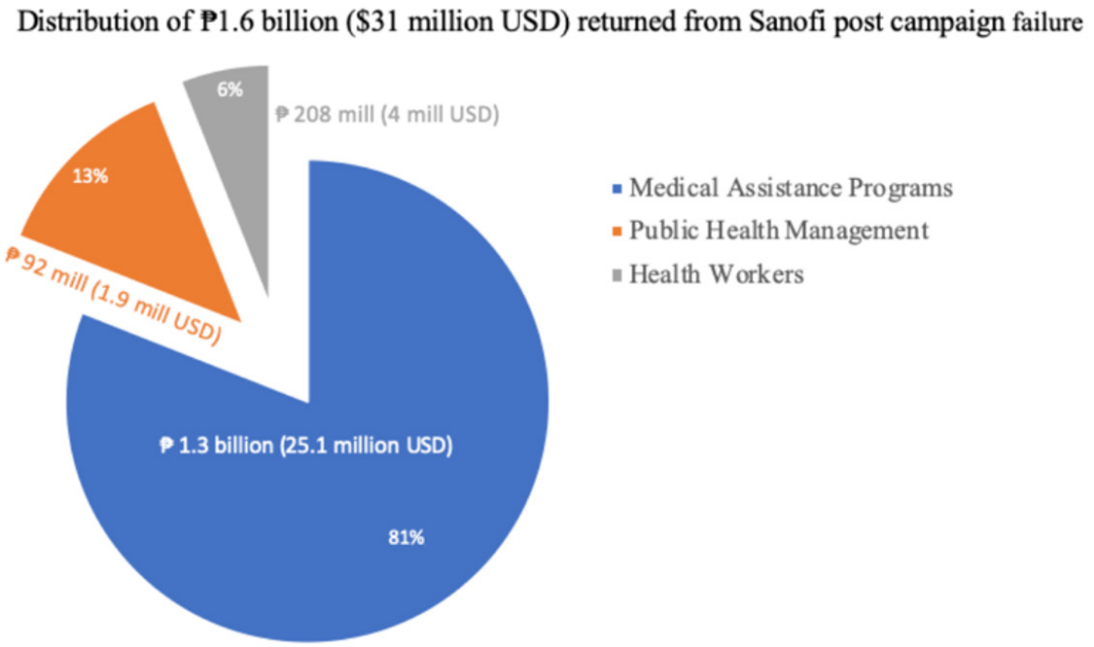

Figure 2: Allocation of $31 million USD returned from Sanofi by the Filipino Department of Health

limited to Brazil and the Philippines (11). Upon negotiating a deal with Sanofi, the Department of Health in the Philippines wanted to purchase three million doses of Dengvaxia to achieve the immunization of one million schoolchildren, nine years of age. Each child was anticipated to receive three doses of the vaccine, each dose 6 months apart, by June 2016. The goal was to reduce up to 80% of the 200,000 annual domestic dengue cases in the Philippines, focusing predominantly on 9-year olds in highly infected areas of Central Luzon, Metro Manila and the Southern Tagalog region (12). As predicted by the ADE theory, it was later discovered that the vaccine actually put people at risk of being more severely affected by the virus, especially if they never had dengue before (2). This raised concerns regarding the true safety and efficacy of the vaccine, and public confidence in vaccines plunged.

This case study focuses on the impact of the 2015 Dengvaxia campaign in the Philippines, which had a goal of vaccinating one million schoolchildren. Sanofi Pasteur's failure to adequately warn the Filipino public about Dengvaxia's effect on ADE, coupled with rushing the implementation of the program by the Department of Health, ultimately led to the shutdown of the campaign in 2017. Therefore, we predict that the media sensationalization of the campaign, which created a public outrage, led to public distrust of the healthcare system and vaccine hesitancy in the Philippines.

Financing

The Dengvaxia campaign, which included the purchase of 3 million doses of Dengvaxia, cost the Filipino Department of Health paid ₱3.5 billion ($67.7 million USD). This amount surpassed the cost of the entire national Filipino vaccination program of 2015, which covered pneumonia, tuberculosis, polio, diphtheria, tetanus, pertussis, measles, mumps and rubella (3).

Protests surrounding the failure of the campaign pushed the Filipino government to ask for a refund of the entire ₱3.5 billion ($67.7 million USD) from Sanofi Pasteur. Settling a compromise, the Filipino government received ₱1.6 billion ($31 million USD) after returning the unused Dengvaxia vaccine vials. The returned funds were mainly allocated towards medical assistance programs for Dengvaxia recipients seeking treatment, as well as public health management and employment of health workers to follow up with complaints of the vaccine recipients (13).

