7TH ASIA DENGUE SUMMIT 2024

Towards Zero Dengue Deaths: Innovation, Collaboration, Action in Asia

5th – 7th June 2024
DoubleTree by Hilton Kuala Lumpur, Malaysia

4th June 2024 Pre-Summit Workshop

Programme Book

Co-convenors:

ADVA Asia Dengue Voice & Action Group

Fondation Mérieux

gdac Global Dengue+Aedes-Transmitted Diseases Consortium

SEAMEO TROPMED Network – Tropical Medicine and Public Health Network

The International Society for Neglected Tropical Diseases

Co-convenor:

Dengue Prevention Advocacy Malaysia

Lead by:

Persatuan Pediatrik Malaysia – Malaysian Paediatric Association

Malaysian Society of Infection Control & Infectious Diseases

Malaysian Society of Infectious Diseases & Chemotherapy

Persatuan Pakar Perubatan Keluarga Malaysia

In collaboration with:

MSPTM Malaysian Society of Parasitology & Tropical Medicine

mma Malaysian Medical Association

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Long term protection (exploratory analysis)[1]

- **61.2% overall vaccine efficacy against VCD** up to 4.5 years after the second dose (95% CI: 56.0, 65.8) (exploratory analysis)[1]
- **84.1% overall vaccine efficacy against hospitalized dengue** up to 4.5 years after the second dose (95% CI: 77.8, 88.6) (exploratory analysis)[1]

Generally well tolerated[1,2]

- No important safety risks observed up to 4.5 years following second dose[1,2]
- No evidence of an increase in disease severity in seronegative patients[1,2]
- No pretesting of serostatus required[1,2]
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1. Qdenga® Package Insert (Product License Numbers: MAL24026010ACZ and MAL24026009ACZ) approved by National Pharmaceutical Regulatory Agency, Malaysia, February 2024. 2. Tricou V, Folschweiller N, Lloyd E, Rauscher M, Biswal S. Efficacy and safety of Takeda's tetravalent dengue vaccine candidate (TAK-003) after 4.5 years of follow-up. Takeda; 2022.

*Incidence of cases: 0.5% Qdenga® vs 2.4% placebo.
†VCD=virologically confirmed dengue.
‡Incidence of cases: 0.1% Qdenga® vs 1.0% placebo.

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Healthcare professionals are asked to report AEFIs to Takeda PV at AE.VMAPS@takeda.com or by scanning the QR code on the right as soon as you become aware of the event.

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For non-Malaysian healthcare professionals, please refer to your country's approved Qdenga® prescribing information.

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WELCOME MESSAGE

Dear Friends and Colleagues,

On behalf of the Asia Dengue Summit Organising Committee, we are pleased to welcome you to the 7th Asia Dengue Summit to be held from 4th – 7th June 2024 in Malaysia. This summit follows the previous six held in Bangkok (2016), Manila (2017), Kuala Lumpur (2018), Jakarta (2019), Singapore (2022) and Bangkok (2023).

Dengue is no more a Southeast Asian or Asian issue. It has become a global issue such that the World Health Organization (WHO) sees it fit to name it as one of the ten threats to global health in 2019. WHO has also set targets for member states to try and achieve by 2030. This ADS is a good forum for policy makers to network and learn how other countries are trying to achieve these goals.

New advances in vector control, modeling methods as well new dengue vaccines will open up new strategies to achieve these goals. Strengthening our early detection and appropriate clinical management will reduce the case fatality rates, thus achieving one arm of the goals. The scientific committee is working to bring to you cutting edge information and latest data on everything related to dengue infection.

Other than the scientific content, I hope that you will avail yourself of the hospitality and excitement of the capital city of Malaysia. The venue is not far from the iconic Petronas Twin Towers, and is connected to a shopping mall that should help to ease the tension from three days of deliberations.

Stay safe & warm regards,

Zulkifli Ismail
Chairman, Organising Committee
7th Asia Dengue Summit 2024

ABOUT US

The Asia Dengue Voice & Action Group (ADVA) was officially set up in 2013 with a mission to identify opportunities to make practical recommendations in dengue-related areas such as improving surveillance and laboratory capacity for dengue disease confirmation with other relevant dengue initiatives, including V2V (vaccine to vaccination) and the Dengue Vaccine Initiative.
ADVA advocates for a collaborative approach to sharing surveillance data and relevant information to ensure the success of dengue prevention through vaccination across regions. ADVA also reinforces the importance of a united front against dengue, and presents a collaborative model for joint effort in the region to prevent the disease through the introduction and implementation of dengue vaccination.
The group has formulated recommendations with an ultimate aim of translating the science of dengue vaccination into messages for policy makers, general public and health care workers.

The Global Dengue & *Aedes*-Transmitted Diseases Consortium (GDAC) is a consortium composed of the Partnership for Dengue Control (PDC), the International Vaccine Institute (IVI), the International Vaccine Access Center (IVAC) at the Johns Hopkins Bloomberg School of Public Health and the Sabin Vaccine Institute. The World Health Organization advises and collaborates with GDAC.

The Southeast Asian Ministers of Education Organization (SEAMEO) is a regional intergovernmental organization established in 1965 among governments of Southeast Asian countries to promote regional cooperation in education, science and culture in the region.

Fondation Mérieux's mission is to fight the infectious diseases that affect vulnerable populations in developing countries, especially mothers and children, by building local capacities. They work in over 20 countries worldwide, in regions prone to infectious outbreaks, and mount their own projects, working closely with local and international partners.

The ISNTD is an independent organisation providing a multidisciplinary global platform to an international network of individuals working in the fields of Neglected Tropical Diseases, diseases of poverty and global development. The aim of the ISNTD is to focus on and highlight the research and programmes of colleagues and organisations worldwide, to ultimately have an impact on the health and prosperity of the world's poorest and most vulnerable, while sharing the goal of reaching sustainable healthcare provision & poverty reduction in the developing world.
The ISNTD believes that this goal cannot be achieved without strengthening the ties between all the parties already involved in NTD alleviation and addressing the socio-ecological and socio-political context of NTDs, in order to achieve not only the cure but also the prevention of NTDs with true and sustainable local leadership.

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ABOUT US

Dengue Prevention Advocacy Malaysia

Dengue Prevention Advocacy Malaysia (DPAM) is Malaysia's first independent dengue prevention advocacy group, jointly established by eight professional bodies and non-governmental organisations (NGOs), alongside several esteemed medical experts with a keen interest in dengue.

DPAM was officially launched on 21st June 2023, in conjunction with the ASEAN Dengue Day. The group is led by the Malaysian Paediatric Association (MPA), Malaysian Society of Infection Control and Infectious Diseases (MyICID), Malaysian Society of Infectious Diseases and Chemotherapy (MSIDC), and Malaysian Public Health Physicians Association (PPPKAM), in collaboration with the Malaysian Society of Parasitology and Tropical Medicine (MSPTM), Malaysian Medical Association (MMA), Asia-Pacific Academic Consortium for Public Health Kuala Lumpur (APACPH-KL), and Rotary International District 3300.

DPAM aspires to synergise efforts by various stakeholders in assisting the Ministry of Health (MoH) Malaysia to achieve its national and global dengue targets through the strengthening of dengue prevention, control and management initiatives in Malaysia. These objectives encompass an annual 5% reduction in dengue cases, maintaining a case fatality rate (CFR) below 0.2% by 2026, and ultimately reducing the CFR to 0% by 2030, aligning with the World Health Organisation's (WHO) target.

DPAM's scope of interest is comprehensive, covering epidemiology, integrated vector management, environment, patient care, laboratory, and vaccines. The group intends to contribute through healthcare professional education & communication, public education & communication, local research, guideline recommendations, as well as policy recommendations. As highlighted in DPAM Resolution Paper, which was released during the group's launch, DPAM will emphasise its efforts on the following key strategies:

Empowering healthcare professionals through educational activities
Rallying the support of relevant stakeholders to conduct consistent and sustainable public education and awareness initiatives
Engaging relevant stakeholders to advocate for adequate financial allocation on key activities such as vector control and research
Conducting dengue-related research in collaboration with other stakeholders
Assisting/supporting MoH in the development or revision of guidelines
Dissemination of research findings through media to mobilise whole-of-society action against dengue.

For any enquiries or further information please contact us at secretariat@dpam.org.my.

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ABOUT US

Tropical Medicine and Infectious Disease (ISSN 2414-6366) publishes authoritative and original articles, critical and systematic reviews, editorials, perspectives, short communications, commentaries, book reviews, letters to the editor and Special Issues on all aspects of tropical medicine and infectious disease. Our aim is to encourage scientists to publish their experimental and theoretical results in as much detail as possible. There is no restriction on the length of the papers. The full experimental details must be provided so that the results can be reproduced. There is, in addition, a unique feature of this journal:

We accept studies showing meaningful but negative results. While there are many journals that focus on tropical medicine and infectious disease studies, none of them actively accept negative results. As a result, most negative data do not end up in the public domain, even if the data were meaningfully negative and the study was well-designed. By accepting such negative results, our journal encourages scientists to share these data, so that they will not need to repeat experiments that somebody else has already done.

The scope of the journal includes, but is not limited to:
• Clinical tropical medicine
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• Tropical infectious diseases
• Parasitology and entomology
• Bacteriology, mycology and virology
• Epidemiological and social science studies
• Chemotherapy and pharmacology
• Immunology
• Disease prevention, control and elimination
• Emerging and re-emerging infectious diseases
• Emerging public health threats
• Global health and One Health

Website: https://www.mdpi.com/journal/tropicalmed

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COMMITTEE

Local Organising Committee:

Professor Datuk Zulkifli Ismail
Professor Ooi Eng Eong
Professor Sharifah Faridah
Dr Koh Kar Chai
Dr Ravindran Thayan
Dr Giri Rajahram
Professor Lucy Lum
Dr Abdul Jabir Jaafar
Dr Jenarun Jelip
Dr Mohd. Rahim Sulong
Dr Wan Ming Keong
Dr David Ng Chun-Ern

Asia Dengue Voice & Action Group (ADVA)
Steering Committee:

Professor Zulkifli Ismail
Professor Usa Thisyakorn
Professor Sri Rezeki Hadinegoro
Associate Prof Daniel YT Goh
Dr Maria Rosario Capeding
Professor Terapong Tantawichien
Emertius Professor Sutee Yoksan

Asia Dengue Voice & Action Group (ADVA)
International Advisors:

Professor Duane Gubler
Professor Tikki Pangestu
Professor Ooi Eng Eong
Emertius Professor Lulu Bravo
Professor Pratap Singhasivanon
Dr Valentina Picot

AGENDA

Wednesday 4th June 2024 – Pre-Summit Workshop

Dengue Vaccination: Bridging Research, Policy and Advocacy for Global Impact

TIME	PROGRAMME	SPEAKERS
1400 – 1410	**Opening address** Dengue in Asia and Malaysia	Zulkifli Ismail
1410 – 1430	**Complexity of Protective Immunity to Dengue**	Ooi Eng Eong
1430 – 1450	**Protection and Pathogenesis in Dengue – The Two Faces of NS1**	Paul Young
1450 – 1510	**Immunological Insights from the Development of TAK-003**	Setoh Yin Xiang
1510 – 1520	**Q&A part 1** Moderator: Azrul Mohd Khalib Panellists: Ooi Eng Eong, Paul Young and Setoh Yin Xiang	
1520 – 1535	**Break**	
1535 – 1555	**TAK-003 Vaccination – Efficacy and Safety in Endemic Countries**	Walid Kandeil
1555 – 1615	**SAGE Recommendation on Dengue Vaccination**	Punnee Pitisuttithum
1615 – 1635	**Dengue Vaccination at a National Level**	Julio Croda
1635 – 1645	**Q&A part 2** Moderator: Azrul Mohd Khalib Panellists: Walid Kandeil, Punnee Pitisuttithum and Julio Croda	
1645 – 1700	**Break**	
1700 – 1755	**Panel Discussion** **Vaccine to Vaccination: Evidence-informed Decision Making and Multisectoral Partnerships for Effective Public Health Policy and Communication Strategy** Moderator: Azrul Mohd Khalib Panellists: Tikki Pangestu, Lokman Hakim Sulaiman, Ooi Eng Eong, Julio Croda and Zulkifli Ismail	
1755 – 1800	**Summary and conclusion**	Azrul Mohd Khalib

AGENDA

Day 1 - Wednesday 5th June 2024

TIME	PROGRAMME	SPEAKERS
0730 – 0900	**Registration**	
0900 – 0930	**Welcome Speech & Opening Ceremony** **Guest of Honor's Speech**	Zulkifli Ismail YB Dato Lukanisman Bin Awang Sauni *Deputy Minister of Health, Malaysia*
0930 – 1000	**Tea Break & Guest of Honor's Tour of Exhibition** **Press Conference**	
1000 – 1115	**Symposium 1: Dengue in Asia** Moderator: Lucy Lum	Adi Utarini Husnina Binte Ibrahim Frances Edillo Basu Dev Pandey
1115 – 1145	**Going Global** ISNTD Video Moderator: Zulkifli Ismail	Zulkifli Ismail Marianne Comparet Katie Anders
	Industry Symposium: Takeda Pharmaceuticals	
1145 – 1150	**Introduction**	Zulkifli Ismail
1150 – 1210	**Dengue Pathogenesis: Antibody-dependent Enhancement, Viral and Host Factors Revisited**	Ooi Eng Eong
1210 – 1230	**Beyond the Bite – Mastering Dengue and Severe Dengue Management**	Chow Ting Soo
1230 – 1250	**Complexity of Developing Dengue Vaccines**	Walid Kandeil
1250 – 1300	**Q&A** Moderator: Zulkifli Ismail	Panellists: Chow Ting Soo Ooi Eng Eong Walid Kandeil
1300 – 1305	**Symposium Closing Remarks** Innovate and Illuminate for dengue, Immunise4Life!	Zulkifli Ismail
1305 – 1400	**Lunch and Posters**	
1400 – 1430	**Keynote** Moderator: Rosario Capeding	Jeremy Farrar
1430 – 1600	**Symposium 2: Emerging Trends** Moderator: Paul Young	Henrik Salje Do Kien Quoc Balvinder Singh Gill Natthawut Ploryngam Saubhagya Danasekara
1600 – 1630	**Tea Break & Posters**	
1630 – 1730	**Symposium 3:** **Insights from Human Infection Studies** Moderator: Ooi Eng Eong	Adam Waickman Panisadee Avirutnan Shirin Kalimuddin
Close of Day 1		

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Day 2 - Thursday 6th June 2024

TIME	PROGRAMME	SPEAKERS
0730 – 0820	**Registration**	
0820 – 0830	**Welcome Back**	Ooi Eng Eong
0830 – 0945	**Symposium 4: Pathogenesis and Immunity I** Moderator: Shirin Kalimuddin	Leah Katzelnick Shirit Einav Nattachai Srisawat Diana Hansen
0945 – 1015	**Tea Break & Posters**	
1015 – 1130	**Symposium 5: Pathogenesis and Immunity II** Moderator: Adam Waickman	Nguyen Lam Vuong Chan Kuan Rong Adriana Zamora Enny Nugraheni David Ng
1130 – 1245	**Symposium 6: Ward Round** Moderator: Jenny Low	Giri Rajahram Lucy Lum Somia Iqtadar Chia Po Ying
1245 – 1345	**Lunch & Posters**	
1345 – 1500	**Symposium 7: Dengue Vaccines 1** Moderator: Tikki Pangestu	Walid Kandeil Louis Macareo Anavaj Sakuntabhai Chao Day-yu
1500 – 1630	**Tea Break & Posters**	
1630 – 1730	**Symposium 8: Dengue Vaccines 2** Moderator: Wan Ming Keong	Michelle Ylade Salisu Garba Amirah Azzeri Chirayus Khawasang
Close of Day 2		

AGENDA

Day 3 - Friday 7th June 2024

TIME	PROGRAMME	SPEAKERS
0800 – 0820	**Registration**	
0820 – 0830	**Welcome Back**	Zulkifli Ismail
0830 – 0945	**Symposium 9: From Vector Biology to Dengue Prevention** Moderator: Katie Anders	Gong Cheng Ng Lee Ching Ami Fazlin Syed Mohamed Eggi Arguni
0945 – 1015	**Tea Break & Posters**	
1015 – 1130	**Symposium 10: Antivirals** Moderator: Ami Fazlin Syed Mohamed	Paul Young Ruobing Li Bhagwat Gunale Napon Nilchan
1130 – 1245	**Symposium 11: Antivirals and Host-directed Therapeutics** Moderator: Pratap Singhasivanon	Sophie Yacoub Steven Lim Sazaly Abu Bakar Isabela Ribeiro
1245 – 1345	**Lunch & Posters**	
1345 – 1500	**ADVA: *NexGen* - Community Participation & Educational Project** **Asia Dengue Voice and Action Group / Junior Achievement** **Dengue Slayers Challenge Grand Final**	
1500 – 1530	**Tea Break & Posters**	
1530 – 1645	**Symposium 12: From Theory to Reality** Moderator: Koh Kar Chai	Lay-Mint Yoshida Martin Hibberd Irish Lobitana Ong Hang Cheng Lee Siew Wah Judith Wong
1645 – 1745	**Symposium 13: Roadmap to Zero Dengue Deaths** Moderator: Tikki Pangestu	Eggi Arguni Rosario Capeding Michael Macdonald Panisadee Avirutnan Suresh Kumar
1745 – 1800	**Prize Presentation for ADVA/JA Dengue Slayers Challenge** **Closing of Summit**	

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ORGANISING COMMITTEE

PROF. ZULKIFLI ISMAIL

Clinical Professor,
KPJ Healthcare University College,
Malaysia

Prof. Zulkifli Ismail is a consultant paediatrician and paediatric cardiologist at a private hospital and Clinical Professor at the KPJ Healthcare University College. He was formerly a professor of paediatrics and paediatric cardiology in the Universiti Kebangsaan Malaysia (UKM). Dr. Ismail has served as the head of the paediatric department and the director of Hospital Universiti Kebangsaan Malaysia (HUKM) as well as the medical director of its private wing, UKM Specialist Centre.

Prof. Zulkifli also served as a past president of the Malaysian Paediatric Association (MPA) and is currently the editor of Berita MPA, a quarterly newsletter publication distributed to fellow members of the Association. He chairs the Positive Parenting Management Committee (www.mypositiveparenting.org) and serves as the chief editor of the Positive Parenting Guide, a quarterly publication aimed to equip Malaysian parents with reliable and practical local information on maternal, child and family care since 2002. He is the Technical Chairman of Immunise4Life (www.ifl.my), a vaccination advocacy programme of the Ministry of Health Malaysia.

Prof. Zulkifli is currently the president of the Asia Pacific Paediatric Association (APPA) and current chairman of the Asian Strategic Alliance for Pneumococcal disease prevention (ASAP). He also serves as a board member of the National Population and Family Development Board (LPPKN), a member of the Ministry of Health Unrelated Transplant Approval Committee (UTAC) and in the editorial board of the Malaysian Journal of Paediatrics & Child Health (MJPCH). He has also served as a reviewer for the Medical Journal of Malaysia and the Philippines Paediatric Infectious Disease Journal.

Prof. Zulkifli has more than 35 publications in peer-reviewed international and local journals in addition to numerous abstracts and articles for the lay-public on various issues involving child health, paediatrics and vaccinology. He has authored or co-authored two books for parents, one for medical students and one for nurses. In 2008, he was conferred the Darjah Panglima Mahkota Wilayah by the Malaysian King that carries the honorific title of ‘Datuk’.

ORGANISING COMMITTEE

PROF. OOI ENG EONG

Duke-NUS Medical School

Prof. Ooi trained in medicine at the University of Nottingham and conducted his doctoral studies on molecular epidemiology at the National University of Singapore. He has been working in the field of dengue for 20 years and his research interest spans dengue epidemiology to molecular pathogenesis of arboviral diseases. His laboratory interfaces clinical studies with virology and immunology to address research questions. He has published in journals such as The Lancet, Science and Nature Medicine. He is a three-time recipient of the Clinician-Scientist (Senior Investigator) Award by the National Medical Research Council of Singapore.

