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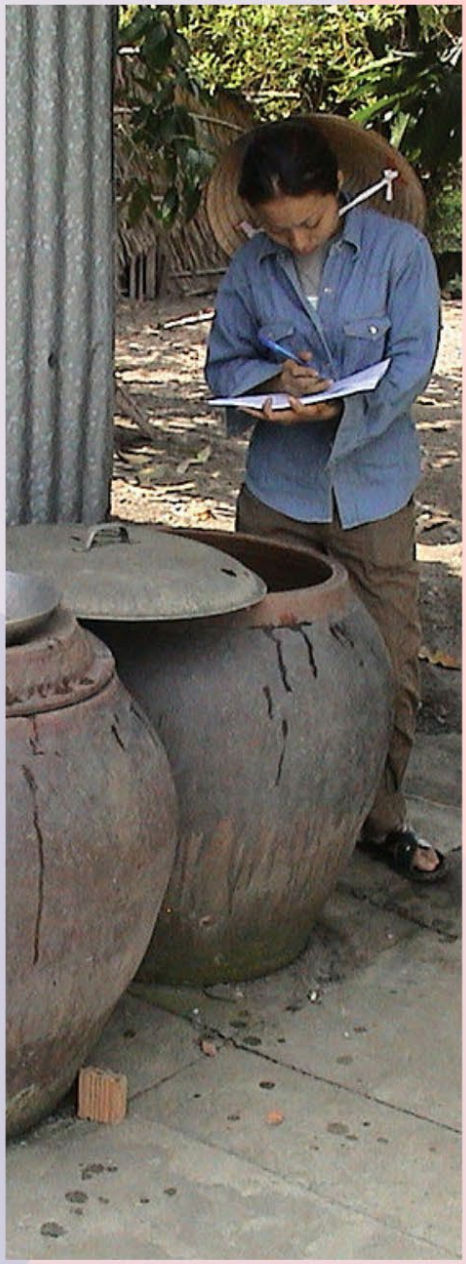
2021 UAB GLOBAL HEALTH CASE COMPETITION

Dengue Management and Prevention in Vietnam, Indonesia, and Cambodia



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All characters and plots described within the case are considered fictional and bear no direct reflection of existing organizations or individuals. The case topic, however, is a true representation of circumstances related to dengue outbreaks in Cambodia, Indonesia and Vietnam. The case scenario is complex and does not necessarily have an ideal solution, thus encouraging a discerning balance of creativity and knowledge.

Provided are informative facts and figures within the case and appendices to help teams create a proposal. The data provided are derived from independent sources, may have been adapted for use in this case, and are clearly cited allowing teams to verify or contest them within their recommendations, if necessary. Teams are responsible for justifying the accuracy and validity of all data and calculations that are used in their presentations, as well as defending their assertions during judging.

Front page image sources: Top right (Xinhua/Agung Kuncahya B.), Bottom left (National Dengue Control Program, Cambodia), Bottom right (Vu Sinh Nam, CC BY 2.0)

Introduction

It's the fall of 2022 and Mariel is reaching the end of her semester internship with the Association of Southeast Asian Nations (ASEAN) in Manila, the capital city of the Philippines. As an MPH student in global health epidemiology & disease control, Mariel always thought mosquito-borne diseases were on the less interesting end of the spectrum compared to high-profile outbreaks like Ebola or COVID-19. In fact, Mariel wouldn't have thought much about applying for the internship had it not been a chance for her to improve her grasp of the Filipino language and visit extended family she hadn't seen in years. However, her time with ASEAN has changed her mind as she spent the semester focused on the epidemic of dengue in Southeast Asia.

During field visits with ASEAN's community health team, Mariel witnessed the difficulty of preventing the spread of dengue, especially in more rural communities where there were fewer resources for eliminating standing water or purifying the water supply for daily use. When she visited her mother's cousins in the southern part of the country, Mariel listened intently when dinner conversations included updates on neighborhood kids who'd had dengue recently.

She kept these experiences in mind as she completed her final assignment, researching how dengue has impacted other Southeast Asian nations, such as Cambodia, Vietnam, and Indonesia. Deaths attributed to dengue are high across the region and countries were looking to increase prevention efforts without repeating the missteps of the initial vaccination program in the Philippines. Mariel was proud of the report she'd put together laying out the history and context of dengue in the region, along with relevant statistics. With ASEAN preparing to expand its dengue prevention focus to Cambodia, Vietnam and Indonesia, she hopes this report would give the new teams the information they needed to plan interventions specific to each country's needs. Mariel's report, included below, will be the starting point for your team to develop its proposal, as detailed in the Team Assignment.

