INA-RESPOND

INDONESIA RESEARCH PARTNERSHIP ON INFECTIOUS DISEASE

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA

NEWSLETTER

June 2023

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HEALTH POLICY AGENCY
MINISTRY OF HEALTH REPUBLIC OF INDONESIA
2023

MASTHEAD

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newsletter

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FEATURES

INA-RESPOND Newsletter

InVITE & PROACTIVE Study Updates

By: Eka Windari R., I Wayan Adi Pranata, Lois E. Bang, Melinda Setiyaningrum, Nur Latifa Hanum, Retna Mustika Indah, Restu Amalia, Riza Danu Dewantara

InVITE

As of June 12, 2023, among the 700 individuals who enrolled in the research, 192 (27.42%) have chosen to discontinue their participation, while 508 (72.57%) are still actively involved. The research is being conducted at three different locations, and all sites are presently at visit 4. The specifics of each site's visits are outlined in Table 1.

It is worth noting that the research has encountered challenges in retaining participants. Out of the 192 individuals who discontinued their involvement, 131 (18.71%) successfully completed the study, whereas 44 (6.29%) withdrew due to personal reasons or loss of interest. Some individuals decided to withdraw voluntarily. Moreover, a few participants did not receive the full vaccine regimen within the required 12-month period, resulting in the exclusion of three subjects (0.43%) from the study. Two individuals (0.29%) were deemed unfit to continue, and one subject (0.14%) failed to comply with study procedures. Regrettably, one subject (0.14%) passed away during the study, and ten individuals (1.43%) had different reasons for discontinuing their participation.

Additionally, the study has been monitoring symptomatic visits among the participants. The details of these visits are presented in Table 2 as of June 12, 2023. It is important to emphasize that while some participants have displayed symptoms associated with COVID-19, this does not necessarily indicate that they have contracted the disease.

The Material Transfer Approval was released on June 6th, 2023, with suggestions from the MTA Committee. These suggestions include making adjustments to the clauses in the MTA document. Furthermore, Biobanking activities can only be conducted within Indonesia, and an Indonesian team will be responsible for conducting inspections and monitoring the research progress to ensure compliance with both the Cooperation Agreement and the Material Transfer Agreement. The applicant is required to furnish a copy of the material receipt as proof and subsequently submit a report on the management of the received material to the Head of the Health Policy Agency (BKPK).

Site	Symptomatic Visit		
	# of visit	Positive	Negative
01	102	61	41
02	14	6	8
03	2	1	1
Total	118	68	50

Table 2. Symptomatic Visit Details per June 12, 2023

Site	Screening / Visit 1	Enrollment Failure	Enrolled	Ongoing	Add. Visit 1	Visit 2	Add. Visit 2	Add. Visit 3	Visit 3	Agree Ext.	Not Agree Ext.	Ext. Visit 4	Ext. Visit 5
01	345	2	343	283	88	326	314	306	315	286	29	224	3
02	228	1	227	130	97	214	191	188	195	151	44	151	30
03	130	0	130	95		130			129	95	35	87	0
Total	703	3	700	508	185	670	505	494	639	532	108	462	33

Table 1. Details of Visits per site per June 12, 2023

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As of June 22, 2023, all 4,336 subjects who were enrolled in the study have completed their participation. The latest site, Site 520, finished its last follow-up visit in May 2023.

Regarding the end-of-study subjects, 3,485 have completed the study up to the 36-month follow-up. However, 506 subjects were lost to follow-up, presenting a challenge in obtaining complete data for their entire study period. 248 subjects passed away during the course of the research, 32 subjects withdrew their consent, due to personal reasons or changes in their circumstances. Moreover, 38 subjects moved away to a city without a PROACTIVE Site. Furthermore, 5 subjects tested HIV negative. Lastly, 2 subjects were temporarily suspended from the study due to their imprisonment. The progress of the study at each site is described in Figure 1.

To ensure a systematic and thorough close-out process, sites that have completed their follow-up period are currently preparing for the site close-out visit, which marks the official conclusion of their involvement in the study.

In June 2023, several sites are scheduled to undergo the close-out visit, including sites 520, 530, 540, 660, 670, 680, 690, and 700. Sites are required to complete all the items listed on the close-out visit checklist, including but not limited to Case Report Form/Source Documents, all AE/SAE/UP Reports, Data Management, Site Regulatory Binder, Logs, Equipment and Supplies, and Specimens. This comprehensive checklist ensures that all necessary documentation and data are properly organized and accounted for, facilitating a smooth and efficient close-out process.

Once a site has successfully completed the close-out visit, the next step is to archive the study documents within one month. These documents will be retained for a minimum of 5 years after the study's completion.

Several sites, such as sites 610, 630, and 560, have already taken proactive measures by sending their study documents to the Secretariat. The Secretariat has collaborated with a trusted vendor to ensure the proper archiving and safekeeping of these vital study documents.