DR. SHARIFAH FARIDAH SYED OMAR

MBChB (Manchester) MMED (UM)

Associate Professor in Medicine and Infectious Diseases
Department of Medicine, Faculty of Medicine,
University Malaya

Head of Unit and Consultant in Infectious Diseases
Department of Medicine
University Malaya Medical Centre

Dr Sharifah Faridah Binti Syed Omar is an Associate Professor at the UM Specialist Centre (UMSC). She is specialized in Infectious diseases and in Internal Medicine. Her clinical interests are Infection, Bacterial Infections, and HIV vaccines. Dr Sharifah is the Vice President of the Malaysian Society of HIV Medicine (MASHM) and has published numerous articles in peer reviewed journals.

ORGANISING COMMITTEE

DR. KOH KAR CHAI

President, Manipal Alumni Association Malaysia
Vice Chair, Confederation of Medical Associations, Asia and Oceania
Treasurer, Commonwealth Medical Association.

Dr Koh Kar Chai is the Past President of the Malaysian Medical Association, the current President of the Manipal Alumni Association Malaysia, Vice Chair of the Confederation of Medical Associations in Asia and Oceania, and the Treasurer of the Commonwealth Medical Association.

He is also a Member and Public Education & Advocacy Lead of Dengue Prevention Advocacy Malaysia (DPAM).

Having graduated from Kasturba Medical College, Mangalore University in 1991, he is now practising as a General Practitioner in Kuala Lumpur and regularly mentors medical students in the field of primary care medicine from various universities.

An active member of the Malaysian Medical Association for almost 2 decades, he has been involved in many policy discussions and decisions on healthcare issues and has served on various healthcare related authorities and bodies both within and without the Ministry of Health, Malaysia as well as the Malaysian Medical Council.

Dr Koh also served as a member of the Malaysian Health White Paper Advisory Council and is a known advocate for equal access to quality, safe and affordable healthcare for all.

DR. RAVINDRAN THAYAN

Molecular Virologist

Current Position: Free lancing Consultancy on Infectious Diseases

Former Position: Head of Infectious Diseases Research Centre, Institute for Medical Research, Ministry of Health Malaysia, Director of WHO National Influenza Centre, Institute for Medical Research, Advisor of Institutional Biosafety and Biosecurity Committee IMR, Committee member of MOH Research Panels, Committee member of MOSTI Research Panels, Committee member of MOH Laboratory SOPs, Algorithm of testing for many viral diseases, MOH Dengue CPG for Adults and Children. Published in many peer reviewed journals as presented in many conferences.

ORGANISING COMMITTEE

DR. GIRI RAJAHRAM

Infectious Diseases Consultant

Head, Department of Medicine,
Queen Elizabeth II Hospital,
Kota Kinabalu, Malaysia.

Dr Giri Rajahram has worked in Sabah in various capacities for over a decade. Beginning as a junior doctor, he went on to complete his Membership of the Royal College of Physicians United Kingdom and a Diploma in Tropical Medicine and Hygiene at the Liverpool School of Tropical Medicine and Hygiene. He is an Infectious Diseases Consultant and is the Head,

Department of Medicine at Queen Elizabeth II Hospital, Kota Kinabalu. He has been involved in collaborative research in examining the epidemiological trends and the clinical aspects of managing *Plasmodium knowlesi* malaria, focusing on improving clinical recognition, patient care and treatment outcomes. This research has informed policy of national and international malaria treatment guidelines. The Australian government awarded him an Endeavour Executive Leadership Award for this work.

Besides clinical duties and research involvement, he has a keen interest in teaching and regularly assists doctors in preparing for medical examinations, including postgraduate membership exams. In the future, he hopes to establish more collaborative scientific and clinical research to address local knowledge-gap and assist in capacity building. He is convinced this helps improve individual patient care and improves community outcomes.

Dr Giri was recently awarded an Oxford-Hoffmann-Keble College scholarship and completed his graduate studies, MSc in International Health at the University of Oxford.

ORGANISING COMMITTEE

PROF. LUCY LUM CHAI SEE

Senior Consultant, Department of Paediatrics,
University of Malaya Medical Center, Kuala Lumpur

Honorary Professor, Department of Paediatrics, Faculty of Medicine,
University of Malaya, Kuala Lumpur

Lucy Lum is a pediatrician with 30 years of experience in dengue management and pediatric intensive care. She collaborated with clinicians in Southeast Asia and Latin America in developing the 2009 revised dengue case classification, evaluation, and clinical research.

Serving as a WHO temporary advisor in dengue outbreak areas in Laos PDR and the Solomon Islands she, together with local healthcare workers, adapted the clinical case management to the minimally resourced environment. In 2012 she was commissioned by WHO Department of Control of Neglected Tropical Diseases to develop a handbook on clinical management of dengue. The Western Pacific Regional Office in 2013, invited her to coordinate the development of a training package in dengue case management, in line with the WHO 2009 Dengue Guidelines. This package serves as the principal training material for the Western Pacific region and Africa.

Before her retirement, she started a second career to promote child health and early childhood nutrition and development focusing on the first 1000 days when the foundation for life-long health is laid. Her collaboration with NGOs in community out-reach programs aims to improve nutrition among young children of urban poor families. Her dream is to live the circular economy with a carbon-neutral footprint where every child can realize his best potential.

DR. MOHD. RAHIM SULONG

Affiliate

Dr. Mohd Rahim Sulong is a Public Health Medicine Specialist who has made significant contributions to public health research and publications especially on communicable diseases. He obtained his medical degree (MD) from Universiti Sains Malaysia in 2000 and later completed his Master of Community Medicine (M.Comm.Med) from the same university in 2009. Currently, he serves as the Head of the Dengue Unit at the Vector Borne Diseases Sector, Disease Control Division under the Ministry of Health Malaysia.

ORGANISING COMMITTEE

DR. WAN MING KEONG

Public Health Physician,
Vector Borne Disease Sector (VBDS), Disease Control Division,
Ministry of Health Malaysia

Dr. Wan Ming Keong currently works as Public Health Physician at the Vector Borne Disease Sector (VBDS), Disease Control Division, Ministry of Health Malaysia. He joined the National Dengue Prevention and Control Program under VBDS in 2020 after serving 1 year of district health service in Hulu Langat, Selangor. He has worked on vector borne disease management since 2013 before pursuing his postgraduate study in public health. He completed his degree in Doctor of Public Health (DrPH) in 2019. His current responsibilities include epidemiological surveillance of dengue, coordination of dengue case management, training and research at the national level. He has been one of the editorial board members for Malaysia's National Strategic Plan for Dengue Prevention and Control 2022-2026.

DR. DAVID NG CHUN-ERN

Pediatric Infectious Disease Specialist

Dr David Ng is a pediatric infectious disease specialist currently serving in Hospital Tuanku Ja'afar Seremban. Completed his fellowship in pediatric infectious disease in Mahidol University, Thailand. His research interests are centered on COVID-19 and a variety of tropical infectious diseases such as dengue, chikungunya and Japanese encephalitis. Beyond his clinical and research pursuits, he is a highly regarded speaker at various local and international medical congresses. He also serves on several key committees related to infectious diseases within the Ministry of Health Malaysia, contributing to policy-making and strategic direction at a national level.

SPEAKERS' BIOGRAPHIES

YB DATO LUKANISMAN BIN AWANG SAUNI

Deputy Minister of Health, Malaysia

Dato Lukanisman, a politician from Malaysia, who as the Sibuti constituency's Member of Parliament since May 2018. Additionally, he serves on the Parliamentary Standing Committee for Health, Science, and Innovation and the Public Accounts Committee (PAC).

Dato Lukanisman is dedicated to making Malaysia's sustainable energy plan a national priority and to making renewable energy a way of life.

Experience:

- **Deputy Minister of Health, Malaysia (Present)**
- **Chairman, Sustainable Energy Development Authority (SEDA) Malaysia (2019-2022)**
- **Parliamentary Information Officer, Special Affairs Department (JASA) (2006 – 2018)**
- **Member of Parliament for Sibuti, Malaysian Parliament (2018 – Present)**
- **Special Assistant, Office of the Member Parliament of Sibuti (2008 – 2018)**

SPEAKERS' BIOGRAPHIES

PROF. ADI UTARINI

Public Health Researcher, Disease Control of Dengue Fever

Professor of Public Health,
Department of Health and Policy Management,
Gadjah Mada University, Yogyakarta.

Formerly the Vice Dean for Research, community service and collaboration at the Faculty of Medicine, Universitas Gadjah Mada (2012-2016), she has been active in strengthening institutional programs to improve research atmosphere and international journal publications. Ranked 311 best Indonesian researchers in all subjects published by Webometrics 2017, she has published her work in more than 25 international health journals. Her research focuses on dengue control, public private mix in Tuberculosis control, malaria control and strengthening quality of care.

She is also currently the Project Leader for Eliminate Dengue Project-Yogyakarta (2013-2019), a project applying Wolbachia Aedes Aegypti intervention to reduce dengue cases in Yogyakarta, funded by the Tahija Foundation, Indonesia. This project (currently introduced as the World Mosquito Program) is a multi-country project coordinated globally by Monash University, Australia. She provides the overall leadership in all aspects of planning and implementation of the research as well as stakeholder engagement with key national and provincial level stakeholders. She completed her Masters degree at the Institute of Child Health, London UK and continued her PhD at the Department of Public Health and Epidemiology, Umea University Sweden.

DR. HUSNINA BINTE IBRAHIM

Deputy Director,
Communicable Disease Control Division,
Ministry of Health Malaysia

Dr. Husnina Binti Ibrahim is a public health physician with extensive experience in the field of infectious diseases. She holds a Master of Community Health (Epidemiology & Biostatistics) from Universiti Kebangsaan Malaysia, which she completed in 2004. Dr. Husnina is currently the Deputy Director of the Communicable Disease Control Division at the Ministry of Health Malaysia, where she is involved in the management and control of infectious diseases.

SPEAKERS' BIOGRAPHIES

DR. FRANCES E. EDILLO

Vector Biology and Genetics,
Biology Department,
University of San Carlos,
Cebu city, Philippines

Dr. Frances E. Edillo is a tenured full-professor in Vector Biology and Genetics from the Biology Department of the University of San Carlos, Cebu city, Philippines. Apart from teaching at the tertiary and graduate levels, she has been leading the Mosquito Research Laboratory in her university. Majority of her group's work aims to understand higher-level phenomena applicable to issues of vector biology, population genetics, public health related to mosquito-borne diseases, and related policies shared with the Department of Health. Hence, she has been contributing to the global efforts in fighting the health and economic burden of dengue and other mosquito-borne diseases. Recently, she has expanded to collaborating on 3D printing project using bone, muscle and pancreatic tissues.

Dr. Edillo was a Monbusho scholar in obtaining her masteral degree in Biology from Toyama University, Toyama, Japan and a Fulbright scholar in getting her PhD in Biology at the University of California at Los Angeles, California, USA. She did her 3.5-year post-doctoral fellowship at Harvard School of Public Health, Boston, Massachusetts, USA. After which, she returned to her alma mater, the University of San Carlos, Cebu city, Philippines. She has collaborated with Brandeis and Yale Universities in the USA and with Institut Pasteur in Paris, France, among others. She was recently one of the recipients of the prestigious Australia Award Fellowship at Queensland University of Technology, Brisbane, Australia in November 2023.

MARIANNE COMPARET

Co-Founder & Director
The International Society for Neglected Tropical Diseases

Dr Katie Anders is a public health researcher and the Director of Impact Assessment at the not-for-profit World Mosquito Program (WMP), based at Monash University where she is also an adjunct Senior Research Fellow in the School of Public Health and Preventive Medicine. She has >15 years experience in epidemiological research and public health practice, with expertise in the design and implementation of field trials, disease surveillance, and clinical research. At WMP, Katie collaborates with partners in 14 countries in Asia-Pacific and the Americas to evaluate the effectiveness, durability, cost-effectiveness and scalability of WMP's Wolbachia mosquito replacement method for control of dengue and other Aedes-borne viruses. She previously worked at the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam, where her research was focussed on the epidemiology of dengue and other viral infections in young children, and prior to that in infectious disease surveillance at the (former) UK Health Protection Agency in London. Katie undertook her doctoral studies through the School of Public Health and Preventive Medicine at Monash University (completed 2015) and a Masters in Control of Infectious Disease at the London School of Hygiene and Tropical Medicine (2005-6).

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DR. KATIE ANDERS

MSc PhD

Director,
Impact Assessment | World Mosquito Program

Dr Katie Anders is a public health researcher and the Director of Impact Assessment at the not-for-profit World Mosquito Program (WMP), based at Monash University where she is also an adjunct Senior Research Fellow in the School of Public Health and Preventive Medicine. She has >15 years experience in epidemiological research and public health practice, with expertise in the design and implementation of field trials, disease surveillance, and clinical research. At WMP, Katie collaborates with partners in 14 countries in Asia-Pacific and the Americas to evaluate the effectiveness, durability, cost-effectiveness and scalability of WMP's Wolbachia mosquito replacement method for control of dengue and other Aedes-borne viruses. She previously worked at the Oxford University Clinical Research Unit in Ho Chi Minh City, Vietnam, where her research was focussed on the epidemiology of dengue and other viral infections in young children, and prior to that in infectious disease surveillance at the (former) UK Health Protection Agency in London. Katie undertook her doctoral studies through the School of Public Health and Preventive Medicine at Monash University (completed 2015) and a Masters in Control of Infectious Disease at the London School of Hygiene and Tropical Medicine (2005-6).

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DR. MARIA ROSARIO Z. CAPEDING

Pediatric Infectious Disease Specialist, Clinician, Researcher Scientist

Head, Medical Research Unit,
Tropical Disease Foundation, Inc

Consultant, Infectious Diseases
Asian Hospital and Medical Center
Philippines

Dr. Capeding is a pediatrician, an infectious disease specialist, and a clinical microbiologist of the Research Institute for Tropical Medicine, Philippines. She is the Head of the Department of Microbiology, Consultant of the Medical Department, and Head of the Dengue Study Group of the said institute. She is the Section Head of Infectious Diseases of the Department of Pediatrics, Asian Hospital and Medical Center, Philippines.

She has engaged in significant researches on the safety, immunogenicity and efficacy of childhood vaccines: Haemophilus influenzae type b, Pneumococcal and Meningococcal Conjugate; Influenza; Hepatitis A; Hepatitis B; DtaP-Hib-IPV-HepB combination vaccine; Typhoid Conjugate; Cholera; Japanese Encephalitis, and Dengue.

She is an accomplished medical researcher though her contributions: 54 original articles and reviews in peer reviewed international and local journals; presented scientific papers in 77 international medical conferences; acted as an expert or member of advisory board to 31 international consultative meetings; and 47 completed and current researches and clinical trials. She is an active member of national and international professional medical societies and global, regional scientific fora. She is also a frequent lecturer to numerous conventions of medical societies, postgraduate courses and local chapter meetings.

Dr. Capeding is an awardee of the 23rd Dr. Jose P. Rizal Memorial Award for Research by the Philippine Medical Association (PMA). She was given the distinction as one of the world's Top Women in Biotech Industry 2014. The paper, Clinical Efficacy and Safety of a Novel Tetravalent Vaccine in Healthy Children in Asia: Phase 3, Randomized, Observer-Masked, Placebo-Controlled Trial, Maria Rosario Capeding, Ngoc Huu Tran, Sri Rezeki, et. al. (The Lancet, 2014. 384:1358-1365 was adjudged Paper of the Year 2014 by the International Society for Vaccines (ISV). She is a recipient of the 2015 Outstanding Professional of the Year Award in the Field of Medicine and Eric Nubla Excellence Award given by the Philippine Professional Regulation Commission.

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DR. JEREMY FARRAR

Chief Scientist
World Health Organisation (WHO)

As Chief Scientist, Jeremy Farrar oversees the work of the Science Division, bringing together experts and networks working in science and innovation from around the world to guide, develop and deliver high quality health policies and services to the people who need them most.

Prior to joining WHO, Dr Farrar was Director of the Wellcome Trust. In his 9 years there, he oversaw a series of major reforms, restructuring and growth, with Wellcome now collaborating with partners around the world and focused on fundamental discovery research and three challenge areas of: infectious diseases; climate and health; and mental health, all with a commitment to ensuring that equity, diversity and inclusion are central to the science they support.

Before joining Wellcome, Dr Farrar spent over 17 years as Director of the Clinical Research Unit at the Hospital for Tropical Diseases in Ho Chi Minh City in Viet Nam. His clinical and research interests have been in integrated health research across a range of infectious diseases and noncommunicable illness including emerging infections, influenza, infections of the brain, dengue, typhoid, malaria, tuberculosis, antimicrobial resistance, opportunistic infections related to HIV and stroke. Dr Farrar was the founding chair of WHO's R&D Blueprint and the founding director of the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC) that led on to the work of the RECOVERY Trial and the UK COVID-19 Genomics UK Consortium.

Dr Farrar trained in neurology and infectious diseases in London, Edinburgh and Oxford in the United Kingdom and in Melbourne in Australia. He has a PhD in Immunology from the University of Oxford in the United Kingdom in partnership with the University of California in San Francisco in the United States of America.

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PROF. PAUL YOUNG

B.Sc (Hons), PhD (London), FAHMS, FASM

Paul Young is Professor of Virology, currently seconded to Research Development in the Deputy Vice-Chancellor's Office of Research and Innovation at The University of Queensland, Brisbane, Australia. He gained his PhD from the London School of Hygiene & Tropical Medicine and joined the University of Queensland in 1991. His research aims to understand the molecular basis of virus induced disease, develop new and improved diagnostics as well as vaccine and therapeutic control strategies for a range of viral pathogens of both human and animal origin.

He began his research work on the dengue viruses almost 4 decades ago and developed a particular focus on the NS1 protein. His group was the first to identify NS1 and a diagnostic biomarker and went on to commercialise its use as a global standard for early dengue diagnosis. His group has published numerous papers on the structure and function of NS1, highlighting roles in virus replication, as a viral toxin, as a vaccine immunogen, as the target of therapeutics and as a circulating biomarker for diagnostics.

Prof Young is President-elect of the International Union of Microbiological Societies and has been the President of the Australian Society for Microbiology (2012-2014), the Australasian Virology Society (2001-2011) and the Asia-Pacific Society for Medical Virology (2012-2015).

PROF. HENRIK SALJE

Professor,
Disease Ecology,
University of Cambridge

Henrik Salje is the Professor of Disease Ecology at the University of Cambridge. The focus of Henrik Salje's research is on answering applied public health related questions, especially with regards to the spread of infectious pathogens. This research program sits at the interface of mathematical modelling, genetics, population biology, big data, public health and field-based epidemiology. By integrating the knowledge base and expertise available from these different fields, he seeks to generate a more complete understanding of the different drivers of disease transmission and optimize our chances of controlling spread. He has degrees from Oxford, Johns Hopkins and Sorbonne Universities.

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KIEN QUOC DO

Pasteur Institute,
Ho Chi Minh City

Kien Quoc Do has been working at Pasteur Institute in Ho Chi Minh City (PI) since 2005. From 2005 to 2012, he had great opportunities to obtain valuable experience in dealing with various outbreaks and epidemics in the South of Vietnam for instance Highly Pathogenic Avian Influenza (HPAI), Influenza Pandemic A(H1N1) 2009, Hand – Foot – Mouth disease (HFMD) and cholera.

He moved to the National Program for Dengue prevention and control in 2012 to pursue his desirable objectives of controlling Dengue since the first day he had come to PI. In addition to routine activities of surveillance and epidemic response, PI has also provided him with a motivating research environment so that he could serve as investigator, research coordinator of many great studies from epidemiological studies to vaccine trials such as: Dengue vaccine trial, EV71 vaccine trial, studies to identify epidemiological features and disease dynamics of Dengue, HFMD, Severe Acute Respiratory Infection and Acute Encephalitis Syndrome. Additionally, he involved actively with many striking outbreak investigations and response of Highly Pathogenic Avian Influenza (HPAI), *Inf A/H1N1pdm, Cholerae*, acute diarrhea, Dengue, HFMD. He was the first to set up and develop the HFMD surveillance system in the South of Vietnam which contributes significantly to the routine activities of HFMD response and EV71 vaccine trial. He was also the founder and paves critical initial steps for the surveillance system of severe viral pneumoniae (SVP), severe acute respiratory infection (SARI), acute encephalitis syndrome (AES) and the one who integrated Zika and Chikungunya into Dengue surveillance system.