Dengue

Virus

Dengue fever is caused by one of the four Dengue viruses (conveniently named Dengue virus 1, 2, 3, and 4). Because there are four variations of the virus, a person can fall ill with Dengue fever more than once, with each reaction being more severe than the previous one. Being a vector-borne disease, the virus is transmitted through the bites of infected female mosquitoes, primarily *Aedes aegypti* (*Ae. aegypti*) and to a lesser extent *Aedes albopictus*. Ae. aegypti is also a known vector for numerous other serious viruses, including the Yellow Fever, Chikungunya, and Zika viruses. The virus may spread from human to mosquito while a person is viremic, meaning the dengue virus is present in their blood. Viremia can last around 12 days total, including up to 2 days prior to being symptomatic, and 2 days after the fever breaks. Some evidence shows that

pregnant mothers might pass the infection to their babies, which could result in preterm birth, low birth weight, and fetal distress (CDC, 2020).

Ae. Aegypti is active during the day and is a frequent feeder. The highest risk of being bitten is in the early mornings and in the evening before sunset. The eggs are viable without being in water for several months, and will hatch once they get in contact with water. *Aedes albopictus* is a very adaptive species to colder conditions as an egg and an adult (CDC, 2019; WHO, 2019). As such, it has now spread to 32 states in the United States and over 25 European countries, mostly due to international trade in products like bamboo or used tires (WHO, 2020b).

Factors contributing to a larger spread of dengue-infected mosquitoes include growing urbanization, climate change (lengthen optimal seasons for mosquito breeding), and globalization (imported cases). Among travelers returning from tropical climates, dengue is the second most diagnosed cause for fever after malaria. For example, in 2012, 11 European countries reported imported cases, including Portugal's outbreak with 2,000 cases (WHO, 2020b).

Symptoms, diagnosis, and treatment

Dengue affects people of all ages. The incubation period, which is the period between exposure to an infectious disease and the appearance of symptoms, is about 4-10 days. Dengue is suspected when a high fever (104°F) is accompanied by two of the following symptoms: severe headache, pain behind the eyes, muscle and joint pain, nausea, vomiting, swollen glands, and rash. The diagnosis can be confirmed with a blood test (CDC, 2019; WHO, 2020b). About 1 in 4 people infected will present with mild symptoms (nausea, vomiting, rash, and muscle pain) easily confused with other diseases, resulting in underreporting. Most people recover within 2-7 days with rest, fluids, and pain/fever relief medications.