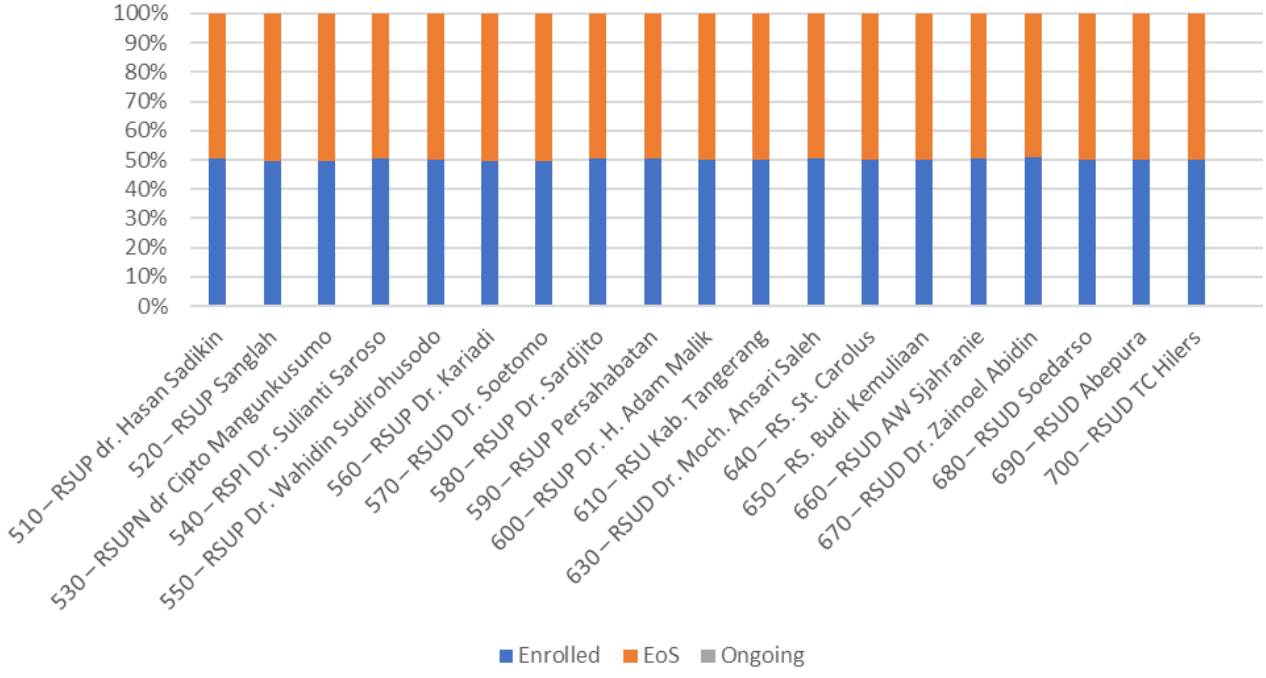


Figure 1. Site's Study Progress

Table 2. Study timeline for Site Close Out Visit (SCV)

Site	Site Name	Site Close Out Visit (SCV)	
		Scheduled	Actual
510	RS Hasan Sadikin, Bandung	Jun-23	15-16 Jun 2023
520	RSUP Sanglah, Denpasar	Sep-23	TBD
530	RS Cipto Mangunkusumo, Jakarta	Jul-23	TBD
540	RS Sulianti Saroso, Jakarta	Sep-23	TBD
550	RS Wahidin Sudirohusodo, Makassar	May-23	24-15 May 2023
560	RS Kariadi, Semarang	Mar-23	30-31 mar 2023
570	RS Soetomo, Surabaya	Apr-23	13-14 Apr 2023
580	RS Sardjito, Yogyakarta	Apr-23	20-21 Apr 2023
590	RS Persahabatan, Jakarta	Jun-23	14-15 Jun 2023
600	RS Adam Malik, Medan	Jun-23	21-23 Aug 2023
610	RSU Kab Tangerang, Banten	Mar-23	08-09 Mar 2023
630	RSUD M. Ansari Saleh, Banjarmasin	Apr-23	05-06 Apr 2023
640	RS St. Carolus, Jakarta	Jun-23	05-06 Jun 2023
650	RS Budi Kemuliaan, Batam	Jun-23	07-08 Jun 2023
660	RSU Wahab Sjahranie, Samarinda	Jul-23	TBD
670	RSUD dr. Zainoel Abidin Banda Aceh	Jul-23	TBD
680	RSUD dr. Soedarso, Pontianak	Sep-23	TBD
690	Abepura	Jul-23	TBD
700	RSUD Dr. TC Hillers Maumere	Aug-23	TBD

INA-RESPOND Newsletter

WHAT IS A DRUG INTERACTION?

By: Nayon Kang, Lucy Chung, David Vallee

FROM OUR PARTNER

A reaction between two (or more) drugs or between a drug and a food or supplement. An existing medical condition can also cause a drug interaction. A drug interaction can decrease or increase the action of the drug(s) or cause adverse effects. [1]

This interaction could result in a range of outcomes, from unwanted effects of clinical significance to no clinically significant impact. The potential for drug interactions increases with polypharmacy, and the management should involve efforts from both healthcare providers, as well as patients. [2]

Different Types of Drug Interactions: [3]

- Drug-Drug Interaction: a reaction between two or more drugs
- Drug-Food interaction: a reaction between a drug and a food or a beverage
    - Grapefruit and grapefruit juice is an example that may lead to an increased levels of a drug that could cause unwanted harmful effects[4]
- Drug-Condition interaction: a reaction that occur when taking a drug while having a certain medication condition
    - Example: Nasal decongestant usage in patients with high blood pressure may cause an unwanted reaction

Mechanisms of Drug-Drug Interactions (DDI)[5,6]

The mechanisms for DDIs can be classified into those related to the pharmacokinetics or pharmacodynamics of a drug. Pharmacokinetic interaction involves mechanisms of what the body does to a drug, such as how it's broken down or removed from the body, and pharmacodynamic interaction involves mechanisms of what a drug does to a body, such as additive or antagonistic effects. Table 1 shows some of the examples of these interactions.