Methodology

For the purposes of this case study, we define program failure as the lack of appropriate pharmacovigilance information prior to vaccine rollout, which in this case

led to 19 deaths among vaccinated children, inadequate communication channels between health authorities, researchers and the general population, and ultimately, the creation of mistrust towards vaccination programs. There are many key points that led to the program failure. Firstly, Filipino authorities did not oblige Sanofi Pasteur to submit results from pharmacovigilance trials. It was later found that the pharmaceutical company had not carried out testing in the complete sample included in the trial, leading to the false assumption that in children above 9 years of age the vaccine was safe, however, age served in part as a proxy for prior dengue infection. In November 2017, Sanofi Pasteur issued an advisory, limiting the use of the vaccine to children who had a previous dengue infection. Again independent researchers argued that there was "no biological basis for a threshold age of 9 years" beyond which Dengvaxia could be assumed to be safe (14). Secondly, after the death of a child who had been vaccinated, the authorities gave a press briefing declaring that the boy's death was unrelated to the vaccine. However, local researchers insisted it was, posting a video on Facebook that warned that if a child had never had dengue before, the vaccine could cause a more severe reaction to dengue.

This lack of appropriate communication channels and the magnified media attention to the vaccination campaign led to public panic (15). Lastly, the program was stopped in December 2017, after more than 830,000 schoolchildren had been vaccinated and 19 deaths due to dengue had occurred amongst vaccinated children, leading to virtually every death in the vaccinated group being blamed on Dengvaxia, even if it was clearly unrelated.

We hypothesize that the failure of the Dengvaxia campaign contributed to increased vaccine hesitancy in the Philippines. Vaccine hesitancy is defined by the WHO as "the delay in acceptance or refusal of safe vaccines despite the availability of vaccination services". It can be caused by factors such as: negative beliefs based on myths, e.g. that vaccination of women leads to infertility; misinformation; mistrust in the health care professional or health care system; the role of influential leaders; costs; geographic barriers and concerns about vaccine safety (16). We analyzed qualitative studies evaluating vaccine acceptance to gain an understanding of the public's reaction to the Dengvaxia program, which provided insights into vaccine hesitancy. We obtained surveillance data on vaccination rates from the WHO and the Department of Health of the Philippines to show correlation with increased vaccine hesitancy after the Dengvaxia campaign. We also obtained data on the incidence rates of measles cases in the Philippines. Given that measles is a highly infectious disease

that can spread very fast when vaccination rates in children decline, we considered it to be an efficient marker for a decrease in vaccine uptake. Using this data, we examined the temporal trends before and after the Dengvaxia program for both vaccination rates and measles cases. Data from the DoH on a national deworming program was used as a proxy for mistrust in health programs and to further illustrate how the Dengvaxia program set the stage for vaccine hesitancy.

Impact

A Sensation, a Scandal, and Significant Misinformation

In an announcement on November 29, 2017, Sanofi stated that vaccinated but not previously infected children were more likely to contract "severe dengue" than those who had not received a vaccination. No context was given, only this fact buried within the announcement. They did not explain what "severe" specifically meant, and this allowed people who just read the announcement to make their own conclusions. In this case, "severe" was directly from the clinical trial's lexicon, but it painted pictures of death in the minds of those who read the announcement. Sanofi also did not provide any statistics or rates of risk, making citizens believe that their children would almost certainly contract a deadly version of the disease.

The government was quick to distance itself from the vaccination campaign, which had been started under a previous regime. Officials during the scare were all different from officials during rollout of campaign, and the control of the government had shifted parties in the interim. The Department of Health (DoH) was struggling to effectively describe how low the risk actually was to the general public. In the age of mass and social media, measured discussion rarely makes headlines. Thus, news agencies in the Philippines ran with reports of Dengvaxia associated deaths, images of childrens autopsies, and stories from grieving parents before anyone within Sanofi or the DoH could confirm or deny the factual basis of these claims. The Centre for Media Freedom and Responsibility found that the three main news agencies in the Philippines focused primarily on the politics of the failure, as reports at these agencies surrounding the Dengvaxia controversy outnumbered reports regarding dengue statistics or other aspects of the disease (17). Posts about the vaccine went viral, including one by prominent public health experts and Dengvaxia critics Dr. Antonio and Dr. Leonila Dans (18). Enormous outrage in the general public soon followed.

Media is not solely to blame for the sensationalization of the campaign(18). The Senate organized a series of public hearings on the campaign, interrogating current and former officials as well as Sanofi executives. The trials were meant to

provide the general public with someone to blame for the disaster, and the finger pointing often fell along partisan lines (18). The politics of dengue are entrenched within the Philippines, and the failure of the campaign offered ammunition to rival politicians. This trial ultimately published a report which called for the prosecution of several key former officials (19,20). The Public Attorney's Office also initiated an investigation that claimed that deaths from the vaccine were not from severe dengue associated with the vaccine, but rather from the vaccine itself. This criminal investigation cited cause of death as viscerotropic and neurotrophic-like diseases, which are listed as side effects of the vaccine. However, Sanofi found zero instances of these side effects through clinical trials, and medical experts say that the actual causes of death in the cases being utilized as evidence by the Public Attorney's Office were unrelated to the vaccine. The claims that the deaths were related to Dengvaxia are likely due to widely shared misinformation; scared parents did not understand why their children died (listed reasons included rabies, enlarged heart, leukemia) and pointed to a public vaccination failure which they had heard so much commotion about (18).