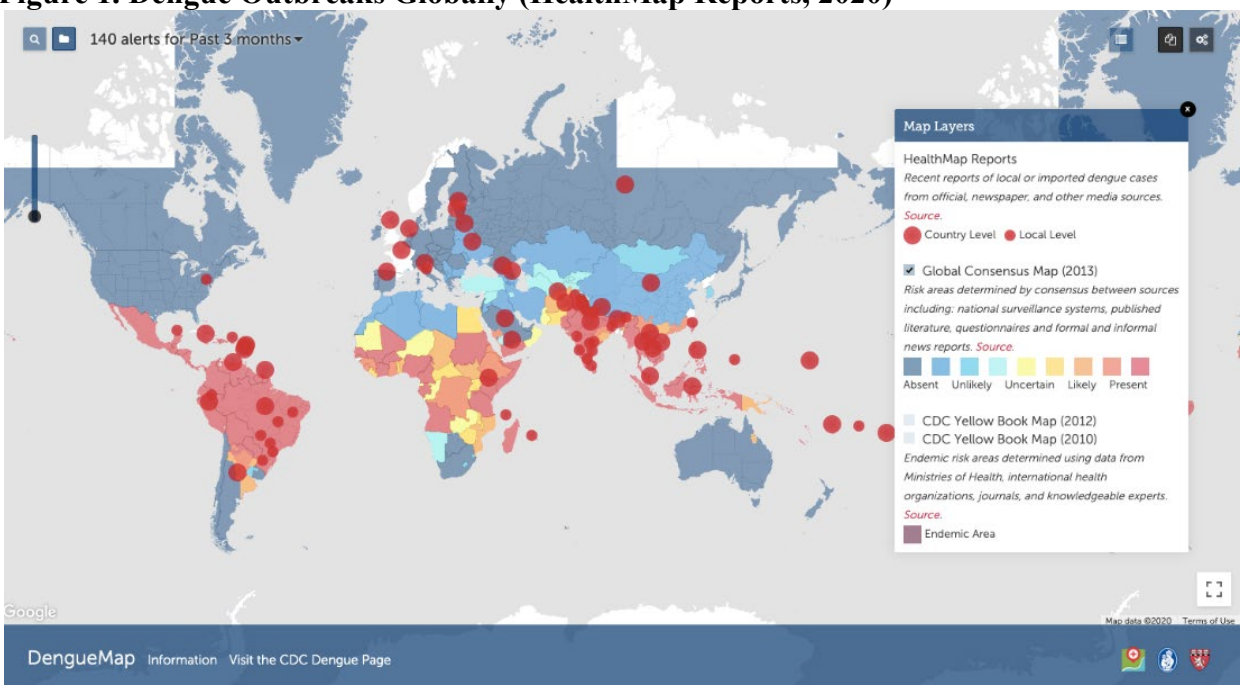
About 1 in 20 symptomatic people develop severe Dengue, and approximately 500,000 cases of severe dengue infection annually require hospitalization (CDC, 2019; WHO, 2020b). Dengue is fatal for 1%-2.5% of cases overall, and up to 20% of those with severe dengue (WHO, 2019). Severe symptoms generally start in the 24-48 hours after the fever decreases to about 100°F, and include stomach pain, persistent vomiting (at least 3 times in 24 hours), rapid breathing, blood in vomit/stool, bleeding from the nose/gums, fatigue, restlessness, and possibly seizures. Severe cases require immediate medical attention or hospitalization. There is no specific treatment available for dengue. Medical help focuses on symptom management (WHO, 2020b).

Usually a person's second infection triggers worse symptoms than experienced with the first infection. The antibodies developed from a person's first infection can make an infection worse, as the dengue virus actually uses the antibodies to help it spread through the body. With a second dengue infection, the individual's blood already has antibodies in it and can lead to a worse infection than previously with a higher risk of severe complications like plasma leakage syndrome (Doucleff, 2019).

Incidence & health impacts

Dengue is a mosquito-borne viral infection. Due to its rapidly growing incidence and relatively high fatality rate, the World Health Organization (WHO) named dengue one of the ten threats to Global Health in 2019 and one of the top WHO strategic priorities for the upcoming five years (WHO, 2019). About half of the world population is now at risk of contracting dengue (Figure 1; HealthMap Reports, 2020). Approximately 390 million dengue infections occur annually in all WHO regions, particularly in The Americas, South-East Asia, and Western Pacific regions. Asia carries about 70% of the global burden. Although dengue infections occur primarily in urban/semi-urban areas during the rainy seasons in tropical and sub-tropical climates, the incidence has risen in less tropical and more temperate countries, including Nepal and some European countries (WHO, 2020b).

Figure 1. Dengue Outbreaks Globally (HealthMap Reports, 2020)



Vaccination as a means of prevention

Philippines program

In 2016, the U.S. Food and Drug Administration approved the vaccine CYD-TDV (Dengvaxia) created by Sanofi Pasteur and it became commercially available to 11 countries, including the Philippines. The Philippines launched a mass vaccination campaign in April of the same year with the goal of inoculating nearly 1 million school children to save thousands of kids' lives and prevent an estimated 10,000 hospitalizations (Reuters, 2016; Doucleff, 2019). Three months after the campaign began, the World Health Organization (WHO) conditionally recommended the

vaccine for all children ages 9 to 16. This recommendation, however, does not address children ages 5 to 9, the most vulnerable age group (Doucleff, 2019; France-Presse, 2019).

The program halted in November 2017 when Sanofi Pasteur advised the government and published an announcement that the vaccine could put previously uninfected people at a somewhat higher risk of a severe case of dengue fever. The company wrote "For individuals who have not been previously infected by dengue virus, vaccination should not be recommended." New studies found that though the increased risk seemed small, it was not an acceptable risk (Douclef, 2019; Soucheray, 2017).