Strategies For Managing DDIs[5,6]

Physicians, pharmacists, and other healthcare providers play an important role in assessing patient's

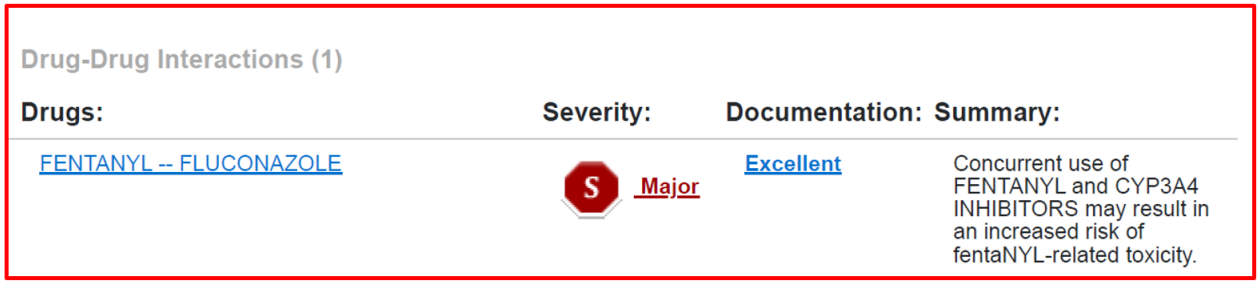
Pharmacokinetic interaction			
Sites/Modes of Interaction	**Types of Interaction**	**Possible Outcomes**	**Examples**
Absorption	Change stomach pH	↑ or ↓ drug absorption and availability	Histamine H_2 Antagonist (famotidine) or proton-pump inhibitors (lansoprazole) increase stomach pH and affect absorption of other drugs
Distribution	Compete for protein binding	↑ or ↓ drug availability and exposure	Warfarin and diclofenac compete for the same protein binding site
Metabolism	Inhibition or induction of isoenzymes (i.e. CYP450) involved in drug metabolism	↑ or ↓ drug concentration and effects	Amiodarone inhibits enzymes that metabolize warfarin and results in increased warfarin concentration
Excretion	Changes in the transport of drugs out of the body	↑ or ↓ drug removal from the body	Non-steroidal anti-inflammatory drugs (ibuprofen) inhibit transport of some drugs in the renal system and lead to increased concentration
Pharmacodynamic Interaction			
Additive/Antagonistic effects	Altered drug response	↑ or ↓ effects of drugs	Additive effects when opioids are given together

Table 1. Examples of Mechanisms of Drug-Drug Interactions[5,6]

medications to ensure safe and appropriate uses. Additionally, patient engagement is also important for gathering accurate and comprehensive medication history to guide future medication therapies and to avoid any potential DDI risks.

Management of drug interactions should be multimodal and below are some important considerations:

1. Identifying potential DDI as well as identifying patients at high risk of DDI, such as those receiving multiple medications for chronic conditions, will be a crucial step.
    a. There are several drug interaction databases that provide information on drug interaction risks, magnitude of interactions, and the severity of risk (Figure 1). Pharmacists, who are familiar with utilizing these databases, can be a great resource in providing comprehensive assessment of DDI risks.
2. Sometimes a DDI is unavoidable and drug interactions will need to be closely monitored.
    a. Therapeutic drug monitoring can be an important instrument in this case, especially for drugs that are routinely monitored, such as warfarin, phenytoin, vancomycin, or aminoglycosides, to guide dose adjustment or alternative dosing strategy.
3. Patient engagement and education are important for reducing DDI risks by:
    a. Clearly communicating current medication regimen to identify any potential DDI risks and 'de-prescribe' any duplicate therapies that could introduce DDI
    b. Ensuring patients understand and communicate any changes made to the current medication regimen to other healthcare providers to avoid future DDI risk.



Drug-Drug Interactions (1)

Drugs:	Severity:	Documentation:	Summary:
FENTANYL -- FLUCONAZOLE	Major	Excellent	Concurrent use of FENTANYL and CYP3A4 INHIBITORS may result in an increased risk of fentaNYL-related toxicity.

Figure 1. Example Result from a DDI Database[7]

DDIs in Clinical Trials and Challenges

Clinical trials involving investigational products (IP) that have never been approved or made available commercially can be challenging due to limited availability of clinical and non-clinical data. Also, the available data will evolve as the pharmaceutical companies continue to undergo different testing to fulfill requirements for the new drug approval processes, but the information may be limited to the research team only. Moreover, in blinded, placebo-controlled trials, some of the DDI management strategies, such as utilizing therapeutic drug monitoring to assess drug levels and guide dose adjustments, may not be feasible to maintain blinding and to avoid sub-therapeutic dosing in participants who may be receiving blinded placebo treatment. When IP is a victim drug in a DDI, the observed outcomes may not reflect the true efficacy of the study product and therefore impact the overall study results. Above mentioned strategies, as well as trial-specific resources, may need to be developed to avoid DDI risks and ensure patient safety and robust results on drug efficacy.

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DCR pharmacy team is happy to hear your thoughts! Please feel free to share your experiences. We can be reached via email at DCRPharmacy@mail.nih.gov

INA-RESPOND Newsletter

DENGUE: PREVENTABLE AND TREATABLE SOON?

By: Herman Kosasih

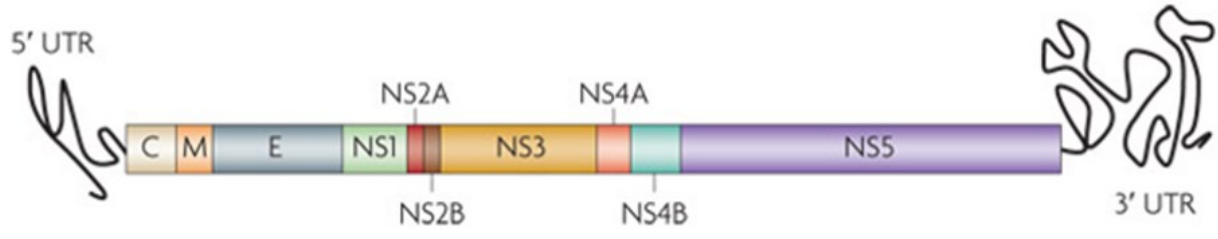
Historically, dengue-like illnesses occurred almost simultaneously in Asia, Africa and North America around 200 years ago. The term 'dengue' originated from the Swahili phrase Ka-dinga pepo, which translates to "cramp-like seizure." It wasn't until 1943 that Ren Kimura and Susumu Hotta successfully isolated the virus (DENV) during an epidemic in Nagasaki. Subsequently, the epidemiology of dengue underwent significant changes.