He firmly believes that his academic knowledge obtained from studies could be applied in routine activities to serve for the supreme objective of Dengue and other communicable diseases prevention and control and vice versa his practical experience in field work will provide him with comprehensive knowledge in conducting and referring research career.

SPEAKERS' BIOGRAPHIES

DR. BALVINDER SINGH GILL

MBBS, MPH, M. Inf. Dis, PHD, AM

Consultant Public Health Specialist
Head of Special Resource Centre
Institute for Medical Research
National Institutes of Health
Ministry of Health Malaysia

Dr Balvinder Singh Gill, a Consultant Public Health Medicine Specialist who currently Heads the Special Resource Centre at the Institute for Medical Research, Ministry of Health Malaysia.

Graduated with a Medical degree in 1994, Masters in Public Health in 2002 and Masters of Infectious Diseases in 2008 under the Directorship of Professor Barry Marshall, Nobel Prize Laureate in Medicine at The Marshall Centre for Infectious Diseases, University of Western Australia. Dr Balvinder then completed a PhD study in 2012 characterizing the factors contributing to the dengue epidemic in Malaysia. The PhD study examined by Professor Duane J. Gubler, was key to the implementation of NS1 testing for the National Dengue Surveillance Program in Malaysia.

Dr Balvinder headed the formation of the COVID-19 modelling team at the National Institutes of Health, Ministry of Health Malaysia which was credited for forecasting the COVID-19 pandemic trends in Malaysia. In addition, Dr Balvinder spearheaded the development of the Information and Documentation Sector which serves as the center for informatics, data management and repository for the Disease Control Division, Ministry of Health Malaysia. He serves as a consultant epidemiologist for WHO-TDR on Dengue Early Warning Response Systems and The National Environmental Health Action Plan (NEHAP).

ASST. PROF. ADAM WAICKMAN

Department of Microbiology and Immunology
Upstate Medical University

Dr. Adam Waickman, PhD is an Assistant Professor in the Department of Microbiology and Immunology and Laboratory Director at the Institute for Global Health and Translational Sciences at SUNY Upstate Medical University in Syracuse, NY. He received his PhD from the Johns Hopkins University School of Medicine in Baltimore, MD, and performed his postdoctoral training at the National Institutes of Health (NIH) and the Walter Reed Army Institute of Research (WRAIR). His group at SUNY Upstate is dedicated to understanding how the interactions between infectious organisms and the human immune system result in pathogenesis and/or durable immunity. His work is primarily focused on viral pathogens – such as dengue, Zika, and SARS-CoV-2 - and leverages "next generation" technologies such as single cell RNA sequencing, multi-parametric flow cytometry, and computational modeling.

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DR. PANISADEE AVIRUTNAN

M.D., Ph.D.

Head, Division of Dengue Hemorrhagic Fever Research &
Siriraj Center of Research Excellence in Dengue and
Emerging Pathogens,
Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok 10700, THAILAND
Email: panisadee.avi@mahidol.edu

Panisadee Avirutnan joined the MD/PhD scholar program of Mahidol University and China Medical Board in 1988. She received Ph.D. (Microbiology) degree in 1998 and Doctor of Medicine (M.D.) degree in 2001 from Mahidol University. She later became a postdoctoral fellow at Washington University in St. Louis, USA between 2006-2011, working on Flavivirus and complement biology. After that she worked for Faculty of Medicine Siriraj Hospital, Mahidol University and was promoted to an Associate Professor in 2013. In 2010, she was appointed Head of Dengue Hemorrhagic Fever Research Division and became a Director of Siriraj Center of Research Excellence in Dengue & Emerging Pathogens in 2019. She oversee clinical cohorts of patients with dengue in three major city hospitals in Thailand. Her research interests are to find specific dengue therapeutics using drug repositioning strategies, to understand molecular mechanisms responsible for protective and pathogenic functions of dengue virus nonstructural protein NS1, to interrogate the mechanism by which the virus evades and exploits the complement system to spread the infection and to search for biomarkers for predicting the development of DHF, the serious clinical syndrome that can be life-threatening.

DR. SHIRIN KALIMUDDIN

Senior consultant,
Department of Infectious Diseases, Singapore General Hospital

Dr. Shirin Kalimuddin is a senior consultant with the Department of Infectious Diseases at the Singapore General Hospital, and a faculty member of the Program in Emerging Infectious Diseases at Duke-NUS Medical School. Her research is directed towards understanding the host response to viral infection, and developing better vaccines and therapeutics for infectious diseases. Most recently, her work has centered on the role of T cell immunity in flaviviral infection and vaccination.

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DR. LEAH KATZELNICK

Ph.D., MPH

Chief, Viral Epidemiology and Immunity Unit
National Institute of Allergy and Infectious Diseases

Dr. Leah Katzelnick pursued a Ph.D. studying antigenic variation among dengue viruses at the University of Cambridge and the National Institutes of Health as an NIH OxCam Scholar and Gates Cambridge Scholar. After receiving her Ph.D. in 2016, she conducted her postdoctoral work at the University of California, Berkeley and University of Florida on determinants of dengue and Zika disease, spending a year in Ecuador and Nicaragua to work closely with research teams conducting longitudinal cohort studies. In September of 2020, Leah became an Earl Stadtman tenure-track investigator and NIH Distinguished Scholar in the Laboratory of Infectious Diseases in NIAID. She is Chief of the Viral Epidemiology and Immunity Unit.

SHIRIT EINAV

Physician-scientist,
Department of Medicine (Division of Infectious Diseases),
Department of Microbiology and Immunology,
Stanford University School of Medicine.

Shirit Einav is a physician-scientist in the Department of Medicine (Division of Infectious Diseases) and the Department of Microbiology and Immunology at Stanford University School of Medicine. After obtaining her MD, Shirit pursued Residency in Internal Medicine at Harvard University (Beth Israel Deaconess Medical Center) followed by fellowship in Infectious Diseases at Stanford University. She joined the faculty at Stanford in 2011. Her basic research program focuses on understanding the roles of virus-host interactions in viral infection and disease pathogenesis. This program is combined with translational efforts to apply this knowledge for the development of broad-spectrum host-centered antiviral approaches to combat emerging viral infections and means to predict their progression to severe illnesses. Shirit is an Investigator at the Chan Zuckerberg Biohub in San Francisco and a Fellow of the Infectious Diseases Society of America (FIDSA).

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PROF. NATTACHAI SRISAWAT

M.D., Ph.D.

Consultant, Clinical Instructor,
Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Dr. Nattachai Srisawat joined the Division of Nephrology, Department of Medicine at Chulalongkorn University in 2011 and is currently working as a clinical instructor. He is actively involved in several centers at Chulalongkorn University (Critical Care Nephrology Research Unit, Tropical Medicine Cluster), King Chulalongkorn Memorial Hospital (Excellence Center for Critical Care Nephrology) and Royal Society of Thailand (Associate Fellow, Academy of Science) in Thailand. He is an active member and having an active association with different professional societies and academies both regional and international level such as be a steering committee of Kidney Disease Improving Global Outcome, AKI controversies conference in Italy. His current research interests involve in tropical infectious disease especially dengue, leptospirosis, Critical Care Nephrology. He has published his contributions and works in national and international text books including reputed professional journals. He also works as an Associate Editor for Nephrology journal and Subject Editor for BMC Nephrology.

DR. NGUYEN LAM VUONG

Lecturer,
Department of Medical Statistics and Informatics (UMP HCMC)

Postdoctoral Researcher,
Biostatistics group at the OUCRU HCMC

Dr. Nguyen Lam Vuong is a medical doctor and researcher with a passion for applying biostatistics to medical research, particularly regarding dengue disease.

Dr. Vuong began his medical career at the University of Medicine and Pharmacy at Ho Chi Minh City (UMP HCMC), graduating with his Doctor of Medicine degree in 2010. He further specialized in the field, completing his residency in Cardiovascular and Thoracic Surgery in 2014 at the same university.

In 2014, Dr. Vuong transitioned to a research career, leveraging his medical expertise in the Department of Medical Statistics and Informatics at the Faculty of Public Health, UMP HCMC. Since 2017, he has focused his research efforts on dengue at the Oxford University Clinical Research Unit, Ho Chi Minh City (OUCRU HCMC).

Dr. Vuong's research journey at OUCRU HCMC began as a Research Assistant (2017-2020). He then pursued a PhD in the Biostatistics group, successfully defending his dissertation titled "Biomarkers, Plasma Viremia, and Clinical Outcomes in Dengue" in February 2024.

Currently, Dr. Vuong holds a dual appointment as a lecturer at the Department of Medical Statistics and Informatics (UMP HCMC) and a postdoctoral researcher in the Biostatistics group at the OUCRU HCMC.

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PROF. JENNY LOW

Senior Consultant,
Department of Infectious Diseases,
Singapore General Hospital

Professor,
Emerging Infectious Diseases Programme,
Duke NUS Medical School

Dr Jenny Low is a senior consultant with the Department of Infectious Diseases in Singapore General Hospital and Professor at the Emerging Infectious Diseases Programme at Duke NUS Medical School. Concurrently, she is the co-director of the Viral Research and Experimental Medicine Centre@ SingHealth Duke-NUS (ViREMiCS) in the SingHealth Duke NUS AMC and deputy clinical and scientific director at the SingHealth Investigational Medicine Unit (IMU). Dr Low has been doing clinical research for more than 20 years. She has a long track record in conducting proof of concept and early phase clinical trials in acute viral diseases. She has tested several first-in-human therapeutics and biologics in humans including a therapeutic anti-yellow fever virus antibody that was published in the *New England Journal of Medicine* in 2020. During the COVID-19 pandemic, among her contributions, she led a clinical study that was among the first to detail the host response to severe COVID-19 which was published in Cell Host & Microbe in 2020. She also led the COVID-19 self-amplifying mRNA vaccine trial that was co-developed by Duke-NUS and Arcturus therapeutics among others. The vaccine is currently licensed for use in Vietnam and Japanese. Her current research focus is on early phase adaptive clinical trials of viral therapeutics and vaccine development as well as understanding the role of the early immune responses in modulating the outcome of infection or vaccination.

ASSOC. PROF SOMIA IQTADAR

BSc,MBBS,FCPS,FRCP(London),FPSIM (Pak)

King Edward Medical University
Lahore, Pakistan

She received her bachelor's degree in sciences in 2001 and completed her bachelor's in medicine & surgery in 2004 from her country's top medical institution, King Edward Medical University where she's serving as Associate Professor in Department of Medicine. Prof. Somia completed her post graduation in internal medicine in 2010 and became fellow of College of Physicians and Surgeons Pakistan and was also awarded FRCP from Royal College of Physicians London in 2021 . She is also trained at Asian Institute of Technology Thailand, Sri Lanka and WHO Singapore in Dengue fever and is currently working as a Master Trainer of Dengue Fever for the government of Punjab, and for WHO for the Asia Pacific. She has served in the capacity of Secretary and later Chairperson of Dengue Expert Advisory Group (DEAG),Pakistan which provides national guidelines on clinical management of Dengue infection and imparts training to doctors and paramedical staff and advises policy makers on Dengue Control .She has more than 50 publications to her name and is author of three books. She is the primary author of Guidelines on Dengue and Pregnancy and COVID-19 for Govt of Pakistan. Prof Somia has also contributed chapters on Dengue in Kumar and Clark and McMaster textbook of Medicine. She is the Secretary General of Pakistan Society of Internal Medicine and recipient of Governors award in year 2021 for her contribution to the field of Medicine.

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DR. CHIA PO YING

MBBS, MMed (Int. Med.), MRCP(UK), FAMS

Infectious Disease Consultant
National Centre for Infectious Diseases,
Tan Tock Seng Hospital

Dr Chia Po Ying graduated from the Yong Loo Lin School of Medicine at the National University of Singapore. She completed her MRCP (UK), Masters in Internal Medicine, specialist training in adult Infectious Diseases as well as her PhD in adult dengue pathogenesis.

Dr Chia is currently an Infectious Disease Consultant at the National Centre for Infectious Diseases and Tan Tock Seng Hospital as well as the dengue champion and arboviral research lead. She is also an assistant professor at Lee Kong Chian School of Medicine NTU and Head of the National Centre of Infectious Diseases Research Office.

PROF. TIKKI PANGESTU

Visiting Professor,
Lee Kuan Yew School of Public Policy,
National University of Singapore,
Singapore

Prof. Pang joined the Lee Kuan Yew (LKY) School of Public Policy after 13 years at the World Health Organisation (WHO) in Geneva, Switzerland as Director of its Research Policy & Cooperation department. In this capacity he worked with countries to strengthen their national health research systems, developed mechanisms and initiatives to improve the efficiency and transparency of global health research, and helped formulate an Organisation-wide research policy.

Prior to his WHO career, Prof. Pang was the Professor of Biomedical Sciences at the Institute of Postgraduate Studies & Research, and Associate Professor/Lecturer at the Faculty of Medicine, the University of Malaya, Kuala Lumpur. He was previously Co-Director of the WHO Collaborating Centre for Dengue & Dengue Haemorrhagic Fever at the University of Malaya, Kuala Lumpur, Malaysia (1982-1995), and a member of the WHO Technical Advisory Group which developed the guideline Dengue Haemorrhagic Fever: Diagnosis, Treatment and Control (1986).

Prof. Pang's main research and academic interests lie in the area of infectious diseases, the impact of genomics on public health, global health governance, national health research systems, knowledge translation, research transparency and accountability, and the use of evidence in health policy development. In these areas, he has published more than 200 scientific articles and 12 books, edited volumes and reports, which includes several major WHO reports, including Genomics and World Health (2002), the World Report on Knowledge for Better Health (2004) and a History of Research in WHO (2010). Prof. Pang's involvement with the LKY School of Public Policy began in 2009 through the ST Lee Project on Global Health Governance.

Prof. Pang is a Fellow of the Royal College of Pathologists (UK), American Academy of Microbiology (USA), Institute of Biology (UK) and the Academy of Medicine of Malaysia. He was the Founding Editor of Health Research Policy & Systems and the Asia-Pacific Journal of Molecular Biology and Biotechnology.

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WALID KANDEIL, MD

Head Global Medical Affairs, Dengue
Vaccine Business Unit, Takeda

Before embarking on a career focused on vaccine development and public health, Walid served as a general practitioner. His growing passion for turning vaccines into practical vaccination strategies led him to his current role as the global medical lead for the dengue program at Takeda's vaccine business unit. With nearly two decades of experience in the vaccine industry, Walid has held positions at prominent companies such as Takeda, AstraZeneca, and GSK. Throughout his career, he has significantly contributed to developing research protocols and has authored numerous publications. Additionally, Walid has delivered many presentations at international conferences, covering a broad spectrum of vaccine-related topics including COVID-19, influenza, pertussis, maternal immunization, human papillomavirus, conjugate pneumococcal vaccines, rotavirus gastroenteritis, meningococcal vaccines, and dengue.

DR. LOUIS MACAREO

MD, JD, MPH

Executive Director, New Products Vaccines Lead

Louis Macareo is currently the EDMA for new products in Global Medical & Scientific Affairs. Louis is an internal medicine physician, attorney and clinical pharmacologist originally from Wilkes-Barre, Pennsylvania. Louis completed his undergraduate degrees in psychology and Arab and Islamic studies at Villanova University. He attended law school at the Catholic University of America and completed his medical degree and a Master of Public Health at Tulane University in New Orleans.

Louis served in the U.S. Army since 1985, first in the artillery and subsequently, for 21 years on active duty as a physician. Louis has been assigned to several locations in the continental United States as well as Egypt, Italy, Kenya, Iraq, and Thailand and has conducted advanced phase drug and vaccine clinical trials and disease surveillance throughout Asia and Africa. His most recent position prior to coming to Merck was as the Chief of the Department of Virology at the Armed Forces Research Institute of Medical Science (AFRIMS), in Bangkok, Thailand where he supervised the conduct of two phase III dengue vaccine clinical trials and conducted arboviral and respiratory disease surveillance studies in a dozen Asian countries as well as the validation of several arboviral and respiratory diagnostic devices.

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PROF. ANAVAJ SAKUNTABHAI

Head of Research Unit
Ecology and Emergence of Arthropod-borne Pathogens Unit,
Institut Pasteur

Representative and Executive Director, Fondation Pasteur Japon, Japan

Anavaj Sakuntabhai, MD, D.Phil.- Professor at the Institut Pasteur, Paris, and Adjunct Professor at McGill Genome Center, McGill University, visiting professor at Kyoto University, the University of Tokyo and Nagasaki University After obtaining the D. Phil. From University of Oxford in 1999, he was appointed as a senior scientist of the Institut Pasteur in 2000 to develop a program on genetics of infectious diseases. He worked on the genetic susceptibility to malaria in populations living in malaria endemic areas in Africa and South-East Asia. He created a research unit of Functional Genetics of Infectious Diseases in 2010. The important project is genetic susceptibility to dengue infection. He proved that asymptomatic dengue infected individuals could transmit the virus to mosquito vector and responded to the virus using T cells, leading to a new concept of dengue and Zika vaccine development. He has significant experience in coordination of international programs, having been coordinator of European FP7 project on Dengue Framework for Resisting Epidemics in Europe (DENFREE). He was involved in investigating two recent global outbreaks, Ebola and Zika. Currently, he is a principal investigator of the Pasteur International Center for Research on Emerging Infectious Diseases (PICREID) supported by the NIH. The project is implemented in West, Central Africa and South-East Asia, linking large observational multicenter cohort studies with basic scientific research and leading to increased preparedness for new epidemic threats. Recently, he created a research unit on Ecology and Emergence of Arthropod-borne Pathogens at Institut Pasteur together with the French National Research Institute for Agriculture, Food and Environment (INRAe). He has been appointed by an executive director of Foundation Pasteur Japan.

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DR. GONG CHENG

Professor at School of Medicine,
Tsinghua University

Dr Cheng's studies focus on the molecular dissection of the mosquito-virus-host interphase, which intend to identify key factors involved in viral pathogenesis, transmission and immunity in mosquitoes/hosts, thus developing novel approaches to control these viral diseases spreading in nature. Multiple mosquito-borne flaviviruses are the pathogens of particular interest. Dr. Cheng has identified multiple key factors in both host blood and mosquito to determine the effectiveness of flavivirus acquisition from infected hosts to fed mosquitoes. Recently, his team demonstrated that mosquito-transmitted flaviviruses can manipulate host skin microbiota to produce a scent that attracts mosquitoes, thus facilitating flavivirus acquisition. Besides, Dr. Cheng's studies aim at understanding the molecular basis of flavivirus infection in mosquitoes and the viral transmission from infected mosquitoes to naïve hosts. Based on a series of findings in flaviviral lifecycle between hosts and mosquitoes, Dr. Cheng made another remarkable achievement to uncover that adaptive mutations in Zika virus (ZIKV) promote the rapid ZIKV transmission between hosts and mosquitoes. These pioneer works offer an insight into the emergence and re-emergence of flaviviruses in nature, thus providing an avenue for disease prevention. According to his original scientific findings and contributions to flavivirus studies, Dr. Cheng has been honored with many awards, such as the New Cornerstone Investigator Program in 2023, the First prize of Natural Science Award of MOE in 2023, the Science Xplore Award in 2022, the First prize of Natural Science Award of Beijing in 2020, the C.C. Tan Award for Life Sciences and Medicine in 2018, the National Science Fund for Distinguished Young Scholar in 2018, etc.

ASSOC. PROF. NG LEE CHING

Group Director,
Environmental Health Institute,
National Environment Agency

Associate Professor Ng Lee Ching is Group Director of National Environment Agency's Environmental Health Institute in Singapore and a WHO Collaborating Centre. She spent 20 years contributing to building laboratory capability for Singapore's public health and developing tools and strategies for mitigation of risks. Dr Ng is also associated with the Nanyang Technological University; serves as Advisor to WHO for dengue and chikungunya surveillance and control and is Director of the WHO Collaborating Centre for Reference and Research of Arbovirus and their Associated Vectors.