By the time Sanofi acknowledged this problem with the vaccine, about 800,000 Philippine children had been vaccinated. The Sanofi study estimated that more than 100,000 of them had never been infected with dengue and should not have received the shot. In response, the WHO changed its recommendation to "only for children who have had a prior dengue infection." However, Filipino parents were not warned about the potential risk and risk communication was lacking from the beginning. On the other hand, in the U.S. territories, Dengvaxia roll-out had included an important restriction: "doctors must have proof of a prior dengue infection to ensure the vaccine will not pose any risks to the child" (Doucleff, 2019).

Sanofi's disclosure caused a nationwide panic as parents stepped out to suggest that the vaccine contributed to the approximately 600 deaths of children who received the vaccine. The Philippine government indicted several government officials over the death of children who received the Dengvaxia vaccine and said the officials acted with "undue haste" in procuring the vaccine and launching the mass immunization campaign. Furthermore, since the Dengvaxia controversy, the confidence in vaccines among Philippine parents has plummeted from 82% in 2015 to only 21% in 2018, a recent study found (Larson et. al, 2018). During this time the proportion of parents who strongly believe vaccines are important fell from 93% to 32%. (Larson et. Al, 2017) As a result, vaccine coverage for childhood diseases in the Philippines, such as the measles, has dropped, WHO says. The Philippines faced a large measles outbreak in 2019 with more than 26,000 cases and more than 355 deaths.

Development of new vaccine

For people without a history of Dengue infection, Dengvaxia essentially acts as a person's first infection of Dengue, triggering the immune system to produce antibodies to the virus. These antibodies do help the body fight the virus, but also make a person's symptoms worse with future successful infections. The protection provided by the vaccine outweighs the risk of exacerbating future infections, but is still important to consider. Following the Sanofi announcement in 2017, a Strategic Advisory Group of Experts (SAGE) working group reviewed new data to conclude that "for countries considering vaccination as part of their dengue control program, a 'pre-vaccination screening strategy' would be the preferred option, in which only dengue-seropositive persons are vaccinated" (WHO, 2018).

Scientists continue to research new vaccine options for dengue that would not have the same limitation as Dengvaxia to only be suitable for those previously exposed to dengue infection. Currently two other live attenuated vaccines, like Dengvaxia (CYD-TDV), are in Phase III of clinical trials. Other vaccine types such as inactivated virus vaccines, subunit vaccines, and DNA vaccines are in Phase I of clinical trials (Deng et al., 2020).

Table 1: Dengue vaccine candidates in use or in clinical trials (Deng et al., 2020)

Vaccine Type	Name	Strategy	Clinical Trial Phase
Live Attenuated vaccine	CYD-TDV	Replacing the prM/E gene of the YF17D virus with genes of the DENV1–4	Evaluation after part of the license
	TV003/TV005	Attenuation by truncating 30 nucleotides in the 3′ UTR of DENV1, DENV3, DENV4, and a chimeric DENV2/DENV4	Phase III
	DENVax	Replacing the coding sequences of DENV2 PDK-53 attenuated vaccine with that of DENV1, DENV3, and DENV4	Phase III
Inactivated virus	PIV	Purified formalin-inactivated virus and adjuvants	Phase I
Subunit vaccine	V180	A recombinant truncated protein containing DEN-80E	Phase I
DNA vaccine	D1ME100	Recombinant plasmid vector encoding prM/E	Phase I
	TVDV	Recombinant plasmid vector encoding prM/E proteins of DENV1–4	Phase I
Heterologous prime/boost	TLAV Prime/PIV boost and reverse order	Initial immune-boost strategy	Phase I

CYD-TDV: the live attenuated chimeric yellow fever 17D virus-tetravalent dengue vaccine; DENVax: the live attenuated tetravalent dengue vaccine; PIV: the purified formalin-inactivated virus vaccine; TVDV: the tetravalent DNA vaccine; TLAV: the tetra-live attenuated virus vaccine.

Outside the Philippines, barriers to disseminating vaccines globally remain from capacity to cost. In low-and-middle-income communities, transferring early-stage technologies for meningitis, rotavirus, typhoid fever, dengue, and varicella vaccines are possible as well as training programs for medical and healthcare personnel to build local or regional clinical trial and vaccine production capacity (Chokshi and Kesselheim, 2008). By transferring technology at early stages by the research community, it allows new platforms, products, and services to be made into products for public use in different communities.