Since the first dengue report in Indonesia in 1968, the disease's epidemiology experienced dynamic transformations. The number of provinces reporting dengue cases increased from two to encompassing all provinces. Incidence rates gradually climbed from 1 per 100,000 people in 1968 to 40 per 100,000 people in 2020, with several peaks reaching 70-100 per 100,000 people every 6-8 years. However, the case fatality rate (CFR) dropped from 40% in 1968 to 0.7% in 2020.

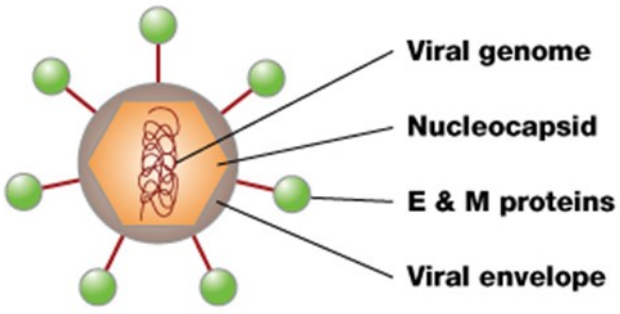
Although the CFR has significantly decreased, dengue remains endemic in over 125 countries, predominantly in tropical and subtropical regions, causing an estimated 390 million infections annually worldwide, with 96 million being clinically apparent. The WHO's goal, outlined in the 2021-2030 Global Strategy for Dengue Prevention and Control, is to reduce the CFR to 0% and the incidence rate by 25%. Considering the substantial advancements in dengue prevention and treatment, which we will briefly discuss here, there is hope that after 80 years since its discovery, dengue will soon become a preventable and treatable disease.

What is Dengue?

Dengue is a febrile illness caused by the dengue virus, a member of the flavivirus genus. It is transmitted by mosquitoes, specifically Aedes aegypti or Aedes albopictus. There are four serotypes of the DENV: DENV-1, DENV-2, DENV-3, and DENV-4. These serotypes interact differently with antibodies, leading to their classification as distinct types. The DENV is a positive-sense RNA virus, meaning it can be directly translated into proteins. The genome encodes ten genes (Figure 1) that is translated into ten proteins.



Guzman, M. G. *et al.* Dengue: A continuing global threat. *Nature Reviews Microbiology* 8, S7–S16 (2010).



The diameter of the DENV is 50 nm. The core of the virus contains the nucleocapsid, which consists of the viral genome and the C proteins. Surrounding the nucleocapsid are the viral envelope and membrane proteins. The seven nonstructural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B, and NS5) play essential roles in viral replication and assembly.

Infection with one serotype of the DENV provides long-term protection against reinfection with the same serotype but only transient cross-protection against other serotypes. Therefore, people living in dengue-hyperendemic areas where multiple serotypes circulate are at risk of experiencing multiple infections.

Clinical classification and disease severity

DENV infection can range from asymptomatic or mild febrile illness to severe disease (life-threatening shock syndrome). The clinical classification of symptomatic DENV infection has undergone revisions. Initially, it was classified into dengue fever (DF), dengue hemorrhagic fever (DHF), and dengue shock syndrome (DSS) (WHO, 1997). However, this classification has been criticized for its emphasis not on the most crucial feature of severe dengue, which is plasma leakage leading to shock. A re-evaluation in 2009 introduced a classification based on the presence of warning signs and severe dengue. The focus of this scheme is to recognize the warning signs early for management decisions. It was also criticized because the criteria for severe dengue was not clear. The concept of expanded dengue syndrome that includes patients with severe organ involvement (liver, kidney, brain, or heart) but without evidence of plasma leakage was then proposed by the WHO South-East Asia Regional Office in 2011. As there are several classifications, institutions/countries may use different classification.

Several factors can influence disease severity in dengue infection. These include the specific serotype or genotype of the virus, secondary infection with a different serotype, age of infants, nutritional status, and genetic factors such as race, specific HLA genes, blood group, and various gene polymorphisms. However, conflicting findings exist regarding some of these factors.

Progress in Treatment

Current treatment for DENV is supportive, managing fever, bleeding, plasma leakage, and shock. While no direct antiviral therapy exists, successful approaches have led to a decrease in mortality rates. However, to further reduce incidence and CFR, effective antiviral drugs that can be used for prophylaxis and for reducing the viral load, duration of viremia and severity are needed. Previous clinical trials with drugs like chloroquine, lovastatin, balapiravir, and celgosivir did not yield significant results. A promising molecule inhibitor, JNJ-1802, blocks the formation of the viral replication by inhibiting complex formation between NS3 and NS4B, has shown positive results in a Phase 2a DENV-3 human challenge study. Participants receiving JNJ-1802 had a lower proportion of detectable DENV-3 RNA, shorter duration of symptoms, and reduced viral load compared to the control group. Larger studies involving all DENV serotypes will be conducted to further evaluate its effectiveness.