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DR. AMI FAZLIN SYED MOHAMED

Herbal Medicine Research Centre,
Institute for Medical Research,
National Institutes of Health (IMR@NIH),
Ministry of Health Malaysia

Ami Fazlin is the Head of Herbal Medicine Research Centre, Institute for Medical Research, NIH Malaysia. Her involvement in herbal research started in 2001 with evidence-based reviews for medicinal herbs and Traditional & Complementary Medicine. The specialization in Clinical Pharmacology and Pharmacometrics has honed her acuity in the design of herbal medicine research at both the preclinical (discovery, standardization, efficacy and toxicity studies) and clinical level. She is the Test Facility Manager for in vivo GLP Lab, IMR and served in the Preclinical and Clinical Cluster (MAFS), Medical Research Ethics Committee, Scientific Review Panel for Phase I study etc. She had published more than 25 articles in the international journals either as corresponding or co-author.

DR. EGGI ARGUNI

MD., MSc., PhD.

Pediatric Infectious Disease Consultant

Dr Eggi Arguni is a pediatrician, lecturer, and researcher at the Department of Child Health and the Center for Tropical Medicine, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada, Indonesia. At Dr. Sardjito General Hospital in Yogyakarta, she is a pediatrician at the Division of Infectious and Tropical Diseases.

Dr Eggi Arguni obtained her Doctor of Philosophy degree in molecular biology and immunology from the Graduate School of Medicine at Chiba University in Japan. Infectious and tropical diseases comprise the bulk of my research, particularly dengue, sepsis, infection control, HIV, and COVID-19 in pediatric patients.

One of her current research collaborations involves working with the World Mosquito Program in Yogyakarta (WMP Yogyakarta), which is an affiliate of WMP Global. They are conducting research to develop a complimentary technology for the dengue vector control through the utilization of a novel approach that employs the non-pathogenic bacterium Wolbachia.

SPEAKERS' BIOGRAPHIES

DR. RUOBING LI

Translational Medicine Expert
Medical lead – Dengue
Translational Medicine Development and Profiling, Biomedical Research, Novartis

Dr. Li joined Novartis as clinical trial lead in Jan 2008. She was trained as hepatologist in the hospital. In 2002, Dr. Li obtained her PhD on internal medicine at health Science center, Peking University, followed by a 2-year postdoctoral fellowship in Microbiology and Immunology department in University of Illinois at Chicago. For the past 16 years, she has been accumulated her experience of drug development with a focus on neglected diseases, malaria and dengue.

DR. BHAGWAT GUNALE

MBBS, MD (Pharmacology)

Life member of Indian Society for Clinical Research

Dr. Bhagwat Gunale is a seasoned professional with over 15 years of experience in the pharmaceutical industry, encompassing clinical research, pharmacovigilance, and medical affairs, alongside 3 years in academia. A life member of the Indian Society for Clinical Research, Dr. Gunale has been instrumental in developing clinical plans for drugs, biologics, and vaccines, including protocol writing and review, preparing clinical trial documents such as Investigator's brochures, clinical study reports, and statistical analysis plans. His expertise extends to medical monitoring, pharmacovigilance activities, and coordination with CROs, investigators, study sites, central laboratories, and collaborators. Dr. Gunale has made significant contributions to regulatory processes through presentations and responses to regulatory authority queries. With over 20 publications in peer-reviewed journals and numerous presentations at CMEs and conferences, his work is well-recognized in the field.

Dr. Gunale's professional journey includes key roles at prominent organizations. Since October 2011, he has been with Serum Institute of India Pvt. Ltd. Prior to that, he served at Glenmark Pharmaceuticals Ltd from January 2011 to September 2011, Emcure Pharmaceuticals Ltd, Pune from January 2009 to January 2011, and Cadila Pharmaceuticals Ltd, Ahmedabad from April 2008 to January 2009. His academic tenure was at Christian Medical College, Vellore, from March 2005 to March 2008.

Dr. Gunale's educational background is rooted in a strong foundation in pharmacology, with an M.D. in Pharmacology from Christian Medical College, Vellore (March 2005 to March 2008) and an MBBS from B. J. Medical College, Pune (August 1998 to December 2003), where he secured a distinction in pharmacology. His commitment to professional development is evident from his participation in various workshops and conferences on vaccine clinical development and pharmacovigilance, including COVID-19 vaccines. Notable certifications include the Vaccine Trials: Methods and Best Practices from Johns Hopkins University, USA, an Advanced Ethics and GCP Course at CMC, Vellore, and a Short Course on Fundamentals of Biostatistics & SPSS, also at CMC, Vellore.

SPEAKERS' BIOGRAPHIES

ASSOC. PROF. PRATAP SINGHASIVANON

Dean,
Faculty of Tropical Medicine,
Mahidol University,
Thailand

Dr. Pratap Singhasivanon is an Associate Professor in the Department of Tropical Hygiene. He obtained his medical degree from Kasturba Medical College, India, before receiving his postgraduate Diploma in Tropical Medicine and Hygiene from Mahidol University. He has a Master of Public Health degree from Harvard University and a Doctor of Public Health degree from the University of Michigan, USA.

Dr. Pratap Singhasivanon is an authority on the epidemiology of tropical diseases, vector-borne infectious diseases, and the application of geographic information system (GIS) in monitoring multi-drug resistant malaria. His primary research area is the epidemiology of malaria, but he has an interest in many other vector-borne diseases that affect populations in Southeast Asia. He often collaborates with medical doctors, specialists and researchers in international health agencies in medical research. Dr. Pratap has established several initiatives to improve the performance of all faculty staff, raising the international profile of the Faculty of Tropical Medicine around the world. He constantly works toward developing and implementing national health policies in Thailand and contributing to the improvement of regulations and planning in Thailand's public health system. Dr. Pratap regularly works closely with Thailand's Ministry of Public Health in both research and human-resource capacity-building and development.

ASSOC. PROF. SOPHIE YACOUB

Head of the Dengue Research Group,
Associate Professor,
Oxford University Clinical Research Unit
(OUCRU-Vietnam)

Sophie is the head of the Dengue Research Group and associate professor at the Oxford University Clinical Research Unit (OUCRU-Vietnam), part of the Centre for Tropical Medicine and Global Health, University of Oxford. She is a Wellcome Trust clinical career development fellow and a Physician in Infectious Diseases and General Medicine and holds an honorary Consultant appointment at London North West University Healthcare NHS Trust in the UK. She has a PhD from Imperial College London and an MSc from the London School of Hygiene and Tropical Medicine.

Sophie is currently leading a large translational programme of dengue research at OUCRU in Vietnam, focusing on pathogenesis studies, clinical trials and innovative technology centered on wearable devices, physiological monitoring and utilizing AI for clinical decision support systems. The overall aim of the group is to improve the management and clinical outcomes of patients with dengue on a national and global level.

SPEAKERS' BIOGRAPHIES

DR. STEVEN LIM CHEE LOON

MBBS (IMU), MRCP (UK)

Fellowship in Infectious Diseases
Ministry of Health, Malaysia

Dr Steven Lim is presently an Infectious Diseases Consultant at Raja Permaisuri Bainun Hospital, a major general hospital and referral centre in the state of Perak, Malaysia. He graduated from International Medical University (IMU) in 2006 and became a fellow of the Royal College of Physicians of London in 2012. He had spent most of his early career serving in Penang General Hospital before obtaining a fellowship in Infectious Diseases (ID) in 2018. He underwent his ID training in Sungai Buloh Hospital, the national centre for infectious diseases, and Alfred Hospital, a major transplant and trauma centre in Melbourne, Australia.

Dr Steven has extensive clinical experience. In addition to providing comprehensive care and treatment for patients, he regularly delivers teaching and training. His areas of interest include HIV, antimicrobial stewardship, Gram negative bacterial resistance and neglected tropical diseases. As an advocate of evidence-based medicine, he actively participates in ID-related clinical guidelines development and clinical research. He has led several clinical trials, notably the I-TECH Study, a pivotal trial that evaluated the efficacy and recommended against the use of ivermectin in the management of COVID-19. He has published peer-reviewed articles and contributed as invited reviewer for local and international medical journals.

Dr Steven serves on the executive committee of the Malaysian Society of Infection Control and Infectious Diseases (MyICID). He is currently a member of the clinical working group of Dengue Alliance, a global partnership between dengue-endemic countries and the DNDi (Drugs for Neglected Diseases initiative) with the primary goal to accelerate research and development for affordable and accessible therapeutics for dengue.

PROF. SAZALY BIN ABU BAKAR

Department of Medical Microbiology,
Faculty of Medicine,
University of Malaya,
Malaysia

Dr. Sazaly Abu Bakar is a professor and Director of the Tropical Infectious Diseases Research and Education Center (TIDREC) and WHO Collaborating Center for Arbovirus Research and Reference (Dengue Fever and Severe Dengue) at University of Malaya in Kuala Lumpur, Malaysia. He received his PhD and post-doctoral training in virology at the University of Texas Medical Branch, Galveston, Texas, USA.

Dr. Sazaly has been involved with dengue research for over 20 years and has also maintained strong research interest in emerging infectious diseases. His research interests include biorisk management, semiochemicals, traditional medicine and natural products (prostate cancer, lung cancer, trace metals, zinc, gene expression, eurycoma), bacteriology (infectious diseases, acinetobacter), and virology (arboviruses, emerging infectious diseases, antivirals, vaccines).

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DR. ISABELA RIBEIRO

Viral Diseases Cluster Director, DNDi

Dr Isabela Ribeiro joined DNDi as a Senior Project Manager in March 2007, after working as a consultant on DNDi projects since 2005. Previously Head of DNDi's Chagas Clinical Programme and Head of Dynamic Portfolio Unit, Dr Ribeiro is now Viral Diseases Cluster Director.

Dr Ribeiro has over fourteen years of drug development experience with a focus on neglected diseases, most recently serving as a consultant to the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (WHO-TDR).

With WHO-TDR, Dr Ribeiro contributed to several projects involving the management of large community-based clinical studies in endemic countries.

A member of the Scientific Advisory Committee of the PDTIS, Oswaldo Cruz Foundation, since 2005, Dr Ribeiro completed a post-doctoral fellowship in infectious diseases and an internal medicine residency at Ohio State University and worked as clinical research fellow based at the Communicable Disease Unit of St. George's Hospital, London, after earning her MD from the Federal University of Rio de Janeiro in Brazil.

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DR. MARTIN HIBBERD

BSc(Hons) PhD

Emerging Infectious Disease
Department of Pathogen Molecular Biology
London School Of Hygiene & Tropical Medicine

Dr Martin Hibberd BSc(Hons) PhD; is Professor of Emerging Infectious Diseases since 2012 and Head of the Department of Infection Biology (since 2022) at the London School of Hygiene and Tropical Medicine (LSHTM).

He has adjunct positions at University of the Philippines, Manila, in Human Genetics (at NIH) and the Genome Institute of Singapore (where he was previously associate director from 2003 to 2016). He also has a visiting position at the Philippine Genome Centre.

He graduated from Brunel University in 1985 in Applied Biology and received his Doctorate from King's College, London in 1994.

He has worked at UK public health agencies, Imperial College London and the Genome Institute of Singapore, before his current job at LSHTM.

He has a broad scientific background spanning both microbial and human determinants of infectious and inflammatory diseases. His current research interests utilize genomic applications to cover both pathogen and host aspects of infectious disease; together with integrating modelling and genomic approaches to understand transmission and outbreaks.

He has over 230 publications, in journals with an impact factor averaging 9, with more than 25,000 citations in total, and an h-index of 79.

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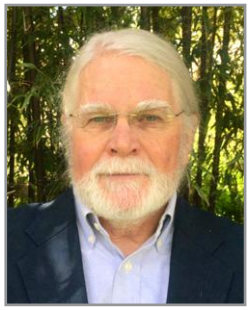

DR. MICHAEL MACDONALD Sc.D

Michael is a Public Health Entomologist, who has been working vector-borne disease control programs since 1977, starting as a Peace Corps Volunteer in the Sabah (E. Malaysia) Malaria Control Program. Dr. Macdonald went on to earn an Sc.D. from Johns Hopkins on research of malaria transmission in Punjab Pakistan and then lived in Burma, Thailand, Cambodia and Zambia with stints in the US and Geneva supporting vector control programs throughout Africa and Asia, working for Johns Hopkins and Boston Universities, USAID, NGOs and UN Organizations, including WFP, UNHCR and WHO.

Michael is currently a consultant with IVCC, the Innovative Vector Control Consortium, hosted by the Liverpool School of Tropical Medicine. IVCC is a Product Development Partnership, building partnerships to develop and deliver innovative vector control solutions that save lives. Since 2018, with support from Australia Aid, IVCC has been working in the Indo Pacific Region to create a toolbox of vector control products to address malaria and other mosquito-borne diseases in the region.

DR. SURESH KUMAR CHIDAMBARAM

Infectious Diseases
Prince Court Medical Centre

Dr. Suresh Kumar A/L Chidambaram is a medical doctor specializing in Internal Medicine (physician) and Infectious Diseases in Kuala Lumpur, Malaysia. He had graduated with an MRCP qualification from the Royal College of Physicians, UK.

He is currently practicing at Prince Court Medical Centre.

DELEGATES' ABSTRACTS

001 Potential public health impact of dengue vaccination with TAK-003 in Malaysia

A Azzeri [1,2], H Jaafar [1,2], R Ting [3], J Langer [4], M Dahlui [2,5]

1. Department of Primary Health Care, Faculty of Medicine and Health Sciences, Universiti Sains Islam Malaysia, Negeri Sembilan, Malaysia
2. Division of Health Research and Case-Mix, Department of Research Development and Innovation, University Malaya Medical Centre, Kuala Lumpur, Malaysia
3 Takeda Malaysia Sdn Bhd, Selangor, Malaysia
4 Takeda Pharmaceuticals International AG, Zürich, Switzerland
5 Centre of Population Health, Department of Social and Preventive Medicine, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Background:

Dengue, a vector-borne disease affecting all age groups, presents a significant health burden in Malaysia. Vaccination with the new dengue vaccine TAK-003 has demonstrated long-term safety and efficacy against symptomatic and hospitalised dengue cases, based on the TIDES study involving over 20,000 children and adolescents. This study aims to model the public health impact of implementing TAK-003 in the national vaccination programme in Malaysia.

Methods:

A static model with a dynamic component was developed. Various vaccination strategies, including routine and catch-up cohorts from ages 7 to 13, were simulated over time horizons ranging from 10 to 30 years to explore optimal cohorts from a public health perspective. Key outcomes assessed were infections and hospitalizations avoided and cost savings from both payer and societal perspectives, compared with no vaccination.

Results:

Our findings indicate substantial public health benefits across all explored vaccination strategies, with the most significant impact achieved through routine vaccination starting at age 7, resulting in a 32% reduction in infections and substantial cost savings over a 30-year period. The inclusion of a catch-up cohort (age 8-11 years) demonstrated an additional 3-4% reduction in infections and increased cost savings.

Conclusion:

Vaccination with TAK-003 in Malaysia offers a substantial reduction in symptomatic dengue cases and hospitalisations while proving to be cost-saving compared with no vaccination. Emphasising younger starting ages and inclusion of catch-up cohorts could maximise these benefits, highlighting the importance of achieving high vaccination coverage and effective program implementation.

002 Dengue Control by using community engagement and health literacy processes in Lua community (minority ethnic group), Bangkok, Thailand.

S. Saritsiri
The 67th Public Health Center, Health Department, Bangkok Metropolitan Administration, Thailand

Background:
The Lua people, a minority ethnic group native to Laos, settled community in Thaweewatthana district, Bangkok and ongoing Dengue outbreak.

Methods:
To investigate and control outbreaks by using community engagement and health literacy.

Results:
The Lua community had 10 rai with 55 households (400 residents), each 40 m2 house with 2 families (10 people). 14 cases, aged 6 to 47, were identified closely houses and communal activities. The first case was found on November 11, 2023, and the last case on January 22, 2024. Patients waited 5 days before seeking medical care, some having severe symptoms. OPD patients returned to crowded, unprotected homes. Mosquito nets were unused, homes remained open, larvae were found in water-filled containers. There was incidence of spraying smog at wrong house because same person's name and on working. The model in controlling COVID outbreaks in slums was used "Everyone in the community must be aware of the disease situation together and assess their risk, monitor yourself and family, and clean the environment". Engaging communities involve education in local languages, promoting health literacy, raising awareness (symptoms, transmission, prevention), and risk assessments. Community participation includes environmental stewardship targeting mosquito life cycle, youth volunteers to explore containers. Community-based house mapping to inform or use symbolic sticks to embroider the layout of houses in the community hall. Community measures were put in place if any house encountered larvae would be fined. The community has learned and ended outbreak.

Conclusion:
Community engagement and health literacy are important for Dengue control.

003 Timing of sample collection for DENV PCR in Kamphaeng Phet, Thailand

Pachcharaporn Thongmarong[1], Kanyarat Phutthasophit[1], Wallika Kulthongkam[1], Thitiman Kaewkao[2], Chinanat Puangsaijai[2], Surachai Kaewhiran[2], Chonticha Klungthong[1], Aaron R. Farmer[1], Darunee Buddhari[1]

1. Department of Virology, WRAIR-AFRIMS, Thailand
2. Kamphaeng Phet provincial hospital, Ministry of Public Health, Thailand

Abstract:

Dengue is a major public health concern in Thailand, including Kamphaeng Phet (KPP) province, an endemic location for dengue in a rural area of northern Thailand. The Department of Virology, WRAIR-AFRIMS has collaborated with Kamphaeng Phet provincial hospital (KPPH) for dengue surveillance program since year 1994. This retrospective study aimed to report the timing of sample collection from dengue clinical diagnosis for Dengue virus (DENV) detection by Polymerase Chain Reaction (PCR) technique in Kamphaeng Phet province during year 1994-2023. During the study period, we identified 18,558 acute febrile illnesses. Of those, 52.4% (9,719 samples) were DENV positive by PCR and 23.9% (3,046 samples) were PCR negative but positive by ELISA. For the PCR positive group, they were further classified as 17.7% (3,278 samples) DENV-1, 33.6% (2,955 samples) DENV-2, 45.2% (2,165 samples) DENV-3 and 52.4 % (1,321 samples) DENV-4. Regarding the timing of sample collection after symptom onset, we found the median of 1 day (IQR 1-4) in dengue positive group by PCR techniques compared to a median of 4 days (IQR 3-6) in dengue negative group ($p<0.001$). The overall sensitivity of DENV PCR testing was 52.4% however, the timing of collection revealed important factors in PCR detection since this PCR would be a useful diagnostic for early diagnosis of dengue viremia, which can be lead to appropriate and prompt management and control of the disease in endemic regions.

004 Increasing age of dengue cases in Rural Thailand from 1994-2023

Natthawut Ployngam[1], Kanyarat Phutthasophit[1], Wallika Kulthongkam[1], Thitiman Kaewkao[2], Chinanat Puangsaijai[2], Surachai Kaewhiran[2], Taweewun Hunsawong[1], Aaron R. Farmer[1], Darunee Buddhari[1]

1. Department of Virology, WRAIR-AFRIMS, Thailand,
2. Kamphaeng Phet provincial hospital, Ministry of Public Health, Thailand

Abstract:

Dengue is a major public health concern in Thailand, including Kamphaeng Phet (KPP) province an endemic area for dengue in rural area of northern Thailand. The Department of Virology, WRAIR-AFRIMS has collaborated with Kamphaeng Phet provincial hospital (KPPH) for dengue surveillance program since year 1994. This retrospective study aimed to report the age distribution changes during the last three decades. Investigators analyzed the febrile illness data and samples to identify dengue infection from 1994-2023. Dengue infection was determined by detection of dengue virus (DENV) of any serotype by polymerase chain reaction (PCR) or serological evidence of infection by enzyme-linked immunosorbent assay (ELISA). During the study period, we identified 18,558 acute febrile illnesses. Of those, 68.8% had confirmed dengue infection based on case criteria. The median age was 18 years (range from 0-98 years old). With the dengue confirmed group, there was an increase in age from 9.8 years (IQR 6-12) from 1994-2003 to 15.7 years (IQR 10-19) from 2004-2013 and 18.8 years (IQR 11-24) during year 2014-2023. This data reflects the overall change in population structure in KPP, and community development from a traditional rural to urban environment can affect the risk of transmission and disease burden in different populations potentially affecting prevention and control strategies. Overall, the impact of this change in risk population provides valuable information for the development and implementation of future prevention and control plans for dengue infection, as well as serving as a guideline for the development of dengue vaccine trials in KPP.