Dengue prevention programs

The WHO provides general guidance for dengue prevention and control at the individual, community and national level. All of these strategies focus on vector control since a significant risk factor for dengue is the proximity of vector breeding sites to human habitation. At an individual level, prevention and protection efforts include using window screens and mosquito nets in sleeping areas, wearing clothing that minimizes skin exposure to mosquito bites, and using mosquito repellants. The use of mosquito nets is most relevant to protecting children who sleep or nap in that day given that Ae. Aegypti is a daytime feeder (WHO, 2020b).

At the household and community level, effective water management practices can eliminate mosquito breeding sites. These practices include: appropriate disposal of solid waste, covers for domestic water containers, insecticides for outdoor water storage containers, and environment management to reduce areas with standing water. At the national level, health authorities may implement emergency vector control measures like spraying insecticides in communities with dengue outbreaks. This is sometimes referred to as fogging. Surveillance of the national mosquito population and screening of sentinel mosquito collections to test for prevalence of the

dengue virus are other outbreak prediction measures that can be carried out at the national level (WHO, 2020b).

Along with programs organized by each country's Ministry of Health, international organizations also play a role in dengue prevention initiatives. One example of support is from the World Mosquito Program, which works in Indonesia and Vietnam. In both countries the World Mosquito Program focuses on the release of mosquitoes that carry the specific bacteria Wolbachia. As the *Walbachia*-carrying mosquitoes breed with wild Ae. Aegypti mosquitoes, more and more mosquitoes carry the Wolbachia bacteria over time. These mosquitoes have a reduced ability to transmit viruses to people, which reduces the risk of transmission and outbreak of mosquito-borne diseases (World Mosquito Program, 2020a; World Mosquito Program, 2020b).

The Mekong-U.S. Partnership grew out of the Lower Mekong Initiative (LMI), which was a decade-long partnership between USAID and the countries of Cambodia, Laos, Myanmar, Thailand, and Vietnam. Both the Mekong-U.S. Partnership and LMI are rooted in broad economic and development goals across areas of agriculture, energy, environment, health, and infrastructure. These goals include a focus on specific global health issues such as Dengue. Activities include support at the national level for coordinated responses to Dengue outbreaks, improving laboratory capacity for diagnosis, and risk communication efforts (Mekong-U.S. Partnership, 2020; USAID, 2020).

Team assignment

ASEAN has created a task force – your team – to provide recommendations to member countries for Dengue prevention and mitigation efforts. ASEAN has never had such health-focused advisory program before. Your team's proposal to one of the three countries will serve as a blueprint for a new and innovative approach to dengue prevention. Your team will act as advisors to the new health promotion & dengue prevention teams in either Cambodia, Vietnam or Indonesia. With the delivery of this case, your team received instructions on how to indicate your country preference. We strongly advise you do not move forward with developing your plan until the country selection has been confirmed by the Sparkman Center for Global Health or the Lister Hill Center for Health Policy.

In your advisory capacity as the new ASEAN team, create a presentation outlining your suggested approach for preventing dengue in the target country, including health programs and policy recommendations. For each program and policy, be sure to include a detailed plan and justification. Remember that these efforts should be based in public health, which the WHO defines as the "art and science of preventing disease, prolonging life and promoting health through the organized efforts of society" (WHO, 2020a). Also keep in mind that while Mariel's report above shares examples of dengue prevention programs already happening in each country, ASEAN wants to see novel approaches and innovative solutions to tackle dengue prevention and vaccine hesitancy in Cambodia, Indonesia, and Vietnam.

Parameters of the presentation include:

- Timeline: 5 year maximum
- Funding: $500,000
    - Teams are allowed to propose strategies for increasing funding, but these proposals must clearly define the funding mechanism and policy parameters.
- Presentation: 15 minutes, followed by 5 minutes for Q&A

On Saturday, February 6th your team will present to a panel of judges with experience and knowledge across the areas of infectious disease, community development, and the geographic regions. After viewing your presentation, judges should be able to answer the following questions:

1. What are the key components of your intervention and how will they positively impact the health of your target population?
2. How will your intervention affect policy in your country? What policies will your country need to put in place in order to achieve your goal? How will those policies be funded and enforced?
3. How will your program address the potential for community distrust of vaccines following the challenges of the Philippines' vaccination program? How will you garner support in the community for your proposed programs and policies?
4. Who, if any, are your community or local partners? What benefit do they bring to your partnership and how does partnering with you benefit them?
5. What is your budget and how is it split across different aspects of your health intervention?