Progress in prevention

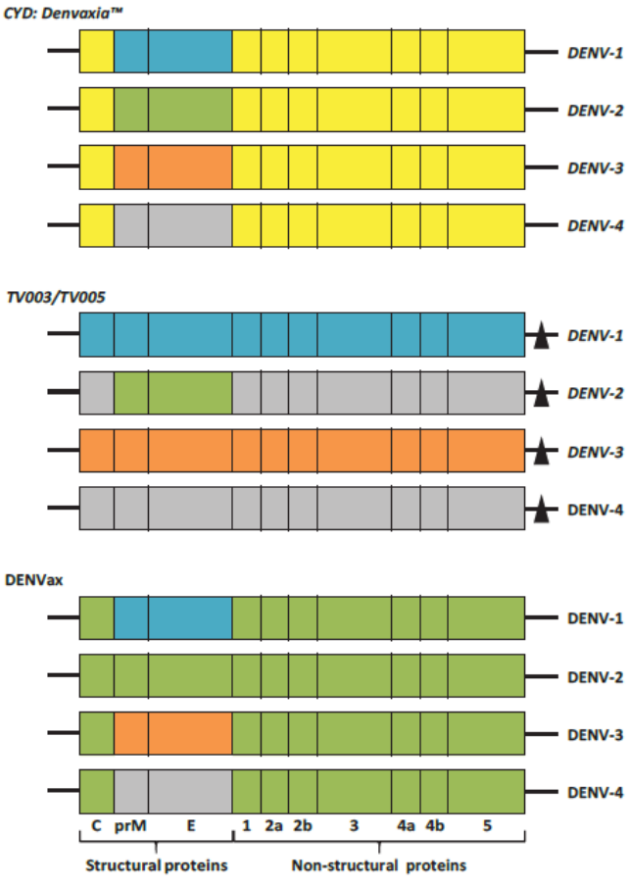
Wolbachia-Infected Mosquito Deployments for the Control of Dengue

Wolbachia-infected mosquito deployments have shown promising results as a novel strategy for dengue control. This approach involves releasing A. aegypti mosquitoes infected with Wolbachia, a bacterium that makes the mosquitoes less susceptible to DENV infection. A trial conducted in Yogyakarta, Indonesia, demonstrated the effectiveness of this method. Over a two-year trial period, the intervention clusters had a lower incidence of symptomatic dengue compared to the control clusters. The efficacy of Wolbachia in protecting against DENV infection was 77.1% (95% CI 65.3-84.9) and was similar across all four DENV serotypes. Furthermore, the efficacy in preventing hospitalization due to dengue was 86.2% (95% CI 66.2-94.3). Following the successful trial, the deployment was expanded to neighboring districts (Bantul and Sleman). The MoH in Indonesia has issued a decree (No 1341/2022) to conduct a pilot project for dengue control using Wolbachia-infected mosquitoes in five cities: West Jakarta, Bandung, Semarang, Bontang, and Kupang.

Progress in vaccine development:

An effective dengue vaccine should provide long-lasting protection against all four DENV types (tetravalent immunity) due to the severe disease potential and short-lived cross-protection between serotypes.

Vaccine development efforts began in the 1920s using methods such as attenuation with ox-bile and chemical treatments. Advances in tissue culture and recombinant DNA technology have greatly contributed to vaccine development. Currently, several candidate vaccines are in clinical trials. TDENV PIV is a tetravalent purified inactivated vaccine undergoing phase I trials. V180 is a recombinant subunit vaccine which has completed phase I trials with favorable tolerability. A monovalent DNA plasmid vaccine showed moderate immunogenicity in early studies. The furthest along in development are three live attenuated vaccines, CYD-TDV (Dengvaxia), TAK-003 (Takeda), and TV-003 (Butantan), using mutation and/or chimeric approaches. The structure of these chimeric vaccines is illustrated in Figure 3 below.



Prompetchara, 2017

CYD-TDV is a yellow fever 17D-dengue chimeric vaccine comprising four strains where the prM and E proteins from each DENV type replace the equivalent proteins in a yellow fever 17D backbone virus. The vaccine demonstrated an efficacy of 57% to 61% against virologically confirmed dengue of any severity caused by any DENV serotype and 80% to 95% efficacy against severe dengue or hos-

pitalization. Efficacy varied by serotype, with rates of 75% for DENV-3 and DENV-4, 50% for DENV-1, and 35% to 42% for DENV-2. However, further analysis revealed that the vaccine increased the risk of severe illness and hospitalization in individuals without previous dengue exposure. Therefore, the WHO recommended the CYD-TDV (Dengaxia) vaccine for individuals aged 9 to 45 years with confirmed prior dengue infection. The mechanisms underlying the vaccine's efficacy in seropositive individuals and the increased risk in seronegative individuals are still uncertain due to limited monitoring and analysis of immune profiles in the vaccinated population.

TAK-003 is a tetravalent vaccine based on an attenuated laboratory-derived DENV-2 virus, which provides the genetic backbone for all four of the viruses in the vaccine The other three virus strains are chimeras generated by replacing the preM and E genes of TDV-2 with those from wild-type DENV-1, DENV-3, and DENV-4 strains.

A phase 3 clinical trial involving >20,000 children aged 4 to 16 years in Asia and Latin America showed that after 18 months follow-up, the vaccine had an overall efficacy of 73.3% and a 90.4% efficacy against hospitalized dengue cases. The vaccine demonstrated higher efficacy in individuals who were seropositive at baseline compared to seronegative individuals (76.1% versus 66.2%). Efficacy by serotype was 69.8% DENV-1, 95.1% DENV-2, and 48.9% DENV-3. The efficacy against DENV-1 and DENV-2 was similar in participants with baseline seronegative or positive, but for DENV-3, efficacy was only among seropositive individuals (61.8%). DENV-4 efficacy was difficult to measure due to insufficient data. The incidence of serious adverse events (SAEs) was similar in the vaccine and placebo groups. TAK-003 appears to be effective in both seropositive and seronegative individuals and has the potential to reduce the burden of severe dengue. However, further evaluation of efficacy and safety, particularly for DENV-3 and DENV -4, is needed.

TV-003 is a live attenuated tetravalent dengue vaccine composed of three attenuated DENV strains with deletions in the 3' untranslated region and a fourth component that is a chimeric virus with prM and E proteins from DENV-2 replacing those of DENV-4 in the DENV4 30 background. The vaccine was developed by the US-NIAID and licensed to Instituto Butantan in 2009.