005 Integrated systems immunology approach identifies impaired effector T cell memory responses as a feature of progression to severe dengue fever

S. I. Studniberg[1], S. Suwarto[2], D. Denis[3], Y. Liao[1], W. Shi[1], A. L. Garnham[4], R. T. Sasmono[3] and D. S. Hansen[1]

1. Monash Biomedicine Discovery Institute, Department of Microbiology, Monash University, Clayton, Victoria, Australia.
2. Division of Tropical and Infectious Diseases, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo National Hospital (RSCM), Jakarta, Indonesia.
3. Eijkman Research Center for Molecular Biology, Jakarta, Indonesia.
4. The Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria, Australia.

Background:

Typical symptoms of uncomplicated dengue (DF) include fever, headache, muscle pains, rash cough, and vomiting. A proportion of cases progress to severe dengue haemorrhagic fever (DHF), associated with vascular permeability, thrombocytopenia, and haemorrhages. Progression to DHF is difficult to diagnose at the onset of fever, which complicates patient triage, posing a socio-economic burden on health systems.

Methods:

To identify parameters associated with protection and susceptibility to DHF, we pursued a systems immunology approach integrating plasma chemokine profiling, high-dimensional mass cytometry and peripheral blood mononuclear cell (PBMC) transcriptomic analysis at the onset of fever in a prospective study conducted in Indonesia.

Results:

After a secondary infection, progression to uncomplicated dengue featured transcriptional profiles with increased cell proliferation and metabolism, and an expansion of ICOS+CD4+ and CD8+ effector memory T cells. These responses were virtually absent in cases progressing to severe DHF, that instead mounted an innate-like response, characterised by inflammatory transcriptional profiles, high circulating levels of inflammatory chemokines and with high frequencies of CD4+ non-classical monocytes predicting increased risk of severe disease.

Conclusions:

Our results suggests that effector T cell memory plays an important role ameliorating severe disease symptoms during secondary dengue and in its absence, a strong innate response is required to control infection. We also provide proof of concept for the potential of system biology approaches to identify discrete populations in the blood predicting reduced or increased risk of DHF to inform vaccine development and to develop diagnostic tools for detection of complicated cases at point of care.

006 Sensitivity and Specificity Evaluation of the Standard M10 Point-of-Care RT-PCR on Archived Dengue Samples from Indonesian Population

MS Santoso[1], D Denis[1], B Rana[1], ME Adiniko[1], L Trianty[2], R Noviyanti[2], RT Sasmono[2]

1. EXEINS Health Initiative, Indonesia
2. Eijkman Research Center for Molecular Biology, Indonesia

Background:

Dengue is a mosquito-borne viral infection with a high global disease burden. The PCR test for dengue usually requires advanced laboratory facilities and specialized storage conditions. The SD Biosensor Standard M10 DENV 1-4 is a multiplex real-time RT-PCR test using an all-in-one cartridge for both extraction and amplification, designed for use in point-of-care settings. This study aims to evaluate its performance on well-characterized archived samples from an Indonesian population.

Methods:

The dengue-positive panel consists of 144 samples confirmed for dengue using CDC RT-PCR dengue serotyping, IgM ELISA and/or whole genome sequencing. The dengue-negative panel consists of 149 samples from febrile samples and healthy volunteers confirmed negative using CDC RT-PCR, NS1 RDT, and IgM ELISA. All samples were tested using Standard M10 DENV 1-4 according to manufacturers' instructions.

Results:

The overall sensitivity and specificity of Standard M10 DENV 1-4 are 91% and 100% respectively. The sensitivities for each serotype are 100%, 96%, 98%, and 62% for DENV-1, DENV-2, DENV-3, and DENV-4, respectively. Post-study improvements on the cartridge done by the manufacturer resulted in improved sensitivity for DENV-4 to 93%. Sensitivity was higher in primary infections at 95%, compared to secondary infections at 88%. The Standard M10 and CDC RT-PCR method has an overall agreement of 91%.

Conclusion:

The SD Biosensor Standard M10 DEN 1-4 is a comparably sensitive, convenient, and easy to use test that has potential to be implemented at point-of-care settings. However, sensitivity varies in different contexts such as immunologic status and infecting DENV serotype.

007 Epitope resurfacing and enhance lipid bilayer interaction on dengue virus-like particle vaccine preparation

DY Chao[1], SR Wu[2], JK Marzinek[3], VR Palur[3]

1. Graduate Institute of Microbiology and Public Health, College of Veterinary Medicine, National Chung Hsing University, Taichung City, Taiwan
2. Department of Dentistry & Institute of Oral Medicine, National Cheng Kung University, Tainan, Taiwan
3. Bioinformatics Institute (A*STAR), Singapore

Background:

Virus-like particles (VLPs) containing dengue virus prM/E proteins have been demonstrated to be a potential vaccine candidate; however, the structure of dengue VLP and how the helix domain of prM/E protein interact with the lipid bilayer are poorly understood.

Methods:

Herein VLP derived from DENV serotype-2 were engineered becoming highly matured (mD2VLP) by modulating the furin cleavage site. The VLPs secreted from transfected COS-1 cells were subjected to (1) cryoEM for 3D construction; (2) lipidomics analysis and molecular dynamic simulation; (3) secretion level analysis; (4) immunogenicity analysis by immunizing the mice.

Results:

mD2VLP showed variable size distribution with diameter of ~31 nm forming the major population under cryo-electron microscopy examination. Furthermore, mD2VLP particles of 31 nm diameter possess a T = 1 icosahedral symmetry with a groove located within the E-protein dimers near the 2-fold vertices that exposed highly overlapping, cryptic neutralizing epitopes. Mice vaccinated with mD2VLP generated higher cross-reactive (CR) neutralization antibodies (NtAbs) and were fully protected against all 4 serotypes of DENV. Through lipidomics and coarse grain modeling analysis, the optimal mutations on helix region to enhance mD2VLP secretion and stability are identified.

Conclusion:

Our results highlight the potential of 'epitope-resurfaced' mature-form D2VLPs and lipid-interacting mutation in inducing quaternary structure-recognizing broad CR NtAbs and enhance VLP secretion to guide future dengue vaccine design.

008 Molecular and Entomological Characterization of the 2023 Dengue Outbreak in Dhading, Central Nepal

Basu Dev Pandey[1],Sandesh Rimal[2], Sabin Shrestha[2], Sunita Wagle Poudel[3], Govinda Bhandari[3], Merveille Kapandji[1], Yuki Takamatsu[1], Ishan Gautam[4], Stefan Fernandez[5], Takeshi Urano[6], Mya Myat Ngwe Tun[1,6], Shyam Prakash Dumre[2], Kouichi Morita[1]

1. Institute of Tropical Medicine, DEJIMA Infectious Disease Research Alliance, Nagasaki University, Nagasaki 852-8523, Japan.
2. Central Department of Microbiology, Tribhuvan University, Kathmandu 44601, Nepal
3. Dhading Hospital, Dhading Besi, Dhading 45100, Nepal
4. Natural History Museum, Tribhuvan University, Swayambhu, Kathmandu 44620, Nepal
5. Armed Forces Research Institute of Medical Sciences, Bangkok 10400, Thailand
6. Center for Vaccines and Therapeutic, Shimane University, Izumo 690-8504, Japan

Background:

Nepal was considered dengue-free until 2004. Since then, sporadic cases have been observed every year, with periodic outbreaks occurring, notably in 2019 and 2022. These outbreaks expanded across all seven provinces and 77 districts with all four serotypes reported. Nepal faced another large outbreak in 2023 after the record-highest number of dengue cases in 2022. However, the dengue virus (DENV) characteristics and vector density in the outbreak area remain poorly understood.

Methods:

Blood samples were collected from dengue-suspected patients In Dhading Hospital in central Nepal and underwent clinical and laboratory evaluations. Initial screening involved 396 samples using (NS1 antigen/IgM/IgG) combo test assay. Randomly selected DENV samples underwent serotyping using RT-PCR. Entomological studies were conducted in the Nilkantha municipality, an area significantly impacted by dengue.

Results:

Out of 396 samples, 278 (70.2%) had confirmed DENV infection. Multiple serotypes (DENV-1, -2, -3) were detected. DENV-2 (97.5%) re-emerged after six years in Dhading while DENV-3 was identified for the first time. Dengue inpatients had a significantly higher frequency of anorexia, myalgia, rash, diarrhoea, nausea, vomiting, abdominal pain, and thrombocytopenia ($p < 0.05$). In this area, *Aedes* mosquitoes largely predominated (90.7%) with the majority of *A. aegypti* (60.7%). We also found high *Aedes* index (20.0%) and container index (16.7%). We confirmed multiple DENV serotype circulation with serotype re-emergence new serotype introduction, and high vector density in 2023.

Conclusion:

These findings call for urgent initiation and scaling up of DENV molecular surveillance in human and mosquito populations for dengue control and prevention in Nepal.

009 A retrospective analysis of Intravenous Fluid Therapy Practice at Hospital Admission for Adults with Dengue

Yvonne MF Chia[1]; James WJ Kang[1]; Felicia CY Lea[1]; Eng Eong Ooi[2,3]; Jenny G Low[1,2,3]

1. Department of Infectious Diseases, Singapore General Hospital
2. Programme in Emerging Infectious Diseases, Duke-NUS Medical School
3. Viral Research and Experimental Medicine Centre @SingHealth/Duke-NUS (ViREMiCS)

Background:

Dengue epidemics in Asia was almost exclusively a childhood disease but is now increasingly prevalent in adults. Guidance of intravenous fluid replacement (IVFR) was however developed for pediatric dengue. Evidence-based fluid replacement guidance especially for older adults with concomitant chronic diseases is lacking. We retrospectively analyzed IVFR use in adult dengue patients admitted to a tertiary hospital.

Methods:

Medical records of patients diagnosed with dengue (confirmed by rapid NS1 kit or laboratory confirmation of RT-PCR, NS1 or IgM) from January 2020 to December 2022 were analyzed. Recovery phase was defined as defervescence for >12 hours with rising platelet count. Appropriateness of IVFR was based on disease severity according to 2009 WHO dengue classification scheme.

Results:

Analysis of the first 30 patients found an almost equal number of males (47%) and females with a median age of 52.5 years (range 15.0-83.0). 20 (67%) patients had at least one comorbidity with hyperlipidemia (33%), hypertension (23%) and ischemic heart disease (10%) being the commonest. Average time from onset to presentation was 4.3 days (95%CI 3.8-4.9). 16 (53%) met WHO classification scheme as requiring IVFR at admission; hypotension, acute kidney injury and/or hemoconcentration. Of these 16, one developed altered mental status and another hemophagocytic lymphohistiocytosis-like presentation. Despite 47% of patients having uncomplicated dengue, all received IVFR at admission, with 8 receiving IVFR beyond recovery phase. One developed fluid overload while another, IV cannula-related thrombophlebitis. There was no mortality.

Conclusion:

Preliminary findings suggest excessive IVFR with lack of standardization possibly contributing iatrogenic complications. We call for development of evidence-based fluid management protocols in older dengue patients.

010 Dengue Viremia Kinetics and Effects on Platelet Count and Clinical Outcomes: An Analysis of 2340 Patients from Vietnam

Vuong NL[1,2*], Quyen NTH[1], Tien NTH[1], Kien DTH[1], Duyen HTL[1], Lam PK[1,2], Tam DTH[1], Ngoc TV[3], Jaenisch T[4,5], Simmons CP[6,7], Yacoub S[1,6], Wills BA[1,6], Geskus RB[1,6*]

1. Oxford University Clinical Research Unit, Ho Chi Minh City, Viet Nam
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Background:

Viremia is a critical factor in understanding dengue pathogenesis, but limited data exist on viremia kinetics. This study aimed to investigate viremia kinetics and its effects on clinical outcomes.

Methods:

We pooled data from three studies between 2000 and 2016, involving 2340 dengue patients with daily viremia measurements after symptom onset. Viremia kinetics were assessed using a random effects model accounted for left-censored data. The effects of viremia on subsequent platelet count and clinical outcomes were examined using a landmark approach with a random effects model and logistic regression model with generalized estimating equations, respectively. Viremia decline rate was derived viremia kinetics model. Its effect on clinical outcomes was assessed by logistic regression models.

Results:

Viremia rapidly decreased following symptom onset, with variations observed depending on the infecting serotype. DENV-1 exhibited the highest mean viremia levels during the first 5-6 days, while DENV-4 demonstrated the shortest clearance time. Higher viremia levels were associated with decreased subsequent platelet counts. Elevated viremia levels on each illness day increased the risk of developing severe dengue and plasma leakage. However, the effect size decreased with later illness days. A more rapid decline in viremia is associated with a reduced risk of the clinical outcomes.

Conclusions:

This study provides comprehensive insights into viremia kinetics and its effect on clinical outcomes in dengue patients. Our findings underscore the importance of measuring viremia during the early febrile phase for dengue studies and support the use of viremia kinetics as outcome for phase-2 dengue therapeutic trials.

011 DENV infection and the integrity of the intestinal barrier: is the gut the tipping point to severe disease?

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Background:

Severe dengue occurs when fever has abated, and viremia as well as NS1 in circulation are decreasing. Warning signs include abdominal symptoms, and additionally, gut leak and elevated levels of LPS in circulation are documented in severe patients.

Methods:

Using mouse models of dengue virus 2 (DENV) infection, we studied the role of the gastrointestinal tract in the development of severe disease.

Results:

Infection was first high in the spleen, followed by the small intestine, large intestine, and other tissues were only infected at the late stage when viremia had decreased. However, following peak of viremia severe gut pathology and dysbiosis appeared in parallel with infection in Lamina propria macrophages. Mucus production was compromised and in some experiments we saw gut leak and bacterial penetration into the tissues. Treatment with broad-spectrum antibiotics one day after DENV infection, significantly reduced gut inflammation without modifying viremia. Kupffer cell infection and the viral RNA load in the liver were significantly reduced after antibiotics treatment. This suggests that bacteria-dependent gut-derived molecules could modify the susceptibility of Kupffer cells to DENV-infection.

Conclusion:

Overall, the data suggests that gut inflammation, a compromised gut barrier, and a dysbiotic metabolome enhancing viral replication in the liver may provide a tipping point for the development of severe disease. We propose that therapies that preserve gut integrity, modulate the microbiome and/or inhibit innate immune activation may prevent the severe form of dengue disease that requires hospitalisation.

012 The epidemiological study of dengue fever among international travelers and foreigners in Hospital for Tropical Diseases.

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Background:
The hospital for tropical diseases had more international travelers and foreigners. Patients were diagnosed as having dengue fever. This aim of the study is to find out the prevalence of dengue patients among outpatient department (OPD) and in-patient department (IPD) of the hospital for tropical diseases.

Methods:
Retrospective date of international travelers and foreigners' patients during 2017 - 2021 in hospital for tropical diseases. Demographic, clinical characteristics and laboratory profiles were collected from dengue patients by using a record review.

Results:
A total of 333 dengue virus infection patients were enrolled, of which 178 (53.45%) were male and 155 (46.55%) were female. Study finding revealed that out of 193 admitted patients with DF 142 (73.58%), DHF 50 (25.91%) and DSS 1 (0.51%) The prevalence of dengue patients among OPD and IPD in 2017 ration 1.59:1 was findings had dengue fever (DF) 32 (82.05%), dengue hemorrhagic fever (DHF) 7 (17.95%), in 2018 ration 1:1.85 was findings had DF 54 (72.98%), DHF 20 (27.02%), in 2019 ration 1:1 was findings had DF 37 (67.27%), DHF 20 (32.73%), in 2019 ration 1:1 was findings had DF 37 (67.27%), DHF 20 (32.73%), in 2020 ration 1.06:1 was findings had DF 14 (82.35%), DHF 3 (17.65%) and in 2021 ration 1:2 was findings had DF 5 (62.50%), DHF 2 (25 %) and DSS 1 (12.5 %) .Patients was symptomatic on admitted to hospital; continuous fever 63.21 %, intermittent fever 34.72%, chill 55.44%, severe headache 65.28%, stiff neck 1.55%, seizure 3.11%, cough 24.87%, sore throat 23.32%, dyspnea 19.69%, muscle pain 74.09%, thigh pain 22.80%, retro-orbital pain 32.64%, rash 17.10%, nausea 40.93%, vomit 36.79%, stomachache 18.13%, diarrhea 23.32%, bleeding manifestation 18.13%, dysuria 5.70%.

Conclusion:
In this study, the ration IPD more than OPD. the majority of the patients admitted day 4 but one patient was symptom least 13 hours before admitted.

013 Simulating Dengue Fever in Saudi Arabia Using a Process-Based Model

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3. Department of Emergency Medicine, University of Washington, USA

Background:

Dengue fever (DF) is a major public health concern in Saudi Arabia, and the Hajj pilgrimage brings together millions of people from DF-endemic countries, increasing the risk of outbreaks. This study developed and validated a process-based model, DyMSiM(P), to simulate DF transmission in Saudi Arabia, incorporating an SEIR model for Hajj pilgrims.

Methods:

DyMSiM(P) is a spatially explicit model that simulates DF transmission between humans and mosquitoes. The model incorporates weather data, mosquito population dynamics, and human demographics to predict the number of DF cases in a given location over time. The SEIR model for Hajj pilgrims simulates the arrival of infectious pilgrims, their interactions with the local population, and their subsequent departure.

Results:

DyMSiM(P) outperformed the original DyMSiM model, with an average R2 of 0.37 and an average RMSE of 78.2. The model accurately captured the seasonal pattern of DF incidence and the impact of weather factors, and it improved the performance of DF prediction during the Hajj pilgrimage.

Discussion:

The limitations of the study include the sensitivity of the entomological component of the model to extremes of temperature and humidity, and the difficulty of assessing the utility of incorporating a pilgrim SEIR model when developing a process-based model for DF in Saudi Arabia.

Conclusion:

DyMSiM(P) is a valuable tool for understanding and predicting DF transmission in Saudi Arabia. It can be used to inform public health decision-making and to develop effective control strategies.

014 Modeling the Role of Weather and Pilgrimage Variables on Dengue Fever Incidence in Saudi Arabia

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Background:

The first case of Dengue fever (DF) in Saudi Arabia appeared in 1993 but by 2022, DF incidence was 11 per 100,000 people. Climatologic and population factors, such as the annual Hajj, likely contribute to DF's epidemiology in Saudi Arabia. In this study we assess the impact of these variables on the DF burden of disease in Saudi Arabia and we attempt to create robust DF predictive models.

Methods:

Using 10 years of DF, weather, and pilgrimage data, we conducted a bivariate analysis investigating the role of weather and pilgrimage variables on DF incidence. We also compared the abilities of three different predictive models.

Results:

Amongst weather variables, temperature and humidity had the strongest associations with DF incidence, while rainfall showed little to no significant relationship. Pilgrimage variables did not have strong associations with DF incidence. The Random Forest model had the highest predictive ability (R2 = 0.62) when previous DF data was withheld, and the ARIMA model was best (R2 = 0.78) when previous DF data was incorporated.

Conclusion:

We found that a nonlinear machine learning model incorporating temperature and humidity variables had the best prediction accuracy for DF, regardless of availability of previous DF data. This finding can inform DF early warning systems and preparedness in Saudi Arabia.

015 Cross-sectional study: Pediatric Severe Dengue Who Had Telemedicine and its Pitfalls (2012-2023).

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Background:

Severe dengue in children primarily manifests as transient capillary leak syndrome leading to dengue shock syndrome (DSS), characterized by fluid accumulation and intravascular volume depletion, often causing severe bleeding during prolonged shock. This study reports a telemedicine-based approach to management and highlights potential pitfalls.

Methods:

This cross-sectional study of pediatric patients with severe dengue in centers without pediatric intensivists who had telemedicine in Malaysia from 2012 to 2023.