Important areas of consideration for your proposal:

- Choice of Target Population: Who is the target population and why did the team choose to target them? You may choose to target a specific area of the country, or another subpopulation.
- Social Benefit/Social Return on Investment: Impact on health outcomes, economic improvement, and productivity at the personal, family, and community levels
- Economic Impact: Direct costs associated with proposed strategies; potential for positive economic impact in the community as a result of your intervention
- Cultural Acceptability: Cultural perceptions of the proposed strategies and the extent to which they have taken in local cultural context and technologies
- Sustainability & Scalability: Plans for how the program will proceed once funding ends; opportunities for this program to expand to other target populations
- Monitoring and Evaluation: Comparison of baseline data to data collected during and after proposed intervention(s) and how this information will be used to inform program improvements and demonstrate impact
- Risk Identification & Mitigation Strategies: Potential challenges/risks associated with recommendation(s) and how those will be addressed, including legal issues & ethical concerns
- Innovation: Are there aspects of the proposal which could be considered particularly innovative or creative; novel application of existing technologies or new products/services proposed?

General resources to support your intervention development:
Public Health 101 slide deck: key definitions, essential services of public health, public health approach (CDC, 2018)

Social-Ecological Model

- ➔ Definition from the Office of Behavioral & Social Sciences Research, National Institutes of Health
- ➔ Explanation of social-ecological model in the context of violence prevention, CDC

Public Policy & Policy-making

- ➔ Observatory of Public Sector Innovation: Public Policy, Organisation for Economic Cooperation and Development
- ➔ "Re-thinking the Policy Making Process for today's needs," Betty Tushabe, TEDxRugando

Examples of past Global Health Case Competition cases & winning presentations

All documents linked here and in References can be accessed to view and download here: References folder

Appendix

Figure 2: Political Map of Cambodia

(Nations Online, 2020)

Figure 3: Political Map of Indonesia

(Nations Online, 2020)

Figure 4: Political Map of Vietnam

(Nations Online, 2020)

Table 2: Key country data

	Indonesia	Cambodia	Vietnam
Population	262,787,403	16,449,519	97,040,334
GDP	**purchasing power parity**: $3.25 trillion **official exchange rate**: $1.015 trillion **growth rate**: 5.1% **per capita**: $12,400 **Gross national saving**: 31.7% GDP	**purchasing power parity**: $64.21 billion **official exchange rate**: $22.09 billion **growth rate**: 6.9% **per capita**: $4,000 **Gross national saving**: 13.7% GDP	**purchasing power parity**: $648.7 billion **official exchange rate**: $220.4 billion **growth rate**: 6.8% **per capita**: $6,900 **Gross national saving**: 29% GDP
Life Expectancy	**total population**: 73.2 years **male**: 70.6 years **female**: 76 years	**total population**: 65.9 years **male**: 63.4 years **female**: 68.6 years	**total population**: 73.9 years (2018 est.) **male**: 71.4 years **female**: 76.7 years
Languages spoken	Bahasa Indonesia (official, modified form of Malay), English, Dutch, local dialects (of which the most widely spoken is Javanese) note: more than 700 languages are used in Indonesia	Khmer (official) 96.3%, other 3.7% (2008 est.)	Vietnamese (official), English (increasingly favored as a second language), some French, Chinese, and Khmer, mountain area languages (Mon-Khmer and Malayo-Polynesian)
Main Religions	Muslim 87.2%, Protestant 7%, Roman Catholic 2.9%, Hindu 1.7%, other 0.9% (includes Buddhist and Confucian), unspecified 0.4%	Buddhist (official) 97.9%, Muslim 1.1%, Christian 0.5%, other 0.6% (2013 est.)	Buddhist 7.9%, Catholic 6.6%, Hoa Hao 1.7%, Cao Dai 0.9%, Protestant 0.9%, Muslim 0.1%, none 81.8%

(Central Intelligence Agency, 2020)

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