A phase 3 study of this single-dose vaccine was initiated in Brazil in 2016, enrolling 16,235 participants aged 2-59 years. Over a two-year follow-up period, the vaccine demonstrated an overall efficacy of 79.6% in preventing dengue illness, with no cases of severe dengue reported. Among seropositive participants at baseline, the efficacy was 89.2%, while in seronegative participants, it was 73.5%. Efficacy against DENV-1 and DENV-2 was 89.5% and 69.6%, respectively, but no data on efficacy against DENV-3 and DENV-4 were available due to limited circulation in Brazil during the study period. However, a previous phase 2 study indicated that 80% of volunteers produced antibodies against all four serotypes.

SAEs related to the vaccine occurred in less than 0.1% of participants within 21 days after vaccination. The frequency of AEs was similar across age groups and among participants previously exposed to dengue or not. Instituto Butantan signed a partnership with MSD in 2018 for further development and MSD plans to conduct a large phase 3 trial in Asia.

The Indonesian Food and Drug Authority (BPOM) approved Dengvaxia in August 2016 and Qdenga in August 2022. Although the Indonesian Pediatric and Internal Medicine Societies recommended it for individuals aged 6 to 45, the government has

not included it in the routine national vaccination program. They are waiting for the Indonesia Technical Advisory Group of Immunization (ITAGI) recommendation.

Summary

Progress has been made in understanding and addressing DENV due to its widespread facilitated by human behaviors and global climate change. However, efforts in understanding DENV's pathogenesis, disease management, prevention, and treatment have resulted in a reduction in global case fatality rates. Achieving the WHO's 2030 target of reducing the burden and incidence of dengue by 25% compared to 2010/2020 and eliminating deaths is becoming more feasible. Advancements in mosquito control, vaccine development, and antiviral discovery hold promise in making dengue preventable and treatable.

Further reading

- Ending the neglect to attain the Sustainable Development Goals: A road map for neglected
- tropical diseases 2021–2030 [https://www.who.int/publications/i/item/9789240010352]
- Safety, Tolerability, and Pharmacokinetics of JNJ-1802, a Pan-serotype Dengue Direct Antiviral Small Molecule, in a Phase 1, Double-Blind, Randomized, Dose-Escalation Study in Healthy Volunteers CID. Oliver Ackaert
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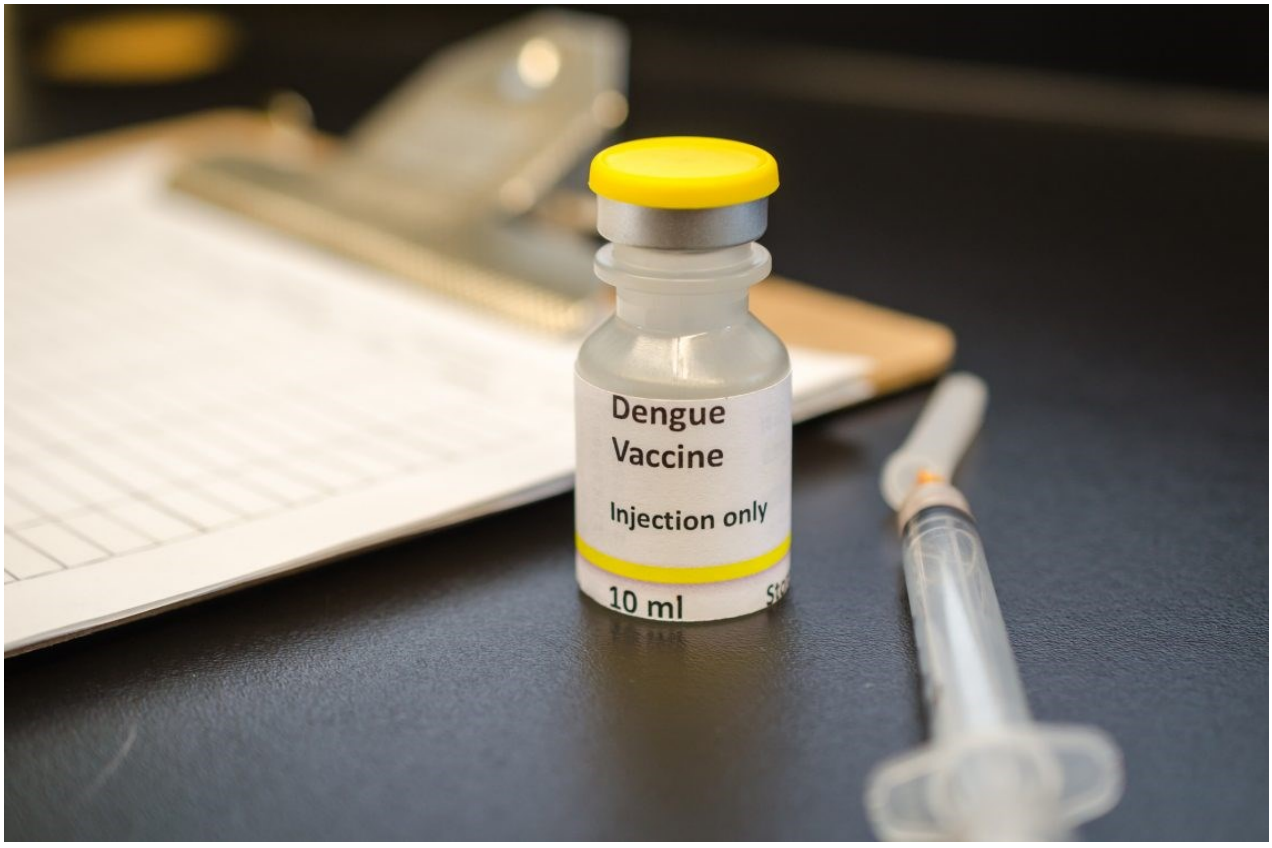

INA-RESPOND Newsletter

OUR SPORTS & LIFESTYLE TEAM PROFILE

By: Caleb L. Halim, Edrick Purnomo Putra, Marco Ariono, Maria Lestari, Monica Surjanto, Risky Dwi Rahayu

Meet our dedicated team of sports medicine physician who are passionate about health, sports, and lifestyle. They have been actively contributing to the INA-RESPOND newsletter, sharing their expertise through insightful articles.