Results:

This study enrolled thirty-five pediatric patients undergoing telemedicine primarily for shock, respiratory distress, severe bleeding, and fluid overload but still in shock, consisting of 23(65.7%), 18(51.4%), 12(34.3%), and 10(28.6%) cases, respectively. The median (IQR) percentage of fluid overload was 9.1 (5.6, 16.2) % at telemedicine. 6% Hydroxyethyl Starch HES (Voluven) was administered to 19 subjects with a median (IQR) total volume of 63.0 (51.2, 75.0) ml/kg throughout the course. The time from telemedicine to de-escalation of fluid therapy was 5.0 (2.0, 9.8) hours. A significant association between the three mortalities (8.7%) and WBC ≥ 25 (p=0.002), lactate ≥ 10 (p=0.006), and BE ≤ -15 (p=0.029) during illness was noted.

Conclusions:

Early use of colloid fluid resuscitation is advocated when multiple crystalloid boluses are needed to prevent recurrent shock and fluid overload. Prompt recognition of occult bleeding is crucial, prioritizing fresh-packed red cell transfusion. Maintaining electrolyte balance and normoglycemia is vital. Gradual intravenous fluid reduction aids excess fluid clearance. Fluid stewardship requires frequent reassessment and meticulous fluid balance, often facilitated by telemedicine sessions until the patient transitions from the critical phase.

016 Comparative Evaluation of Five Rapid Diagnostic Test for Dengue Diagnostics

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Background:
Every year, dengue outbreaks cause substantial humanitarian and economic hardship worldwide. Dengue causes a wide spectrum of disease. Primary dengue can range from subclinical disease to flu-like symptoms. Although less common secondary dengue is associated with increased morbidity and mortality. Accurate, efficient and rapid diagnosis of dengue in acute stage is essential as delay in diagnosis increases the risk of severe dengue and can lead to poor disease outcome. In dengue-endemic areas, laboratories and clinics have for a while now relied on simple and cost-effective serological rapid diagnostic tests (RDTs) to diagnose dengue.

Methods:
This study evaluated the performance of five commercially available RDTs which can detect NS1 antigen and IgM/IgG antibodies: SD Bioline Dengue Duo, Atron Dengue virus IgG/IgM and Ag cassette, Standard Q Dengue Duo, Humasis Dengue combo kit and ALL Test Dengue Combo Rapid Test. Well characterized archived dengue and non-dengue serum samples at Aga Khan University, Pakistan were used. Each RDT was evaluated separately and in combination for the diagnostic parameters [non-structural (NS1) antigen and/or immunoglobulin M (IgM) positive].

Results:
430 serum samples were evaluated (255 NS1 ELISA positive and 175 negative NS1 ELISA) Compared to the reference NS1 enzyme-linked immunosorbent assay (ELISA) samples, sensitivity of RDTs ranged from 65.1% to 94.12% with best overall sensitivity shown by Atron Dengue virus IgG/IgM and Ag cassette (94.12%) All RDTs showed a specificity of >99%. Atron Dengue virus IgG/IgM and Ag cassette (96.78%) had the highest diagnostic accuracy.

Conclusion:
In conclusion, Atron Dengue virus IgG/IgM and Ag cassette showed the highest sensitivity and diagnostic accuracy, while Standard Q Dengue Duo and ALL Test Dengue Combo Rapid Test showed the highest specificity. Moreover, these results confirm that combining antigen- and antibody-based RDTs can have huge value for dengue diagnosis and that very good commercial tests exist and should be used.

Keywords:
Dengue, diagnosis, diagnostic parameters, rapid diagnostic tests, serology

017 Dengue in Bali: Virus Surveillance Reveals Serotype Shifts and Genotype Replacement in the Last 10 Years

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Background:

Bali, the most popular tourist destination in Indonesia, has a high occurrence of dengue fever. Despite the annual outbreaks and serious health risks, there is a lack of consistent and thorough virus surveillance in the region. This study aims to monitor viral transmission dynamics in Bali.

Methods:

During 2018-2020 and 2022, we enrolled individuals with dengue symptoms at hospitals in Bali. We conducted clinical evaluations, collected blood samples, and determined the DENV serotypes using RT-PCR and genotypes through genome sequencing. Alongside retrospective genomic data from the last 10 years, the current genomic data were phylogenetically analyzed.

Results:

We recruited a total of 62 and 66 patients with confirmed dengue between 2018-2020 and 2022. Serotype data was obtained for 49 and 48 individuals in each respective year. The most common serotype in 2018-2020 was DENV-1 (31.9%), followed by DENV-3 (27.7%), DENV-4 (21.3%) and DENV-2 (19.1%). In 2022, DENV-3 was the most prevalent serotype (58.3%), followed by DENV-2 (29.2%), and DENV-1 (10%), with an increase number of severe dengue. Compared with data from the last ten years, serotype shifting was clearly observed, with emerging multiple lineages and a replacement of Genotype IV of DENV-1 with Genotype I over the years. The Cosmopolitan, Genotype I, and Genotype II were the predominant genotypes for DENV-2, DENV-3, and DENV-4, respectively.

Conclusion:

Our findings show the genetic diversity and dynamic nature of dengue virus in Bali, emphasizing the importance of routine virus surveillance to predict and manage future outbreaks based on serotype and genotype patterns.

018 The amino acid substitution D29V in the prM protein contributes to clinically-tested dengue vaccine strain attenuation

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Background:

Despite decades of dengue vaccine development, our understanding of the molecular basis of virus attenuation remains incomplete. We thus explored the genetic and mechanistic basis of attenuation of dengue virus serotype 2 (DENV2) PDK53 strain, a key component of the clinically-tested TAK003 vaccine.

Methods:

We constructed an infectious clone of wild-type DENV2 16881, based on published full genome sequence and from which PDK53 was derived. Using site-directed mutagenesis, we substituted each of the 5 amino acid PDK53 mutations onto the 16681 infectious clone.

Results:

In addition to the previously identified NS1 G53D substitution, we identified a aspartate-to-valine substitution at amino acid position 29 of the prM protein that altered both DENV2 replication and type-I interferon (IFN) induction; the latter functionally limited plaque size of the mutant virus. This prM D29V substitution impaired neither virion assembly nor virus maturation. Instead, immunoprecipitation with mass spectrometry, as well as cell fractionation studies found that wild-type prM bound host high mobility group box 1 (HMGB1) protein to localize this protein in the cytosol; mutant prM, in contrast, lost the ability to bind HMGB1. We also observed that binding of wild-type prM to HMGB1, a ubiquitously expressed protein involved in gene transcription regulation, was critical to limit transcriptional response to wild-type 16681 infection. The loss of binding driven by the prM D29V substitution resulted in differential expression of large number of genes upon mutant and PDK53 infection, amongst which are type-I IFN and the IFN stimulated genes that attenuated infection.

Conclusion:

The interaction between prM and HMGB1 is a hitherto undefined mechanism of DENV evasion of virus-restrictive host response to infection. We suggest that this interaction could be exploited for developing new attenuated DENVs.

019 Asymptomatic Dengue Infection Among Healthy Residents of the Indonesia-Malaysia Border Sebatik Island, North Kalimantan Province, Indonesia

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Background:

Dengue fever, caused by the dengue virus (DENV), is a major concern for global health. Many people infected with the virus experience symptoms like high fever, severe headaches, and joint-muscle pain. However, a large number of cases shows no symptoms at all, making it difficult to control the spread of the disease and highlighting the risk of virus transmission.

Methods:

A mass blood survey to assess the transmission of vector-borne diseases was carried out on Sebatik Island, Indonesia in September 2023. A total of 291 healthy individuals participated with ages ranged from 6 to 76 years (median 32 years). Dengue RDT screening was first applied, followed by RT-PCR serotyping and whole genome sequencing.

Results:

Among all participants, 37 (12.7%) tested positive for NS1, 82 (28.2%) for IgG, and no IgM positive cases. Further RT-PCR testing confirmed 21 cases of DENV infection, with all four serotypes represented: 2 cases of DENV-1 (9.5%), 1 case of DENV-2 (4.8%), 8 cases of DENV-3 (38.1%), 3 cases of DENV-4 (14.3%), and 7 (33.3%) cases of mixed infections. Whole genome sequencing revealed the genotypes of the DENV, and phylogenetic analysis showing close relationships to DENV strains from Malaysia, Singapore, and other cities in Indonesia.

Conclusion:

This study highlights the high prevalence of asymptomatic dengue infections on Sebatik Island and the complex nature of transmission dynamics, emphasizing the need for comprehensive surveillance and control efforts. Collaboration among regions is crucial in containing the spread of dengue fever and minimizing its impact on public health.

020 Forecasting Dengue Cases in Malaysia: Comparative Analysis between ARIMA/ SARIMA, Deep Neural Network and Long-Short Term Memory

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Background:

The escalating incidence of dengue fever on a global scale has raised significant concerns. Forecasting techniques play a pivotal role in strengthening dengue control and outbreak management. Hence, this study aimed to develop and evaluate the accuracy of time series autoregressive integrated moving average (ARIMA)/seasonal ARIMA(SARIMA), deep neural network (DNN), and long-short-term memory (LSTM) in forecasting dengue cases in districts of east and west Peninsular Malaysia.

Methods:

Weekly dengue cases were obtained from January 2015 to Mac 2023 for Timur Laut and Kota Bharu districts. The data were decomposed to determine the structural pattern and subsequently split into training, validation, and test datasets. Using the Box-Jenkins method, ARIMA/SARIMA models were developed. For DNN and LSTM models, the architecture (depth and width) was optimized based on performance and complexity. Grid search was employed for hyperparameter tuning to identify optimal settings. The final models were used for rolling one-step forecasts, and accuracy was assessed using root mean squared error (RMSE).

Results:

A total of 428 data points were analyzed, revealing a 4-year cycle of dengue outbreaks in both districts, notably in 2015 and 2019. Kota Bharu exhibited more pronounced seasonality than Timur Laut. In Timur Laut, the LSTM model showed superior performance with the lowest RMSE (RMSE=4.200), surpassing DNN (RMSE=4.202) and ARIMA (RMSE=4.234). Conversely, in Kota Bharu, the SARIMA model performed best with the lowest RMSE (RMSE=5.400), outperforming LSTM (RMSE=5.440) and DNN (RMSE=5.612).

Conclusion:

The LSTM was the most accurate model for forecasting dengue cases with complex patterns. In contrast, the SARIMA was the best model for forecasting dengue cases exhibiting seasonality. Integrating the model into the early warning dengue system may assist the health authority in managing dengue outbreaks more efficiently.

021 Mutations in NS1-G53D and NS2B-I114T Attenuates Clinical Isolates of Dengue Virus Serotypes 2, 3 and 4

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Background:

Dengue is an acute arboviral disease that affects an estimated 100 million people globally each year. There are four types of dengue virus (DENV1-4), all of which are transmitted principally by *Aedes aegypti*. Although vaccines containing recombinant chimeric viruses have now been licensed in some countries to prevent dengue, a vaccine that contains purely full genome DENVs that elicit the full range of DENV-specific humoral and cellular immune responses remains to be developed. In this study, we explored if attenuating mutations identified in DENV-2 would also attenuate wild-type DENV-3 and -4.

Methods:

We used DENV-3 (D3/SG/05K863DK1/2005) and DENV-4 (D4/SG/06K2270DK1/2005), which were isolated from acutely ill dengue patients, as the wild-type (WT) virus in this study. Infectious clones with mutations that were previously identified in DENV-2, namely NS1-G53D and NS2B-I114T were generated using site-directed mutagenesis and Gibson assembly. Virus genome stability and viral replication kinetics were performed on mosquito and/or mammalian cells.

Results:

Introducing both NS1-G53D and NS2B-I114T substitutions into DENV-3 and DENV-4 produced stable mutants through 2 - 4 passages in C6/36 cells and produced consistently small plaques on plaque assay. The double mutant viruses showed increased viral replication and IFNß response in mammalian cells. Furthermore, there was reduced viral replication in *Aedes aegypti* mosquitoes infected with DENV-3 double mutants; mutant DENV-4 infection in mosquitoes is in progress. Immune gene profiling in infected monocyte derived dendritic cells showed gene expression profiles suggestive of features observed in DENV-2 PDK53.

Conclusion:

Engineering of mutations that attenuate DENV through the same mechanisms may produce novel mutants with features suitable for further development as live attenuated vaccines. Four DENVs bearing the same mutations and hence mechanism of attenuation may minimise the potential of competition between serotypes in a tetravalent formulation.

022 Performance Evaluation of Dengue Rapid Diagnostic Kits for Dengue

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Background:

Dengue remains endemic in Malaysia despite various efforts have been taken in controlling the disease burden and the vector. One of the key measures is to diagnose dengue early at the healthcare facilities. In Malaysia, rapid diagnostics tests (RDTs) are increasingly used to confirm recent dengue infections due to their ease of use and short turnaround time for results at the primary healthcare clinics and emergency departments. The evaluation aims to determine the sensitivity and specificity of the dengue kits and to assess the limitations in conducting the tests.

Methods:

5 different rapid, in-vitro, immunochromatographic based dengue kits received were evaluated using in-house characterised panel sera for NS1Ag, IgM and IgG for dengue. All kits are combination kits of NS1Ag and IgM/IgG. Testing procedure was based on the manufacturer's kit instructions. Sensitivity and specificity of each kit were calculated and compared. The manufacturer's origin was also identified in the evaluation.

Results:

2 dengue kits were manufactured in Malaysia while 3 dengue kits were manufactured outside Malaysia. The sensitivity and specificity of the all evaluated kits ranged from 79-100% and 28-100%, respectively.

Conclusion:

The evaluation showed a variability of the dengue rapid diagnostic kits' performances, which may have impacts on the early diagnosis in the clinical settings. The findings elucidated that further development in dengue diagnostics is required in the country. Effective, affordable and accessible dengue RDTs are required as a point of care testing, testing for any clinical trials in searching for the treatment and prevention of dengue.

Keywords:

Dengue, rapid diagnostics kits, Malaysia

023 Unraveling Dengue Virus Diversity in Asia: An Epidemiological Study based on Genetic Sequence and Phylogenetic Analysis

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Abstract:
Dengue virus (DENV) is the causative agent of dengue fever. Although most infected individuals are asymptomatic or present with only mild symptoms, severe manifestations could potentially devastate populations in tropical and subtropical regions. In hyperendemic regions such as South Asia and Southeast Asia (SEA), all four DENV serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) have been prevalent for several decades. Each DENV serotype is further divided into multiple genotypes, reflecting the extensive diversity of DENV. Historically, specific DENV genotypes were associated with particular geographical distributions within endemic regions. However, this epidemiological pattern has changed due to urbanization, globalization, and climate change. This presentation traces the historical and recent genetic epidemiology of DENV in Asia from the 1950s to the present. We analyzed envelope sequences from a database covering 16 endemic countries across three distinct geographic regions in Asia. These regions include Bangladesh, Bhutan, India, Maldives, Nepal, Pakistan, and Sri Lanka from South Asia; Cambodia, Laos, Myanmar, Thailand, and Vietnam from mainland SEA; and Indonesia, the Philippines, Malaysia, and Singapore from maritime SEA. Additionally, we describe the phylogenetic relationships among DENV genotypes within each serotype, along with their geographic distribution, to enhance the understanding of DENV dynamics.

024 Transcriptional landscape of wild-type and attenuated dengue virus strains

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Background:

Dengue vaccines are conventionally characterised as virus strains that exhibit a small plaque phenotype. However, emerging studies suggest this phenotype inadequately informs virus attenuation, as it may arise from immune restriction or slow viral growth. In this study, we investigated transcriptional profiles after infection as an alternative approach to differentiate wild-type from attenuated viral strains.

Methods:

A549 cells were infected with 9 different DENV-1 wild-type and 2 attenuated virus (PDK13 and WP-delta30) strains. Total RNA was sent for bulk RNA-sequencing after 24 hours post-infection at an MOI of 10. DESeq2 was used examine the differential expression (DE) profile of wild-type and attenuated strains. Principal component analysis (PCA) and differential analysis was performed to determine the gene expression differences between uninfected, wild-type and attenuated strains. Over-representation analysis with gene ontology biological process library was conducted with clusterProfiler. Graphs were plotted with ggplot2.

Results:

Wild-type DENV-1 strains induced different host transcriptional responses compared to the attenuated DENV-1 strains. PCA revealed TRIML2, BCL2A1, SNHG19, EIF2AK3-DT, and MT-ND3 expression distinguished wild-type from attenuated DENV-1 strains. Attenuated strains induced upregulation of small molecule metabolic processes, namely monocarboxylic acid and fatty acids, and downregulation of innate immune and pathogen-sensing responses compared to wild-type strains. Moreover, we identified 19 DE genes between PDK13 and WP-delta30, where the latter vaccine has greater clinical efficacy.

Conclusion:

Our studies suggest different transcriptomic responses induced by wild-type and attenuated viruses, and between attenuated strains with differing clinical efficacy.

025 Acceptability of a dengue vaccine amongst the public in Singapore

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Background:

The recent 2020 dengue outbreak in Singapore which reported the highest case numbers in history, highlights shortfalls in current approaches to controlling dengue. Dengue vaccination has great potential to work alongside vector control in reducing the public health burden. In Singapore, there is a unique distribution of dengue infections, where a higher burden is seen amongst the elderly population aged 60 and above. This presents a challenge for Singapore as most research and vaccine trials do not include this age group. In this study, we aim to gather insights on the acceptability of the dengue vaccine amongst the public in Singapore, including those aged 60 and above.

Methods:

We developed a survey to measure the acceptability and attitudes towards dengue vaccination in Singapore, as well as their knowledge of existing or future dengue vaccines. Favourable vaccine characteristics were further probed to act as determinants of attitude. Alongside this, knowledge, attitudes and practices for the current dengue situation were measured. An emphasis is placed on reaching population makeup for specifically the elderly group. The responses of this survey will be analysed using logistic regression.

Results:

NA

Conclusions:

Results from this study can provide valuable insights for dengue vaccination roll-out in Singapore for current and future vaccines by providing information on public sentiments. Dengvaxia is currently the only available option in Singapore, however due to being fairly new, it has not received large scale promotion. Hence, our study can inform prioritizations and measures for promotion to ensure optimal uptake.

026 Assessing Sentiments on Dengue Vaccine in the Key Stakeholders: A Qualitative Study

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Background:
Singapore remains vulnerable to cyclical dengue epidemics of increasing magnitudes with low levels of population immunity against the four dengue serotypes. In anticipation of the licensure of the second dengue vaccine in Singapore in coming years and its potential integration into the nation's core prevention strategy, this study seeks to elicit opinions of key stakeholder groups on dengue vaccination.

Methods:
In-depth interviews will be conducted with three key stakeholder groups invested in dengue prevention and care in Singapore, 1) scientists studying related topics, 2) policymakers, and 3) frontline healthcare workers. The study team will recruit a convenient sample by snowball sampling until thematic saturation is reached. A literature review was conducted on vaccination decision making by policymakers, research and policymaking gap, and healthcare workers' opinions on vaccine implementation, to provide theoretical scaffolding for the topic guide. The semi-structured topic guide comprises five sections: 1) dengue situation in Singapore, 2) understanding on dengue vaccines and their role in the national strategy, 3) public acceptability 4) programme-implementation considerations, and 5) the research to policy process in Singapore pertaining to dengue and dengue vaccination. The interviews will be conducted virtually through Zoom. Transcripts will be transcribed verbatim and analysed using thematic analysis.

Results:
This is a protocol for a study in progress. Data collection has yet to commence.

Conclusions:
The consolidated opinions of stakeholders with varied technical backgrounds may form a valuable evidence base for policymakers in their decision process to introduce a new dengue vaccine in Singapore and highlight key programmatic considerations to optimise implementation.

027 Diagnostic performance of dengue NS1 rapid tests in Rural Communities in Cebu, Philippines

C De Guzman, GL Magsakay, MSG Bargo, KA Agrupis, MV Crisostomo, M Ylade, J Deen

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Background:

Dengue fever is an important public health problem in the Philippines. Early, rapid confirmation of dengue is critical for prompt clinical management. We aimed to assess the performance of BiolineTM dengue NS1 Ag rapid test against RT-PCR in detecting acute dengue infection in rural communities.