Vaccine Hesitancy

This brings us to our primary impact of the Dengvaxia failure: increase in vaccine hesitancy. The situations described above created an environment which was rife for further misunderstandings regarding vaccines and other health interventions. Qualitative and quantitative data shows that people in the Philippines were scared,

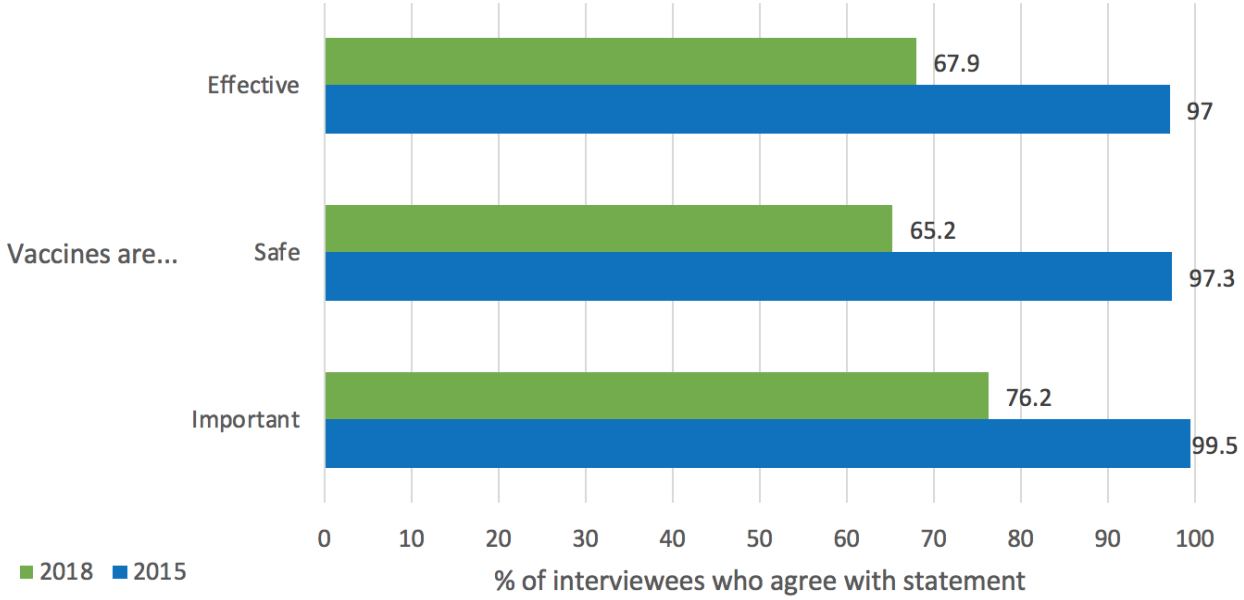

Figure 3: Percentage of interviewees who agree with statements listed in 2015 (1000 surveyed) vs. 2018 (2500 surveyed). Data taken from the Vaccine Confidence Project™.

and that this fear was easily spreading. Interviews and focus groups in Quezon City, Philippines revealed that acceptability of the dengue vaccine was associated with parental experience with vaccination and dengue, trust in public health institutions, and communication received by parents. Following the dengue vaccination campaign, parents regretted the experience, trust in public institutions was eroded and the communication strategy was deemed inadequate. This led to low vaccine acceptability post-vaccine suspension (21). As displayed in Figure 3, there has been a dramatic shift in the perceptions of Filipinos regarding the safety, efficacy, and importance of vaccinations following the Dengvaxia program failure. Those "strongly agreeing" with the statements listed in the table decreased by an even more significant degree (15)

A study which sought to qualify the impact of Dengvaxia on mothers' perceptions of the program and of vaccines in general found that participants felt fear, empathy, and anger over the Dengvaxia associated deaths. Most participants knew why vaccines were important. Additionally, most participants stated that they had or were planning on giving their children vaccines, but specified that they were only confident in vaccines which had been on the market for a long time period. Two women stated that they were scared of injecting their children with vaccines following the Dengvaxia failure (22). This might impact the rollout of new vaccines, which could harm future public health initiatives within the country. Even routine health interventions, like the administration of deworming medications, have been greeted with scepticism. In an interview with the Phillipine Daily Inquirer, a mother said she would not allow health workers to give her two children deworming tablets and has shunned all drugs from the DoH: "Be it a vaccine, a chewable, a syrup, I said no. I have my options to bring my sons to a hospital or our family doctor for deworming or whatever it is in the DOH program. I don't trust their services now after the Dengvaxia controversy" (23).

Rise in vaccine-preventable diseases, and fall in vaccine coverage

The Dengvaxia controversy extended further beyond vaccine hesitancy in the Filipino population. Figure 4 demonstrates data from the DoH's Annual Report (24), which shows the proportion of fully immunized children in the Philippines from 2015 to 2018. There is a clear downward trend of vaccinated children which starts after 2016 (25), which correlates with the height of the Dengvaxia controversy.