With diverse specializations in sports medicine, including exercise therapy, injury prevention, nutrition, and performance optimization, our team brings a comprehensive approach to the topics they cover. Their articles aim to provide valuable insights and practical advice that enhance overall well-being.

Through their contributions, our team of specialist doctors empowers readers with the information they need to make informed decisions about their health and incorporate physical activity into their daily lives. From debunking common myths to offering exercise tips, discussing the benefits of various sports, and exploring lifestyle modifications, their articles are informative, engaging, and applicable.

We are grateful to have these passionate experts as part of our INA-RESPOND newsletter team. Their dedication to delivering valuable content inspires and motivates individuals to lead active, healthy, and fulfilling lives.

Stay tuned for their upcoming articles, where they will continue to explore the intersections of sports, health, and lifestyle, bringing you the latest insights and practical advice from our esteemed team of sports medicine physician.

Dr. Marco Ariono, Sp.KO, is a dedicated sports medicine specialist based at the prestigious Indonesia Sports Medicine Center. With a deep passion for sports, particularly football, Dr. Marco combines his expertise in diagnosing and treating sports-related injuries with personalized exercise programs. His goal is to optimize athletic performance, facilitate injury recovery, and improve overall health and well-being. Dr. Marco stays at the forefront of the field, continuously seeking advancements to provide comprehensive care. With a commitment to ongoing professional development, he ensures the highest level of dedicated expertise for his patients.

Dr. Marco Ariono is known for his exceptional care and support to athletes and individuals seeking to

lead active lives. By combining his medical expertise with personalized treatment plans, he has successfully helped numerous patients recover from sports-related injuries and enhance their athletic performance. Driven by a patient-centric philosophy and a holistic approach, Dr. Marco addresses the physical, mental, and emotional aspects of recovery. His commitment to staying updated with the latest advancements in sports medicine ensures that his patients receive the most effective and comprehensive care available.

Dr. Caleb Leonardo Halim, Sp.KO, is a passionate sports medicine specialist practicing at the Royal Progress Hospital and Royal Sports Performance clinic. With a strong background as a fitness enthusiast, Dr. Caleb has elevated his love for exercise by becoming a specialist in sports medicine.

For over 10 years, Dr. Caleb has dedicated himself to studying strength training, suspension training, and powerlifting. His expertise lies in understanding the biomechanics of movements and tailoring exercise prescriptions to meet individual needs. Whether it's the senior population, individuals with diabetes and obesity, or those with sports-related injuries, Dr. Caleb focuses on providing specialized care to address their unique challenges.

Driven by a deep passion for promoting a healthy lifestyle, Dr. Caleb is committed to helping his patients achieve healthier, stronger, and fitter bodies. With his expertise and dedication, he strives to make a positive impact on the lives of those he treats. If given the opportunity, he will work tirelessly to guide individuals towards their fitness goals and improve their overall well-being.

Dr. Monica Surjanto, Sp.K.O, is a dedicated sports medicine doctor who graduated from the Sports Medicine Faculty at the University of Indonesia in 2019. Currently, she holds positions at the Sports Clinic and Jakarta National Sports Committee, where she focuses on providing comprehensive care in the field of sports medicine.

Dr. Monica's main interest lies in utilizing exercise therapy to address non-communicable diseases such as obesity, diabetes, osteoarthritis, osteoporosis, and low back pain. Her expertise enables her to develop personalized exercise programs that

promote health and well-being while effectively managing these conditions. Additionally, she possesses a keen interest in the prevention and treatment of musculoskeletal injuries resulting from physical activity and sports, catering to both the general public and athletes.

With her extensive knowledge and passion for sports medicine, Dr. Monica strives to make a positive impact on the lives of her patients. She remains dedicated to staying updated with the latest advancements in her field, ensuring that she provides the highest level of care and treatment options. Dr. Monica's commitment to improving the well-being of individuals through exercise therapy and injury prevention solidifies her role as a valuable asset in the field of sports medicine.

Dr. Risky Dwi Rahayu, M.Gizi, Sp.KO, is a passionate sports medicine doctor dedicated to promoting active and healthy lifestyles. With a focus on optimizing the health and performance of athletes, she works with a regional athlete's development organization and applies the "exercise is medicine" concept to assist less physically active individuals at an exercise center. Dr. Risky has extensive experience in sports event medical teams and has served as the team doctor for the Indonesia National Women's Football Team. She combines clinical expertise with a passion for research and knowledge-sharing, ensuring the highest level of care for her patients. In her leisure time, she enjoys reading, music, and movies, further enriching her perspective as a sports medicine doctor.

Dr. Risky Dwi Rahayu's commitment to promoting active lifestyles, her involvement in sports events, and her passion for research make her an invaluable asset in the field of sports medicine. Her multifaceted approach to patient care and dedication to continuous learning contribute to her ability to make a positive impact on the lives of athletes and individuals seeking optimal health and performance.

Dr. Maria Lestari, BmedSc, Sp.KO, is a dedicated Sports Medicine Doctor affiliated with RS MMC & EKA Hospital. With a passion for women's health, she specializes in addressing issues such as low energy availability and sarcopenic obesity. Dr. Maria completed her postgraduate sports medicine diploma from the University of Otago in 2018 and her residency at *Ilmu Kedokteran Olahraga FKUI* in 2021. She is also an accredited strength and con-

ditioning specialist from the International Sports Sciences Association (ISSA).