Methods:

We analysed dengue NS1 rapid test and RT-PCR results in blood samples collected from children presenting with an acute febrile illness as part of an observational study (ClinicalTrials.gov, NCT038303618) conducted in rural communities in Cebu, Philippines. We assessed the diagnostic performance of NS1 rapid test against RT-PCR, overall, by day of collection related to the onset of the illness and by dengue virus (DENV) serotype.

Results:

We included 903 specimens in this analysis. Overall, the sensitivity, specificity, and accuracy of NS1 rapid test were 53.85% (95%CI: 50.59%-57.10%), 86.64% (95%CI: 84.43%-88.86%) and 64.45% (95%CI: 61.27%-67.51%), respectively. The NS1 rapid test sensitivity was most optimal on samples collected during the first two days of illness (sensitivity: 70.45%, 95%CI:62.98%-77.93%) & accuracy: 76.92%, 95%CI: 69.37%-83.07%). The sensitivity of NS1 was highest for DENV4 (92.15%, 95%CI: 90.03%-94.26%), and lowest for DENV3 (47.13%, 95%CI:43.20%-51.06%).

Conclusion:

The low sensitivity of NS1 rapid test could be improved by conducting the test earlier during the illness. In our setting, a negative NS1 rapid diagnostic test result should be cautiously interpreted, especially after the second day of illness.

028 Deletions Within the 3' Untranslated Region Hindered Translation Initiation, Leading to Attenuation of a Dengue Virus 3 Vaccine Strain

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Background:

Phases I-III clinical trials of TV003, a live attenuated dengue vaccine, have demonstrated promising safety, immunogenicity, and efficacy. This vaccine was attenuated via nucleotide deletions in the 3′ untranslated region (3'UTR), yet the precise mechanism underlying this attenuation remains elusive. To bridge this knowledge gap, our investigation focused on the DENV-3 component of TV003, which was derived from wild-type DENV-3 Sleman/78.

Methods:

Using Gibson assembly, we rescued Sleman/78, as well as two mutants: one with 30 nucleotide deletions in dumbbell (DB) II (Sleman/78Δ30, that was shown in clinical trials to be insufficiently attenuated), and another with an additional 31 nucleotide deletion in DBI (Sleman/78Δ30/31, which is a component of TV003) in the 3'UTR, for in vitro investigations. Host protein binding partners of the 3'UTR of these viruses were identified using RNA-affinity chromatography coupled with mass spectrometry.

Results:

The replication kinetics of Sleman/78Δ30/31 in both Huh-7 cell lines and primary monocyte-derived dendritic cells (MODC) were slowest among the 3 viruses. It also produced the smallest plaque sizes in BHK-21 cells. RNA-affinity chromatography found ribosomal proteins (RPs) and translation initiation factors (TIFs) as binding partners of wild-type 3'UTR; binding of these groups of proteins was reduced in the Δ30 and Δ30/31 3'UTRs, with Δ30/31 3'UTR showing the fewest interactions with RPs and TIFs. This loss of binding corresponded with the slowest translation of the respective DENV proteome. Similarly, replacing the open reading frame of these three DENV-3 genomes with eGFP gene also produced reduced eGFP expression with Δ30/31 compared to the other two 3'UTRs.

Conclusion:

Beyond its role in forming the pan-handle structure of the DENV genome, the 3'UTR, particularly through the DBI and DBII secondary structures, plays a pivotal role in recruiting factors involved in translation, reduction of which contributed to attenuating wild-type DENV-3 Sleman/78.

029 Elucidating the mechanism of attenuation in the DENV4 PDK48 live-attenuated vaccine candidate

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Background:

Caused by infection with any one of four dengue viruses (DENV1-4), dengue is a major vector-borne disease and global health concern. However, the DENV-host interactions that underpin pathogenesis still remain poorly defined. We utilise the wild-type DENV4 1036 strain and its clinically attenuated derivative PDK48 to interrogate the genetic determinants of pathogenesis.

Methods:

PDK48 differs from its pathogenic 1036 parent by only seven non-synonymous nucleotide changes in its genome. We used Gibson assembly to construct mutant 1036 infectious clones that each harbour one of these mutations, and compared their plaque size and replication kinetics against those of 1036 and PDK48.

Results:

We identified a E345K substitution in the envelope (E) protein and G32W substitution in the non-structural 3 (NS3) protein that reproduce the small plaque phenotype of PDK48. However, only the NS3 G32W mutant can recapitulate the slower replication kinetics of PDK48 in Huh7 cells. This mutation, which occurs in the protease domain of NS3, does not directly impair proteolytic activity but may allosterically inhibit other enzymatic functions of NS3 or disturb its interactions with other viral and host factors. Neither mutation contributes to the reduced infectivity of PDK48 in *Aedes aegypti* by an infectious bloodmeal, suggesting that different mechanisms underlie the attenuation of PDK48 in the mammalian host and mosquito vector.

Conclusions:

A single NS3 G32W mutation is important for both the plaque size and replication of PDK48 in mammalian cells. However, identification of the precise mechanism by which it affects the virus life cycle and fitness is in progress. We envision that our findings will allow us to better understand the genetic determinants of DENV attenuation and provide fresh insights into DENV-host interactions underpinning dengue pathogenesis.

030 The anti-dengue effect of oral and intraperitoneal administration of *Schizophyllum commune* aqueous extract in AG129 mice

E Kavithambigai[1], MAR Mohd Ridzuan[2], M Amirudin[2], MJ Nur Hana[2], MN Farhan[2], K Khayri Azizi[1], T Emmanuel[1], KSY Sheila[1], MZ Zarina[1], AW Manisya Zauri[1], A Muhammad Afif[1], K Jeevanathan[1], H Amir[1], Z Azlina[3], WM Adham[2], AP Phazlyana[2], CY Keong[2], SM Ami Fazlin[2], MZ Rozainanee[1],W Kah Hui[4], S Vikineswary[5] and T Ravindran[1]

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Background:

Schizophyllum commune aqueous extract (ScASE) had been reported for anti-dengue activity in in-vitro studies using plaque reduction assay and real time RT-PCR. The objective of this study to explore whether this mushroom extract may protect AG129 mice from dengue virus infection when given orally and intraperitoneally.

Methods:

AG129 mice were categorised into five groups of six: mock-infected mice, DENV 2-infected mice, DENV 2-infected mice that were either orally or intraperitoneally treated with ScASE (500 mg/kg), and positive control mice that were treated intraperitoneally with celgosivir (15 mg/kg). For four days, the treatment doses were administered twice daily. Blood samples were collected for assessment of DENV titer, NS1 Ag and inflammatory cytokine levels. Blood, liver, spleen, kidney, and large intestine were collected during sacrifice and tested for blood profile, DENV titer and histopathological alterations. Extracted RNA from spleen samples were selected for transcriptomic analysis.

Result:

The treatment of AG129 mice with 500 mg/kg of ScASE resulted in complete recovery from dengue infection, similar to those treated with celgosivir. In comparison to DENV-infected mice, there was a considerable decrease in the amount of viral RNA and antigens in the blood and organs. The production of inflammatory cytokines associated with dengue severity was reduced in ScASE-treated mice. There were no significant differences in blood cell profile or histopathological effect between treated and mock-infected mice. The results for spleen transcriptomics are pending for analysis.

Conclusion:

This preliminary data suggests that administering ScASE intraperitoneally can protect AG129 mice from dengue infection, indicating potential for development as an anti-dengue therapeutic drug.

031 Assessing the Antiviral Activity of Oral Remdesivir VV116 Against Serotype 2 Dengue Virus Infection In Vitro

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Background:

Dengue fever remains a pressing issue in tropical regions, prompting the need for cost-effective and efficient drug discovery methods. This study investigated the potential for repurposing the investigational COVID-19 drug oral remdesivir, VV116 as an antiviral agent against serotype 2 dengue virus (DENV-2) in human liver (HepG2 and Huh7) and monkey kidney (Vero) cell lines.

Methods:

Cells (HepG2, Huh7 and Vero) were infected with DENV-2 and treated with VV116 at various concentrations (0.196 to 100 µM). High-content imaging assay and plaque reduction assay were performed to detect fluorescent-labelled intracellular viral particles and measure infectious viral counts, respectively. Concurrently, cellular cytotoxicity was assessed through Hoechst nuclei fluorescent staining and counting. Half-maximal effective (EC50) and cytotoxic concentrations were determined by dose-response curve analysis. The window between antiviral activity and cytotoxicity was determined by selectivity index (SI) ratio calculation.

Results:

The data showed that VV116 treatment reduced the intracellular viral particles and infectious viral count, respectively, in both HepG2 and Vero infected cells with an EC50 of <5 µM. The VV116 treatment also reduced the intracellular viral particles and infectious viral count in Huh7 infected cells but with higher EC50 value (>10 µM). The SI value for VV116 was high (SI>10) against DENV-2 infections in HepG2 and Vero cells.

Conclusion:

The oral remdesivir VV116 showed potent antiviral activity in vitro against DENV-2 infections in HepG2 and Vero cells. Further analysis, particularly in vivo pharmacodynamic and pharmacokinetic studies, are warranted to fully evaluate its effectiveness and safety profile.

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032 Clinical characteristics and outcomes of congenital dengue in two newborns

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Background:

Congenital dengue, though rare, poses significant diagnostic and management challenges in neonates.

Methods:

We describe two cases of congenital dengue in newborns delivered to symptomatic mothers who were tested positive for dengue NS1 antigen just before labor. The neonates were hospitalized since birth and closely monitored for signs of dengue, with diagnostic confirmation through NS1 antigen detection and polymerase chain reaction (PCR) for serotype identification. Serial serology tests documented the duration of NS1 positivity and timing of IgM and IgG seroconversion.

Results:

Patient 1 was a term baby who developed tachypnea within 30 hours of life and fever on day 5, testing positive for Dengue NS1 antigen. DEN4 was detected. NS1 positivity persisted until day 19 of life, with IgM and IgG seroconversions occurring on day 9 and day 19, respectively. This neonate required respiratory support but no intravenous fluids. Patient 2, a term baby, developed fever and jitteriness on day 5 of life and was tested positive for NS1. This patient experienced transaminitis and severe thrombocytopenia, requiring platelet transfusions. DEN 1 was identified. NS1 remained positive until day 13, with IgM and IgG seroconversions on day 9 and day 13 of life.

Conclusion:

These cases underscore the importance of considering dengue in the differential diagnosis for neonates presenting with fever, thrombocytopenia and rash in dengue-endemic regions. The extended NS1 positivity and timing of seroconversion illustrate the unique kinetics of dengue serology in neonates. Prompt recognition and appropriate supportive care are crucial, reducing unnecessary antibiotic use and improving outcomes.

033 Self-testing for Dengue: Paving the Way for Democratizing Dengue Diagnostics

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Background:

Dengue fever poses a significant burden on public health globally, with its prevalence increasing in recent years. Early diagnosis of dengue is crucial not only to help distinguish against other febrile illnesses but also to facilitate appropriate medical interventions. The current practices, however, require febrile patients to seek testing at healthcare facilities, which may pose challenges, especially in regions where resources are limited. The lesson learned from the COVID-19 pandemic highlights the importance of accessible and rapid diagnostic tools, instigating the need to re-evaluate the diagnostic approaches for other infectious diseases, including dengue. A diagnostic approach that empowers a febrile person to perform his or her test is therefore needed. Here, we evaluated if the dengue NS1 rapid diagnostic test assay could be applicable and acceptable as a home self-test kit. A lateral flow immunochromatography test (ICT) using NS1 was converted as a possible self-test kit by providing the kit with a test device, an alcohol swab, lancet, disposable dropper, assay buffer, and test manual.

Methods:

Twenty participants were recruited for the study. The participants performed the test based on the test manual provided in the self-test kit under the observation of trained observers. These observers recorded all the actions performed by the participants to evaluate the effectiveness of the instruction manual, ease of use, accuracy, and satisfaction. The results of the test were interpreted by the participants using a given interpretation table.

Results:

Eighty percent (80%) of the study participants successfully obtained the expected results.

Conclusion:

Findings from the study suggested that a self-test diagnostic is a viable approach for the early detection of dengue.

034 Dissecting the immune cell subsets involved in severe dengue progression and pathogenesis

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Background:

The molecular mechanisms involved in severe dengue progression is critical for therapeutics and vaccine development. Candidate biomarkers have been suggested to classify patients with severe and mild dengue, but the immune cell subsets that contribute to the differential expression of these biomarkers remain poorly understood. We thus investigated the expression levels of various severe dengue biomarkers in different immune cell subsets in severe dengue patients, and determine the immune cell characteristics that contribute to severe dengue progression and pathogenesis.

Methods:

We first identified genes that were most consistently different between severe and mild dengue patients across multiple cohorts. The abundance of these genes were then analysed using publicly available single-cell RNA-sequencing (scRNA-seq) datasets. The performance of the predictive dengue genes was determined by calculating the area under receiver operating characteristic curves (AUROCs).

Results:

We identified 10 genes that were differentially expressed between severe and mild dengue patients across multiple cohorts. The differential expression of these genes were specific to severe dengue but not for other viruses. These predictive genes were also highly expressed in platelets, M1 macrophages, cytotoxic NK cells and exhausted CD8 T cells in patients with severe dengue compared to mild dengue patients, indicating the involvement of these immune cell subsets in facilitating severe dengue progression and pathogenesis.

Conclusion:

Platelets, M1 macrophages, cytotoxic NK cells and exhausted CD8 T cells could be the major immune cells involved in severe dengue progression and pathogenesis.

035 Recent Trends in Dengue Research in the Philippines (2018-2023): A Scoping Review

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Background:
Dengue is hyperendemic in the Philippines. A previous review described the trends in dengue research in the country from January 1958 to December 2017 (60 years). We aimed to provide an update on dengue research in the Philippines during the last 6 years.

Methods:
We conducted a scoping search for full text studies written in English from January 2018 to December 2023 on 4 available academic search engines. Published original work on dengue research in the Philippines and on Filipinos that reported objectives, methods, and results, or descriptive epidemiologic and case reports were included. Articles were sorted according to themes.

Results:
We identified and screened 1,327 articles. After removing duplicates (43, 3.2%) and ineligible articles (1,176, 88.6%), 108 (8.1%) studies were reviewed. Twenty-eight (26%) were descriptive epidemiology studies and case reports, nineteen (18%) were socio-behavioral and economics studies, seventeen (16%) were entomologic and vector control studies, eleven (10%) were clinical trials and vaccine effectiveness studies, eleven (10%) were modeling studies, eight (7%) were virologic and serologic response studies, five (5%) were dengue diagnostics studies, three (3%) were investigations on markers of dengue severity, two (2%) were on burden of disease, two (2%) were on dengue therapeutics, and two (2%) were on mobile application development for improved dengue surveillance.

Conclusions:
With the considerable number of dengue studies on the Philippines within the last 6 years, 3 new themes emerged: mobile application development, dengue therapeutics, and dengue vaccine effectiveness assessment. More research efforts are needed in these areas to support dengue surveillance, treatment, and prevention.

036 Effectiveness of a single-dose mass dengue vaccination in Cebu, Philippines: A 5-Year case-control study

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Background:

In April 2016, the Philippine Department of Health launched a 3-dose CYD-TDV mass vaccination campaign of 9- to 14-year-old children in three northern regions, expanded in July 2017 to Cebu Province, but was discontinued in December 2017 after the first dose had been administered.

Methods:

From 15 February 2018 to 28 February 2023, we conducted a multi-center case-control study in Cebu province to assess the effectiveness of a single-dose CYD-TDV against hospitalized VCD. Eligible children to receive the dengue vaccine in mid-2017 and admitted as suspected dengue were enrolled, collected with blood sample for dengue RT-PCR, obtained with clinical & socio-demographic information, and followed until discharge. Vaccination status were compared between VCD cases and neighbourhood controls of the same sex and age-group.

Results:

We included 584 VCD cases and 1168 controls in the analysis. Of the 584 case, 397(67.8%) presented as dengue with warning sign(DWS), 8(1.4%) had severe dengue (SD), and 1(0.2%) died. All dengue virus serotypes were detected, but serotype 3 was the most common (287/584, 49.1%). One dose of CYD-TDV was associated with 21% (95%CI:-7 to 41%; p=0.1129) overall protection against hospitalized VCD and 31% (95%CI: 6 to 49%; p<0.0001) protection against more severe presentations of dengue during the 5-year period following vaccination.

Conclusion:

A single dose of CYD-TDV conferred 31% protection against DWS and SD for at least five years. The study is limited by an absence of pre-vaccination dengue serostatus of the participants but majority in this age group and location are likely dengue seropositive.

037 Baseline innate immune gene expression is reprogrammed by dengue virus infection

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a. Hansi Dean and Ralph Braun were employees of Takeda Vaccines, Inc. at the time this research was conducted.

Background:

Infection elicits adaptive memory responses against the pathogen and, in some cases, trained immunity through reprogramming of innate immune cells. Human dengue virus (DENV) infection mostly targets myeloid-derived cells such as monocytes and macrophages. However, the impact of DENV infection on innate immune cells has never been investigated.

Methods:

Two independent human volunteer cohorts were used to demonstrate that DENV infection can lead to long-lasting reprogramming of immune gene expression. Bulk whole blood RNA sequencing was conducted to determine differences in baseline gene expression.

Results:

This reprogramming differentiates the innate immune response to live attenuated tetravalent dengue vaccination, in vaccine recipients with or without prior DENV infection. Several gene modules uniquely found in baseline seropositive individuals after vaccination correlated with neutralizing antibody titers measured at one year after the first of a two-dose vaccination regime. Remarkably, we found that DENV infection but not live attenuated dengue vaccination reprograms gene expression of innate immune markers including those implicated in dengue pathogenesis and disease severity.

Conclusion:

Our findings suggest a hitherto unknown but lasting effect of DENV infection on the innate immune system that impacts vaccination outcome and potentially also secondary dengue pathogenesis.

038 Genomic Surveillance of Dengue Virus in Jambi, Indonesia: Insights from 10 Years Longitudinal Study

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3. Eijkman Research Center for Molecular Biology, National Research and Innovation Agency, Indonesia.

Background:

Dengue virus (DENV) surveillance is critical for monitoring the virus serotype and genotype. Serotype distribution is known to be dynamic, with shifts often associated with outbreaks and increased disease severity. Previously, DENV-1 was reported as the dominant serotype in Jambi, Sumatra, but subsequent studies have been lacking. This study aims to monitor changes in serotype and genotype distribution a decade after the last surveillance.

Methods:

Sera from suspected dengue patients were tested for the NS1 antigen and IgM/IgG antibodies. Serotyping was performed using RT-PCR, while genotype determination involved sequencing of envelope genes. Additionally, clinical, hematological, and demographic data were recorded.

Results:

A total of 206 samples were collected between 2018-2020 with an additional 435 collected in 2023-2024. DENV-1 was the dominant serotype in 2014-2015. Interestingly, DENV-3 was the dominant serotype found both in 2018-2020 and 2023-2024 samples. All other serotypes were detected in the 2018-2020 cohort and no DENV-2 was detected in 2023-2024. Genotype analysis confirmed that DENV-1 (genotype I), DENV-2 (Cosmopolitan), DENV-3 (genotype I), and DENV-4 (genotype II) have been circulating in Jambi since 2015, with new lineages emerging in the phylogenetic tree. Notably, clade replacement was observed in DENV-1 with previous strains from 2014-2015 was no longer dominant.

Conclusion:

Our study reports a DENV serotype shift and the introduction of new lineages in Jambi after a decade. This study highlights the dynamic nature of serotype distribution over time and the significance of surveillance in endemic regions. Continuous DENV surveillance is vital for predicting future DENV transmission patterns.

039 Assessing the Cost Effectiveness of Dengue Vaccination with TAK-003 as Part of the National Immunization Program in Indonesia

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5. Takeda Pharmaceuticals International AG, Zürich, Switzerland

Background:

Dengue fever, a mosquito-borne viral disease, poses a significant public health burden in Indonesia. The TIDES program evaluated the efficacy, safety and immunogenicity of a novel vaccine candidate, TAK-003, in >20,000 children and adolescents in eight dengue-endemic countries across Asia and Latin America. TAK-003 is approved in Indonesia for the prevention of dengue disease for people aged 6-45 years. The purpose of this study was to assess the public health impact and cost-effectiveness of TAK-003 as part of the national immunization program in Indonesia.