Figure 5 shows WHO-estimated vaccine coverage in the Philippines from 2010 to 2018 (26). As with Figure 4, there is a clear downward trend. Beginning from 2016, there was a decrease in coverage of

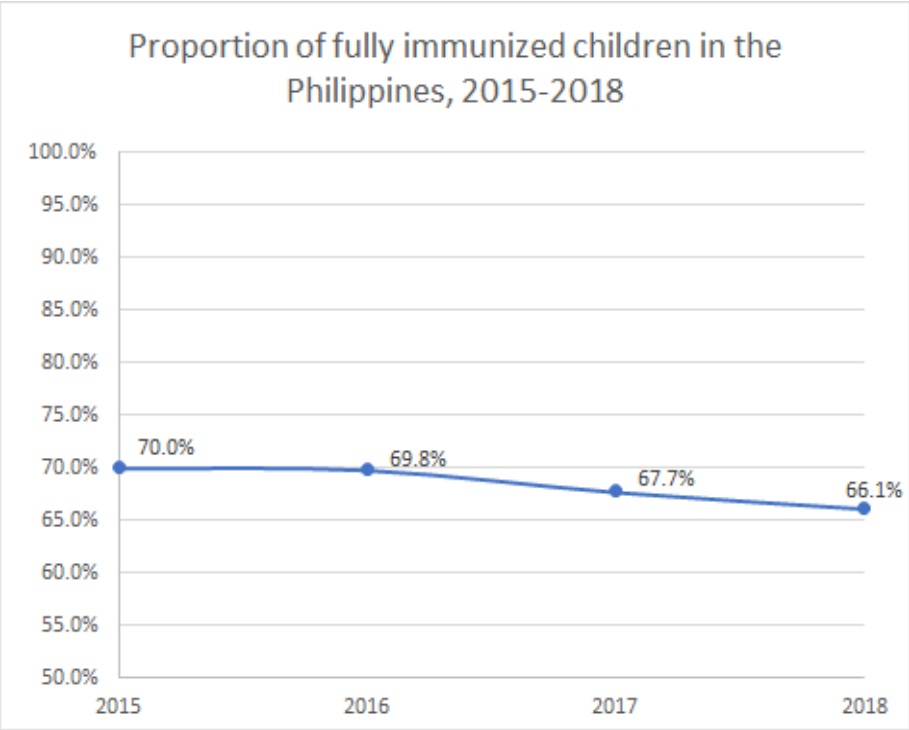

Figure 4: Proportion of fully immunized children in the Philippines, 2015-2018

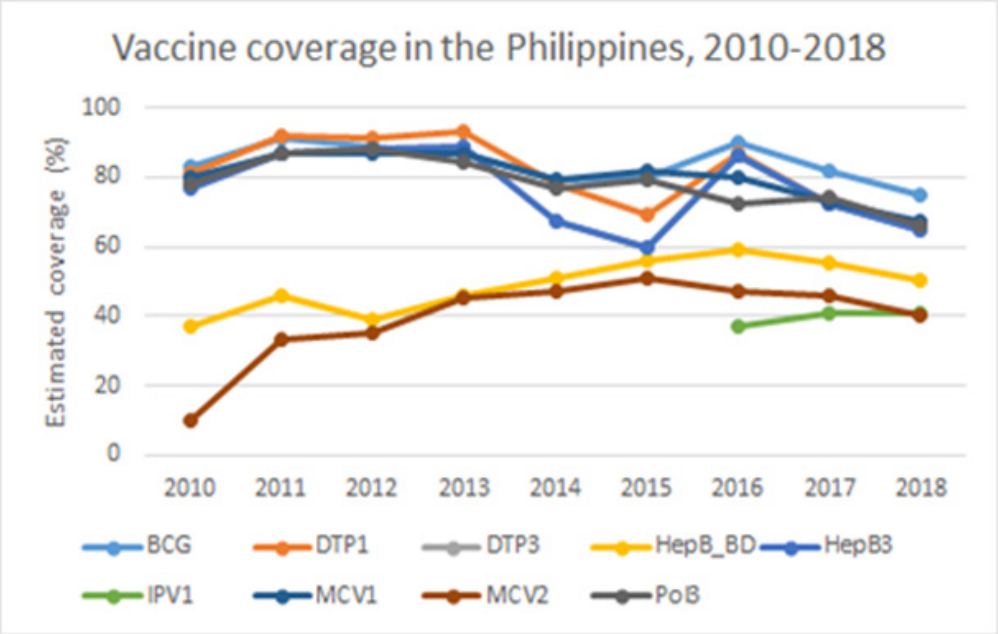

Figure 5: Vaccine coverage in the Philippines, 2010-2018. Vaccination data for BCG (Bacille-Calmette Guerin), DTP (diphtheria, tetanus and pertussis), hepatitis B, IPV (inactivated polio vaccine), MCV (measles containing vaccine) and Pol3 (oral polio vaccine).

the following vaccines: BCG, DTP, HepB, IPV, MCV, and Pol. This decrease in vaccine coverage correlates with an increased mistrust in the government public health agency, and increased vaccine hesitancy as a direct result of the media campaign surrounding the Dengvaxia campaign. Furthermore, Figure 5 demonstrates MCV coverage coupled with incidence of measles in the Philippines. As vaccine coverage decreases from 2016 onwards, measles cases rise, with an outbreak in 2018. According to WHO-estimated data, there were 20,827 measles cases in 2018 with 199 deaths. In 2017, there were 2,428 measles cases. In 2016 and 2015, there were 716 and 619 cases, respectively (26).