In addition to her clinical practice, Dr. Maria serves as a Medical Officer for the Professional Footballers' Association of Indonesia (APPI) and is a senior investigator in the Cluster for Sports and Exercise Studies at IMERI FKUI. Her involvement in these roles allows her to contribute her expertise to support the well-being of professional footballers and contribute to research in the field of sports and exercise.

Outside of her professional pursuits, Dr. Maria enjoys traveling, weightlifting, running, and cooking. These hobbies contribute to her well-rounded lifestyle and enhance her understanding of the importance of physical activity and healthy nutrition.

Dr. Maria Lestari's commitment to women's health, her expertise in sports medicine, and her involvement in professional organizations and research make her a valuable asset in the field. Her dedication to continuous learning, combined with her diverse interests, enables her to provide comprehensive care to her patients and promote a holistic approach to health and well-being.

Dr. Edrick Purnomo Putra is a passionate sports medicine doctor with a particular interest in the "Exercise is Medicine" field. He focuses on utilizing exercise prescription as a tool for the treatment and prevention of non-communicable diseases. Dr. Edrick is dedicated to promoting the importance of physical activity and its benefits for overall health and well-being.

In today's world, the role of sports medicine doctors has become increasingly vital, especially with the rising prevalence of non-communicable diseases in society. Dr. Edrick recognizes the importance of raising public awareness about the significance of a healthy lifestyle. He believes that providing access to information and consultation

is essential to ensure individuals can engage in physical activity safely.

Outside of his medical practice, Dr. Edrick indulges in his passions for art, traveling, and learning foreign languages. These interests deepen his understanding of different cultures and viewpoints and add to his well-rounded attitude to life.

With his commitment to the "Exercise is Medicine" field and his belief in the importance of promoting a healthy lifestyle, Dr. Edrick Purnomo Putra serves as an advocate for physical activity and its positive impact on health and well-being. His dedication to providing safe and effective exercise prescriptions makes him an invaluable resource for individuals seeking to improve their overall health through physical activity.

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With their expertise and commitment, our team of specialists strives to make a lasting impact on the health and well-being of our readers. Stay tuned for their valuable contributions as they continue to share their knowledge and passion for health, sports, and lifestyle through the INA-RESPOND newsletter.

INA-RESPOND Newsletter

COMIC CORNER

FEEDING ADVENTURES: NOURISHING INFANTS AND YOUNG CHILDREN WITH LOVE AND LAUGHTER

By: Aly Diana

Source: https://www.istockphoto.com/id/vektor/pengasuhan-orang-tua-dan-anak-gaya-hidup-gm1202164528-345022798

I think most of us are parents, grandparents, or have siblings who are parents. At some point, we need to learn about how to feed our little ones to help them grow and develop. While it may seem simple, being a responsible adult can be challenging. We may know some recommendations, like breastfeeding exclusively for six months and introducing solid foods at six months, but there are other practical suggestions we might not be aware of. Let's learn together and give our little ones the best start in life. Remember, it's important to give them our full attention and maintain eye contact during feeding to strengthen the bond between us.

Following evidence-based feeding recommendations is crucial for the healthy growth and development of our children. Breast milk provides complete nutrition for the first six months and helps create a strong bond between parent and child. It's important to remember that most mothers can breastfeed, and seeking expert guidance can overcome any challenges. Please don't give up without consulting an expert.

Introducing solids at around six months is another important recommendation. This complements breastfeeding and helps meet the nutritional needs of growing infants. It exposes them to new tastes and textures, supporting their oral motor skill development. As parents and grandparents, we have the opportunity to provide a diverse and nourishing diet that sets the stage for healthy eating habits.

Promoting self-feeding is a valuable practice that fosters our child's development and independence, and it can start as early as nine months. Contrary to some misconceptions, self-feeding does not reduce the intake of nutritious food or increase the risk of choking when introduced appropriately and under supervision. In fact, it allows children to explore different textures and flavors, encouraging acceptance of a wide range of nutritious foods. Encouraging self-feeding provides numerous benefits, including fostering independence, enhancing fine motor skills, promoting a varied and nutritious diet, and establishing a positive mealtime experience for both child and parents.

During mealtime, it is important to create a happy and relaxed atmosphere. Trusting our children's natural hunger cues and avoiding pressuring them to eat beyond their needs is crucial. As long as they are gaining weight, staying active, and appearing healthy, they are likely receiving sufficient nourishment. It is best to avoid engaging in battles over unfinished food and resisting the temptation to offer unhealthy options. By consistently offering food and allowing children to listen to their bodies, we can help them develop a healthy relationship with food. Less pressure during mealtime results in less stress for both parents/caregivers and children, which is beneficial for everyone involved.

When it comes to bottle feeding, it's worth noting that infants who are exclusively breastfed and have their mothers available do not typically require bottles. However, in certain situations where bottle feeding becomes necessary, it's important to be mindful of best practices. One practice to avoid is letting infants fall asleep with a bottle, especially if it contains milk or sugary liquids. Prolonged exposure to these liquids can increase the risk of tooth decay. Responsible bottle feeding techniques, such as holding the infant during feeding and avoiding propping the bottle, are important to ensure their safety and oral health. As the children reach one year of age, it is advisable to transition them away from bottle feeding and introduce a cup. This promotes their oral and overall development, as well as independence.

Remember, every child is unique. If you're unsure, seek help. Consulting healthcare professionals for personalized advice is always recommended. Resources like the UNICEF Parenting website provide evidence-based guidance on feeding practices, child development, health, and building nurturing relationships, which can make the learning process easier.

Let's embark on these feeding adventures together, filled with love and laughter, and create a nurturing environment where our little ones can thrive and grow into healthy individuals. This knowledge can also help us spread the word and guide others who may have misconceptions or misinformation.

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