According to the DoH's measles surveillance program as seen in Table 1, data from January 1st to July 27th 2019 shows 39,856 cases of measles, with 538 deaths (27). Compared to the same time period in 2018, which had 12,469 cases and 107 deaths, this represented a 220% increase in measles cases since the fallout from the Dengvaxia campaign. Of the measles cases in 2019, 75% were unvaccinated or had unknown vaccination status. These cases were calculated from laboratory confirmed (3,301) cases, epidemiologically-linked (1,442) or measles compatible/clinical measles (35,383) cases. Lab confirmed cases show positive results for measles-specific antibodies, and epi-linked cases are defined as those who have had close contact with a lab-confirmed or another epi-linked case. In 2018 (28), confirmed measles cases were calculated only from either laboratory-confirmed or epidemiologically-linked cases, with 5,120 total cases (and 59 deaths). Of these confirmed cases, 89% were unvaccinated or had unknown vaccination status. However, there were still 13,287 measles compatible/clinical measles cases which were not analyzed. Clinical measles cases are defined as a suspect case for which no blood sample was taken, not an epidemiological link, or lab results are still pending. Comparing confirmed cases with 2017, which had 791 cases with 17 deaths, 2018 had a 547% increase in numbers of measles cases. These results differ slightly from WHO estimated cases, which may be the result of variations in the disease surveillance or access to data.

Furthermore, Figure 6 demonstrates WHO estimated data of pertussis and diphtheria cases (26) in the Philippines, both of which show a rising incidence which correlates with decreased vaccine coverage. The number of cases was increasing before the Dengvaxia controversy, perhaps pointing to an increase in overall vaccine hesitancy or other reasons for decreased vaccine uptake. However, from 2017 to 2018, there is a larger increase in cases, with a jump of 339 pertussis cases in 2018 (from 88 in 2017) and 183 diphtheria cases (from 68 in 2017) which may be correlated with

increased vaccine hesitancy from the Dengvaxia campaign.

Why are there measles outbreaks?

Measles is a highly communicable disease. On average, 90% of those exposed to measles will get the disease unless they have been vaccinated, or have already been infected (29). When a community has low immunization coverage, the likelihood of measles outbreak increases. The WHO recommends that a vaccine coverage of about 95% of all children is required in order for a community to be fully protected against measles (30). This includes protection for the vulnerable members of the population such as infants that are too young to receive vaccination, individuals who may be immunocompromised, or older adults. The results of the Dengvaxia campaign, which was heavily sensationalized in the media, pointed towards distrust in the government public health system and vaccine programs according to the qualitative studies surveyed. Decreased vaccine coverage was observed after the Dengvaxia campaign, subsequently decreasing herd immunity to measles, allowing for this highly infectious disease to spread as seen in Figure 7, and pointing towards increased vaccine hesitancy.

Deworming in the Philippines

Increased distrust in government public health programs manifested not only in vaccination campaigns, but impacted other programs as well. In 2015, the DoH introduced a deworming program called OPLAN: Goodbye Bulate, which targeted public school children aged 5-18 years and preschool children aged 1-4 years (31). This program aimed to combat the high prevalence of soil-transmitted helminth diseases in the Philippines, and administered anti-helminth drugs albendazole and mebendazole in January and July of every year with a target of 85% coverage. In 2015, the program enrolled 11,740,245 children out of a target of 14 million, reaching a coverage of 84%. In 2016, the program's success continued, with 15,853,687 public school children (82.4%) enrolled in the program (32). In January 2017, the deworming coverage among enrolled public school-age children was 84.5% (17,060,163 children were dewormed out of 20,194,252) (25). However, since the Dengvaxia campaign, the program coverage fell to 45% in 2018, representing approximately a 40% decrease in coverage (24) as seen in Figure 8. According to an article in the Philippine Daily Inquirer, the low deworming rates in 2018 were due to parents who refused to sign consent waivers, citing the Dengvaxia controversy as the reason behind their fear of DoH health programs (23).

Funding for the Department of Health

The Dengvaxia controversy was also correlated with budget cuts to the DoH. Under the 2020 National Expenditure Plan

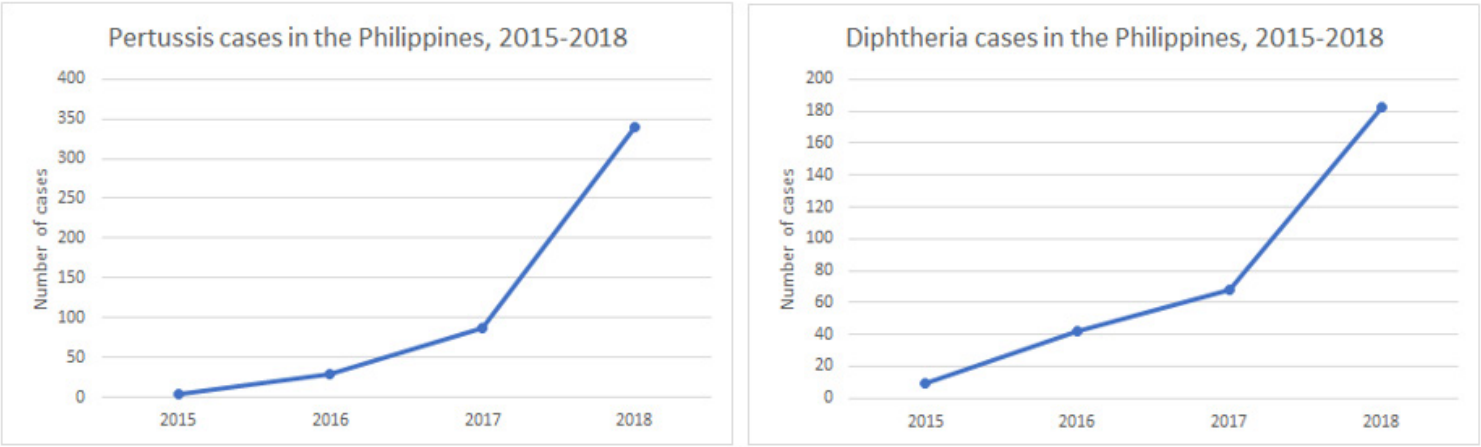

Figure 6: Pertussis and diphtheria cases in the Philippines, 2015-2018.

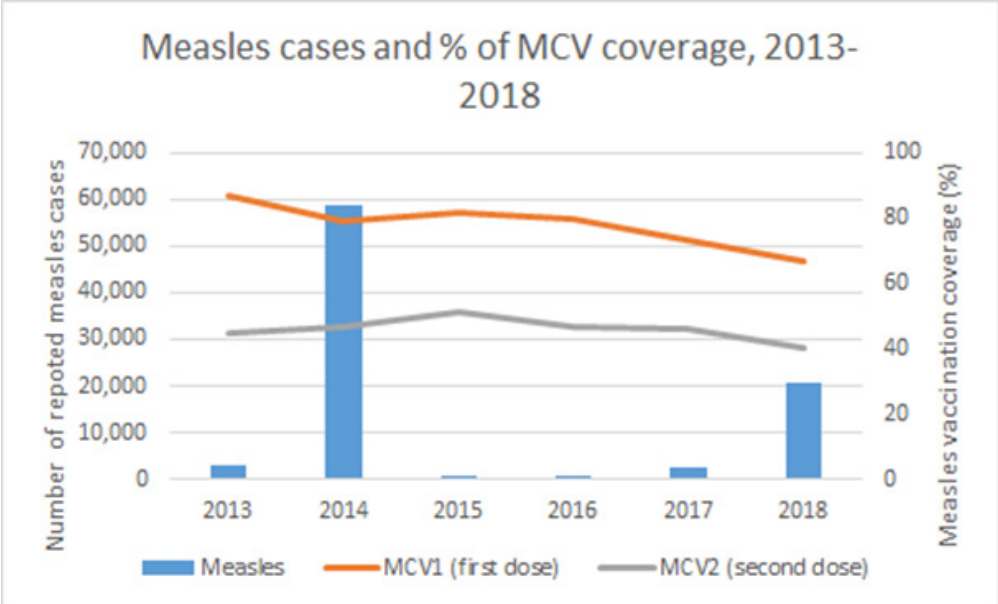

Figure 7: Measles cases and % of MCV coverage in the Philippines, from 2013-2018.

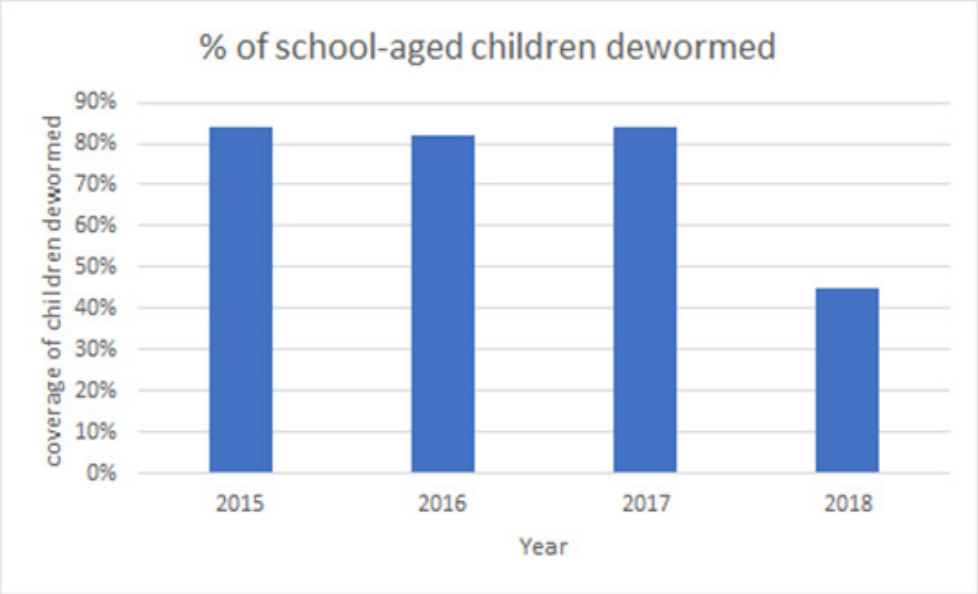

Figure 8: Decrease in coverage of the DOH deworming program, 2015-2018.

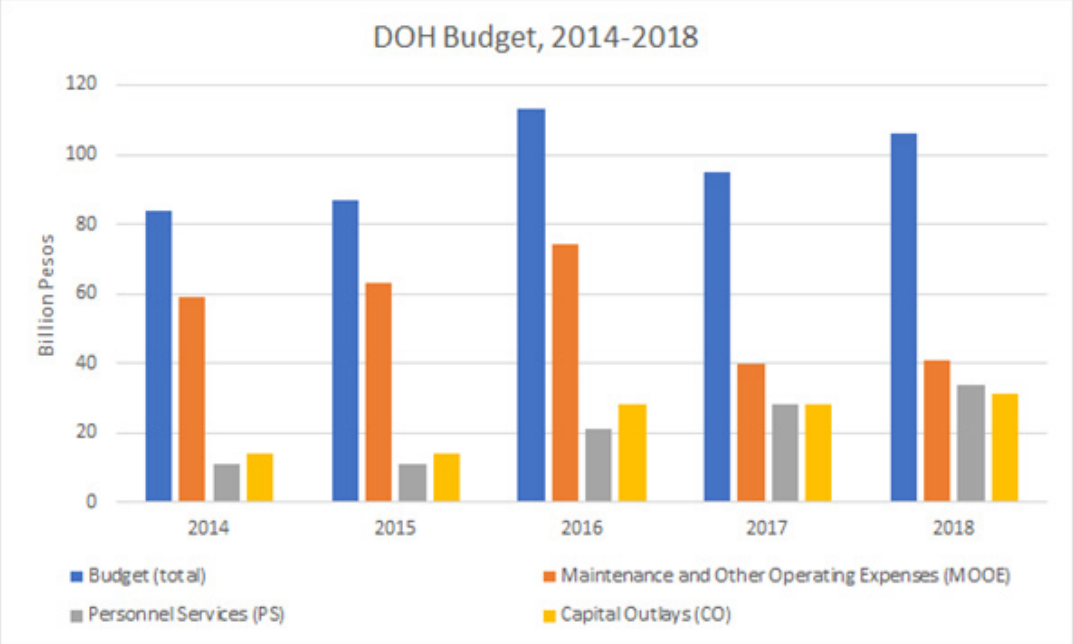

Figure 9: DoH budget from 2014-2018, broken down by PS, MOOE, and CO.

created by the Department of Budget and Management, the health department has a combined allocation of ₱160.15 billion (US$3.1 billion), of which ₱92.2 billion (US$1.8 billion) is allocated to the DoH. This amount is 5% lower than the 2019 appropriation of ₱169.45 billion (US$3.3 billion). This comes in just as President Rodrigo Duterte is set to implement Universal Health Care. The DoH's Human Resource for Health Deployment Program (HRHDP) will be heavily affected (from ₱8.5 billion (US$166 million) in 2019 to ₱2.45 billion (US$48 million) in 2020), which could lead to the loss of over 10,000 health personnel, such as nurses, dentists and medical technologists (33). The 2019 budget was already decreased from the 2018 budget for the DoH by about 17% (25), which received around ₱106 billion (US$2 billion). Figure 9 shows the DoH budget from 2014 to 2018, which is publicly available on the DoH's website (34). In 2016, a special provision of the budget was included for purchasing the Dengvaxia vaccine. In 2017, the budget dropped from ₱113 billion (US$2.2 billion) to ₱95 billion (US$1.9 billion). Large cuts were made to Maintenance and Other Operating Expenses (MOOE) in 2016 as well as in 2019, which is used for medicines, medical supplies and other operational expenses in public hospitals. Budget for MOOE for government hospitals and facilities, was reduced by ₱1.5 billion from the 2016 budget. According to the Manila Times, the cuts in the budget were supposed to be allocated for vaccines and facility enhancement programs (35).

Zooming in on the 2019 DoH budget in comparison to the 2018 budget (Table 2), cuts were made in three different programs: Health Policy and Standards Development, Health Systems Strengthening, and the Public Health program (36). The Health Policy program aims to ensure the alignment of policies, programs and standards towards sectoral goals on equity, access and quality of care. The Health Systems Strengthening Program provides technical support (service delivery) to local government units to ensure high quality health care services, and contains the Health Facilities Enhancement Program (HFEP) and the HRHDP. This program was decreased by 94% going from 2018 to 2019, and cuts to the HRHDP affect medical centres in the Philippines. The Public Health Program, the biggest program in the DoH, was cut by 12%, and includes programs for immunization, prevention and control of infectious diseases, and family health. On the other hand, the Epidemiology and Surveillance budget was increased by 403%, due to surveillance for children who received Dengvaxia (37). While the Dengvaxia controversy may not necessarily be behind the cuts to the health budget, public outcry and distrust of DoH public health programs during this period may be linked to the

funding of the Philippines' Department of Health. Furthermore, cuts to hospitals may exacerbate negative opinions of the healthcare system, in turn creating a feedback loop of fear and distrust.

In summary, the Dengvaxia controversy was heavily sensationalized by both the media and the Senate, leading to public outrage. The campaign was quickly stopped, but the fallout from the campaign affected many Filipino families, who began to feel as though they could not trust what government programs provided. This led to an increase in vaccine hesitancy immediately after the controversy, correlated with a decrease in vaccine coverage and an increase in incidence of vaccine-preventable diseases such as measles, pertussis, and diphtheria. Moreover, the outrage from the campaign affected other health programs such as the DoH's deworming program, leading to a decrease in coverage. Since the campaign, funding for the DoH has dropped, with budget cuts for healthcare facilities and supplies such as vaccinations. However, the evidence cannot prove that the Dengvaxia campaign was responsible for causing these massive changes, nor can it fully explain the decrease in vaccine uptake and measles outbreak. These data can only show that the Dengvaxia controversy is correlated with vaccine hesitancy, and future studies will need to be done in order to fully assess the direct impact the Dengvaxia campaign had on the Filipino population.

Limitations

This case study is not without its limitations. Firstly, the data used for vaccination rates, measles incidence and deworming is ecological. This constrains the inferences that can be made to comparisons between prevalences, without being able to assess cause and effect, as well as limiting the inferences that can be made about changes in vaccination behavior over time. It is therefore impossible, due to the confines of our study, to directly ascribe casual relationships between Degnvaxia and vaccine hesitancy, vaccination coverage, or vaccine preventable diseases. However, the observations that were made in this study could serve as the basis for the hypothesis of longitudinal studies.

Secondly, the data used in the analysis was not collected for the purpose of measuring vaccine hesitancy. Thus, the causes for a shortfall in rates may be due to reasons completely out of the scope of hesitancy such as stock outs or lack of vaccination programs in certain areas. It is also important to note that since the data was not specifically collected for our outcome, it may not depict the entire population exposed to the Dengvaxia program. Additionally, the impacts of a decline in vaccination coverage might not be seen for several years. Such was the case in the 2014 measles outbreak in the Philippines, it is thought to be caused by a decrease in vaccination coverage in 2011. At this time, vaccine confidence was

Table 1: Measles disease surveillance data from the DoH

	2019 - Jan. to July	2018 - Jan. to July	% change	2018 - Jan. to Dec.	2017 - Jan. to Dec.	% change
Measles incidence	39,856 cases	12,469 cases	↑ **220%**	5,120 cases (lab confirmed & epi-linked)	791 cases (lab confirmed & epi-linked)	↑ **547%**
Deaths	538 deaths	107 deaths	↑ 403%	59 deaths	17 deaths	↑ 247%

Table 2: % change in budget by program between 2019 and 2018

Operations by Program	% change from 2018 budget
Health Policy & Standards Development Program	↓ 28%
Health Systems Strengthening Program	↓ 94%
Public Health Program	↓ 12%
Epidemiology & Surveillance	-↑ 403%

high, as shown in the figures above, but vaccine coverage was lower than surrounding years. Notwithstanding, given that the controversy surrounding the vaccination program was presented in media outlets throughout the whole country, we believe that this could have contributed to vaccine hesitancy and would be captured in subsequent surveillance data.

Thirdly and most importantly, vaccine hesitancy is the result of multiple factors which we were not able to measure for this case study. There are many factors beyond the Dengvaxia program that may influence hesitancy in the Philippines. These may include, but are not limited to; geographical barriers, personal beliefs or complacency. These factors are hard to measure and more so through indirect data sources. All these factors combined may influence vaccination rates overall and may subsequently confound our results. It would be necessary to carry out longitudinal studies with a representative sample of the population, in order to obtain data that would allow us to control for confounding factors and thus provide better insight into the association between the Dengvaxia program and vaccine hesitancy.

Future Implications

The Philippines have recurring DHF epidemics every 2-3 years (6) A national epidemic of dengue was recently declared in the Philippines as infections doubled since 2018, killing 662 people, many of them being children. However, following the Dengvaxia controversy, there are little resources available in order to protect the population not only against Dengue, but also against the social drivers of Dengue propagation. Dengvaxia will not be used in the current epidemic, a decision supported by the WHO. With the loss of the public trust in vaccination campaigns in the Philippines, an increase in vaccination rates and awareness campaigns is necessary to prevent future outbreaks and stop the increasing incidence of diseases like measles.

With the current Dengue outbreak in the Philippines, a clear identification of the source of vaccine hesitancy is needed to assist advocacy efforts for resource allocation that can positively impact vaccination rates by the re-introduction of Dengvaxia or other preventive measures for outbreak control. Given that there is qualitative information available on the populations knowledge, attitudes and practices regarding vaccination, it would be important to use these findings towards creating social outreach programs to regain the public's trust in vaccination. Strategies could include media campaigns on social networking platforms which feature trusted community leaders or social influencers to bring to attention the benefits of vaccination. One of the main shortfalls that should be targeted is the lack of a robust vaccine safety monitoring program. Currently the pharmacovigilance monitoring system that is in place uses web based

technology to keep track of adverse events, however, it may be useful to implement other safety procedures. Many resources are available through the WHO such as a manual on surveillance of adverse events following immunization and activities supporting countries to ensure quality of vaccines (26, 29).

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