Methods:

We developed a static model with a dynamic component, incorporating various vaccination strategies for routine and catch-up cohorts aged 9 to 12, simulated over a 20-year period (time horizon varied in sensitivity analyses). We estimated infections and hospitalizations avoided, and associated costs from both payer and societal perspectives, compared to a scenario with no vaccination. We assessed the incremental-cost-effectiveness ratio (ICER) using cost per Disability-Adjusted Life Year (DALY) averted as the outcome measure with model inputs and assumptions varied in sensitivity analyses.

Results:

All vaccination strategies demonstrated cost savings (dominance) from both a payer and societal perspective and substantial public health benefit through reductions in dengue cases and hospitalizations. In the routine vaccination strategy of 9-year-olds the relative reduction in hospitalizations were estimated to be 57%, which increased to 60%-66% across the 4 catch-up cohorts examined.

Conclusion:

The inclusion of TAK-003 to Indonesia's national immunization program may offer an opportunity to deliver public health benefits and achieve cost savings for both payers and society.

Funding: Takeda

040 Reported mosquito control strategies implemented in rural households in Cebu, Philippines

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Institutions and Country: Institute of Child Health and Human Development, National Institutes Health- University of the Philippines, Manila (Philippines)

Background:

Dengue is an acute febrile illness transmitted by the female *Aedes aegypti* and other mosquito species. Vector control remains the primary method of dengue prevention. We compared the reported mosquito control strategies implemented in households of children who were virologically confirmed dengue (VCD) and those who were non-VCD in the rural communities in Cebu, Philippines.

Methods:

We analysed data on reported vector control strategies collected as part of an observational study (ClinicalTrials.gov, NCT038303618).

Results:

We included data from 1,752 households. Overall, the most common vector control strategies in these households were disposal of stagnant water (594/1,752, 33.9%), burning of mosquito coil during daytime (887/1,752, 50.6%) and use of chemical repellent (262/1,752, 15.0%). Other interventions such as recent fogging in the neighbourhood (1,174/1,752, 67.0%), burning of dried leaves (363/1752, 20.7%), and cleaning the house/surroundings (18/1752, 1.03%) were also reported.

Conclusion:

Based on these current practices, there is a strong need for the implementation of evidence-based vector control interventions.

041 Genomic Surveillance of Dengue Virus in Patients Admitted to a Teaching Hospital in Kuala Lumpur, Malaysia from 2022 to 2023.

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4. Hospital Canselor Tuanku Muhriz, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

Background:

Malaysia is a dengue hyper-endemic country with all four serotypes of dengue virus (DENV) circulating simultaneously. In our pilot study, it was found that DENV4 was the most prevalent in 2022. Thus, this study aims to assess the serotype trends of dengue infections in the teaching hospital, Hospital Canselor Tuanku Muhriz (HCTM).

Methods:

Serum samples of NS1-positive dengue patients were collected from April 2022 until December 2023. Viral RNA was extracted using Qiagen Viral RNA Extraction Kit. cDNA was synthesized using the ReverTra Ace cDNA Synthesis Kit. Multiplex PCR was performed using EasyTaq PCR reagents with a universal forward primer and four virus-specific reverse primers, each with a final concentration of 200 µM. The band was visualized using gel electrophoresis for DENV1 (493bp), DENV2 (148bp), DENV3 (291bp), and DENV4 (408bp).

Results:

From 312 viral RNA samples, 80 samples (25.6%) were successfully serotyped. Seventy-four samples were monotypic infections whilst 6 samples were coinfection. In monotypic infection, the most prevalent serotype is DENV2 (n=56, 70.0%), followed by DENV4 (n=17, 21.3%), DENV1 (n=8, 10.0%) and DENV3 (n=5, 6.3%). For the coinfection, the number of cases for DENV1/DENV2 (n=2, 2.4%), DENV1/DENV3 (n=2, 2.4%) and DENV2/DENV4 (n=2, 2.4%). In 2022, DENV4 (n=10, 13.5%) is the dominant serotype but DENV2 (n=42, 56.8%) replaced DENV4 in 2023 to become a dominant serotype.

Conclusion:

In this preliminary study, DENV2 successfully displaced DENV4 to become the predominant serotype in 2023.

Keywords: dengue, surveillance, serotypes, Malaysia

042 Seroprevalence of neutralizing antibodies against DENV-1 and DENV-4 among patients admitted to a teaching hospital in Kuala Lumpur

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Background:

Dengue is a public health problem in Malaysia since 1902. All four serotypes of dengue virus (DENV) co-circulate in Malaysia with an incidence rate of 80.7 per 100,000 population in 2021. Previous studies reported that more than 90% of the Malaysian adult population were dengue seropositive. Nonetheless, studies on neutralizing antibody levels against all four serotypes in the Malaysian population still lacking. This study aims to determine the presence of neutralizing antibodies against DENV-1 and DENV-4 in dengue patients admitted to a teaching hospital, Hospital Canselor Tuanku Muhriz (HCTM) in Kuala Lumpur.

Methods:

A total of 445 serum samples from dengue patients admitted to HCTM from 2021-2024 were used in this study. Presence of neutralizing antibodies against DENV-1 0144 strains and DENV-4 TVP360 strains was determined using plaque reduction neutralization assay. Patient socio-demographic data were collected via medical records. Data analysis was performed using chi-square and logistic regression, and p-value<0.05 was considered significant.

Results:

Of 445 serum samples, 149 primary dengue infections and 296 secondary dengue infections. Majority of them are male (n=232, 52.1%), aged 18 – 35 years (n=179, 40.2%) and Malay (n=272, 61.1%). In primary dengue infection patients, 83.9% and 65.1% have neutralizing antibodies against DENV-4 and DENV-1, respectively. In secondary dengue infection patients, 98.3% and 96.3% have neutralizing antibodies against DENV-1 and DENV-4, respectively. Type of dengue infection was associated with age (p<0.001)

Conclusion:

In this preliminary study, majority of primary dengue infection patients had neutralizing antibody against DENV-4 than DENV-1 because DENV-4 is predominant serotype in 2021.

Keywords: antibody, dengue, primary, secondary, serotype

043 An Epitope-Directed Discovery of Potently Neutralizing Antibodies with Minimal Infection Enhancement Activity

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Background:

The envelope protein domain III (EDIII) of dengue virus is known to be a target of various potently neutralizing antibodies. 3H5 is a mouse anti-EDIII that binds to the lateral-ridge region and shows potent neutralization of the dengue virus with negligible antibody-dependent enhancement (ADE) activity. We aimed to engineer an EDIII antigen that selectively displays 3H5 epitope to investigate whether other antibodies binding to the same region as 3H5 exhibit similar neutralization potency with minimal ADE.

Methods:

We genetically introduced engineered N-glycosylation sites onto the surface of dengue serotype 2 EDIII to shield other known EDIII epitope, which are either associated with ADE or exhibit low-to-moderate neutralization, enabling selective display of the lateral-ridge binding epitope of 3H5.

Results:

The resulting glycosylated EDIII was successfully used as a bait antigen to select scFv antibodies that bind to the same epitope region as 3H5 (on-site) from a dengue-immune scFv-phage library. In contrast, a parallel selection using a wild-type non-glycosylated EDIII antigen failed to identify on-site scFv. Additionally, the selected on-site antibodies were shown to possess potent neutralizing ability, while minimally enhancing infection, similar to the template antibody, 3H5.

Conclusion:

These results indicate the potential use of this glycosylated EDIII as a dengue immunogen to selectively elicit antibody responses toward a desired neutralizing epitope of the dengue virus. Furthermore, the scFv-phage selection also demonstrates the advantage of using a 'focused' antigen in an epitope-directed antibody discovery campaign.

044 Dengue virus diversity in a prospective phase 0 study of dengue infection in Nha Trang, Vietnam

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Background:

Dengue disease is caused by dengue viruses (DENV-1–4). Viral diversity across and within serotypes impacts disease outcomes and efficacy of interventions such as vaccines. Our previous viral genomic sequencing work demonstrated that these viruses persist over many years despite mosquito control measures highlighting uninterrupted viral transmission chains even when the reported dengue incidence was low.

Methods:

Whole blood was collected in Paxgene RNA stabilisation vacutainers from index cases and household contacts enrolled in this prospective phase 0 study of DENV infection in Nha Trang, Vietnam (April 2022–February 2023). Total RNA was extracted and a pan-dengue RT-qPCR was performed to identify samples for DENV whole genome sequencing. A DENV capture-sequencing protocol was deployed, together with library preparation followed by Illumina MiSeq sequencing. An analytical pipeline was developed to enable high-quality consensus genomes for phylogenetic analysis.

Results:

From 130 index cases and 301 of their household contacts, to date, DENV RNA was detected by RT-qPCR in 51 participants and 29 DENV whole genome sequences were obtained. Based on phylogenetic analysis, 10 DENV-1 Genotype I infections were identified, 17 DENV-2 Genotype II Cosmopolitan, and 2 DENV-4 Genotype I. DENV-1 and DENV-4 genomes closely matched our previous study conducted from 2016–2019, the DENV-2 Genotype II Cosmopolitan strains showed more divergence, possibly because of a new introduction.

Conclusion:

The complex dynamics of viral diversity, as observed in Nha Trang, highlight the challenges to tackle dengue and the need for an integrated approach of antivirals, vaccines, vector control, diagnostics, and community involvement.

045 Electrolyte and metabolic abnormalities and dengue severity in adults

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Background:

Dengue is a major public health problem in the tropical and subtropical regions of the world. Patients with dengue are susceptible to dehydration because of high fever, vomiting, anorexia and diarrhoea during the febrile phase. The risk of hospitalization increases with reduced oral fluid intake and promoting a high fluid intake at home could help reduce the need for hospitalization.

Methods:

We conducted an observational study involving 585 suspected dengue patients who sought treatment in the University of Malaya Medical Centre between October 2017 and March 2021. A targeted history of oral intake was obtained, assessed as a percentage of the baseline. The first blood biochemistry upon presentation to hospital till 24 hours post admission was obtained. These included serum sodium, potassium, urea and glucose level, and urine ketones. The primary outcomes were electrolyte and metabolic abnormalities and final dengue severity.

Results:

502 adults with laboratory confirmed dengue were included in the analysis.

Significant associations between significant ketonuria with reduced food intake below 50% of usual, hyponatremia with nausea and myalgia, significant ketonuria with anorexia, nausea, vomiting, mucosal bleeding, chest discomfort, lethargy and myalgia; hypoglycemia with vomiting, and hyperuremia with anorexia were observed. These electrolyte and metabolic abnormalities were significantly associated with dengue severity.

Conclusion:

Hyponatremia is the most common electrolyte abnormality while significant ketonuria is the most common metabolic abnormality among dengue patients. These, including hypokalemia and hyperuremia were significantly associated with dengue severity. Prevention of these abnormalities should be the focus of management during the febrile phase.

046 Prospective Phase 0 Study of Dengue Infection in Index Cases and Household Contacts in Nha Trang - Vietnam

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Background:

Dengue is a global health concern, with half of the world population at risk of infection and no antiviral available. This Phase 0 study investigated potential dengue transmission between index case (IC) and household contacts (HHCs) and assessed operational feasibility of a Phase 2 trial for the novel JNJ-1802 dengue antiviral.

Methods:

The study was conducted in Nha Trang, Vietnam (April 2022–February 2023). Dengue ICs were identified within 72 hours after self-reported onset of fever. Their adult HHCs with no dengue signs and symptoms were enrolled within 48 hours of a dengue-confirmed IC. Blood samples and questionnaires were obtained twice a week for four weeks and a follow-up visit took place at day 40. Dengue virus RT-qPCR, NS1 and anti-DENV IgM/IgG ELISA were performed to assess characteristics of dengue transmission.

Results:

Of the 301 enrolled HHCs, 91.7% (276/301) completed 10 follow-up visits. At baseline, all HHCs were asymptomatic, of which 87.4% (263/301) had a prior dengue infection based on anti-DENV IgG and 1 HHC was DENV RNA-positive.

During follow-up visits, 5 HHCs (1.7%) had DENV infection based on virology parameters: Two participants became positive for only DENV RNA, 1 participant for both DENV RNA and NS1 and 2 participants became positive for NS1 only. IgG seroconversion was detected in 6.0% (18/301).

Conclusion:

Operational feasibility of a dengue index case design for the Phase 2 study was demonstrated. With blood sampling twice a week, dengue transmission was detected in 1.7% (based on virology) to 6.0% (based on serology) infections.

047 Assessing the contribution of NK cells in vaccine efficacy

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Background:

The quality and quantity of innate immune responses are known to influence the adaptive immune response and outcome of the vaccine. However, the role of natural killer (NK) cells in vaccine outcomes is poorly understood as these cells are challenging to handle, and represent a minority among the peripheral blood cells. To investigate in greater detail, we curated a NK cell pathway database with information on the genes involved in various NK cell subsets and functions. Furthermore, we explored how the NK cell pathways are altered by vaccines and how these pathways impact vaccine efficacy.

Methods:

To build the NK cell pathway database, we combined the NK cell related genes and pathways from the Blood Transcription Modules, MSigDB, single-cell RNAseq databases and existing literature. We then used the NK cell pathway database to determine the NK cell involvement in response to different vaccines. Finally, we leveraged on a RTS,S malaria vaccine challenge study to understand whether NK cell pathways can influence vaccine efficacy.

Results:

The database consists of 185 NK-cell related pathways, and cluster analysis revealed that there were no highly overlapping pathways. Flow cytometry confirmed the results obtained from the NK-cell related pathway analysis, where the live-attenuated Yellow Fever vaccine (YFV) was shown to induce CD56dimCD16hi NK cell subset activation both transcriptional and translational levels. Interestingly, different types of vaccines and adjuvants induced different numbers and types of NK cell pathways. Viral vector vaccines were found to be associated with the greatest increase in NK cell responses while toxoid vaccines were associated with the least. Finally, using the RTS,S malaria vaccine challenge study, we observed that the greater NK cell activation and stress was negatively associated with vaccine efficacy. These results indicate that exaggerated NK cell responses may reduce vaccine efficacy.

Conclusion:

Our findings suggest that the extent of NK cell activation and stress may influence vaccine efficacy.

048 Association *Salmonella typhi* coinfection based on Tubex reactivity in dengue patient with dengue severities: focusing in TNF-α, IL-6, TLR-4 and TLR-6 plasma level

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Background:

Indonesia is an endemic area of dengue virus (DENV), typhoid, malaria, leptospirosis and other arboviruses. Therefore, the possibility of coinfection in DENV patients can occur. Co-infections may lead to severe manifestations, missed or delayed diagnosis and treatment of DENV infection. The aim of this study is to define incidence of coinfection in DENV patients with Salmonella typhi in Bengkulu, Sumatera, Indonesia 2020. In addition, we also evaluated characteristics of immune responses in coinfection DENV patients with different disease severities.

Method:

Adult subjects more than 16 years old with fever and other clinical symptoms of DENV less than 3 days were included in this study. DENV infection was confirmed by NS1 antigen test and RT-PCR. DENV disease severity was classified into DD and DHF based on hematocrite value. Tubex TF were conducted to confirm Salmonella typhi infection in the convalescent phase. The examination of TNF-α, IL-6, TLR-4, and TLR-6 was performed by ELISA method..

Result:

Sixty-three subjects met the study criteria and DENV-2 was the most dominant serotype. Monoinfection and coinfection cases were found in 24 subjects and 39 subjects respectively. The levels of IL-6, TLR-4, and TLR-6 in the monoinfected and coinfected groups showed significant differences.

Conclusion:

Coinfection caused an increasing in plasma IL-6, TLR-4, and TLR-6, whereas TNF-α and IL-6 caused more severe disease in DENV patients.

049 Assessing the Public Health Impact of Dengue Vaccination in Indonesia: A Mathematical Modeling Approach

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Background:

This study evaluates the potential impact of dengue vaccination programs in Indonesia, focusing on identifying effective implementation strategies for children aged 1 to 18 years old.

Methods:

An aged-structured serotype-specific dynamic transmission model for dengue was developed and calibrated using age-stratified seroprevalence data from Indonesia (2014), while also considering the dengue virus (DENV) serotypes prevalent. Various vaccination scenarios were examined by systematically varying assumptions regarding vaccine efficacy against symptomatic infection (VES, 50-90% for each serotype), asymptomatic infection (VEA, 15-81% for individual serotype, proportional to VES), vaccine coverage rate (VCR, 50-90%), vaccine duration of protection (VD, 5-20 years), and vaccination targeted age (VTA, 1-18 years). A total of 122,473 scenarios were evaluated. The main outcome is cumulative dengue cases over 20 years since the start of a vaccination program.

Results:

Across all scenarios and serotypes, the effectiveness of dengue vaccination decreased as VTA increased. Compared to no vaccination, the most effective scenario (VES: 90%; VEA: 90%; VCR: 90%; VD: 20 years; VTA: 2-year) could prevent approximately 177.85 million cumulative infections (56.50% reduction in all cases). The reduction varied slightly by serotype: DENV1 (R01: 3.1, 63.14%), DENV2 (R02: 3.6, 56.23%), DENV3 (R03: 2.7, 78.79%), and DENV4 (R04: 2.2, 77.39%), where R0i represents the basic reproduction number of DENVi. This scenario also could avert 47.50 million dengue symptomatic cases (31.66% reduction) and 7.50 million hospitalizations (3.26% reduction).

Conclusions:

Routine vaccination of young children with an effective dengue vaccine could lead to a substantial reduction in dengue cases across all 4 serotypes within two decades in Indonesia.

050 Olfactory response of laboratory strain *Aedes aegypti* and *Aedes albopictus* towards different attractive sugar baits (ASBs)

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Background:

The effective control of *Aedes* mosquitoes is increasingly challenging due to the presence of insecticide resistance in populations of mosquitoes. Hence, attractive toxic sugar baits can be used as an alternative strategy to insecticides. The introduction of suitable attractant into baits are very crucial since it will determine the number of mosquitoes attracted towards it.

Methods:

The testing of no-choice and choice assay by *Ae. aegypti* and *Ae. albopictus* towards different group of ASBs (mango, Chrysanthemum and mix) was performed. In addition, olfactory preference index by mosquitoes was calculated using preference index formula. Then, the obtained data was tested through independent t- test to determine the significant differences, ($p < 0.05$) between ASBs.

Results:

Both of the mosquitoes species showed repellency towards Chrysanthemum ASBs since the preference index in nochoice assay showed negative values, (-0.60, -0.56 and -0.78) for Ae.aegypti while (-1.00, -0.25 and -0.56) for *Ae. albopictus* respectively. However, the preference index towards mango and mix ASBs indicates positive values. For the choice assay in Ae. *aegypti*, the pairing of mango and mix ASBs shows statistically significant value ($p <0.05$) while in *Ae. albopictus*, the pairing of mango and flower showed ($p < 0.05$).

Conclusion:

This study had proved that mango as an effective attractant to attract the mosquitoes through olfactory response compared to other natural attractants. Thus, sustain released of the natural attractant odour can be a major part of the Attractive Toxic Sugar Bait in attract and kill mechanism to overcome mosquito-borne diseases in future.

051 Prior dengue infection and single-dose dengue vaccination on the risk of subsequent virologically confirmed dengue: A five-year prospective cohort study in Cebu, Philippines

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Background:

In 2016, a three-dose dengue vaccination program using CYD-TDV, Dengvaxia was implemented in high burden regions in the Philippines. The program extended to Cebu in 2017. Further analysis of CYD-TDV showed that an increased risk for severe dengue was seen among dengue-seronegative participants. Dengue vaccination was halted, offering one dose in Cebu. We assessed the effect of baseline dengue serostatus and CYD-TDV on subsequent risk of virologically-confirmed dengue (VCD).

Methods:

We enrolled 2,996 children in a prospective cohort study in Cebu. Baseline sera were collected and tested by indirect IgG ELISA and focus reduction neutralization test (FRNT). Receipt of CYD-TDV was ascertained through review of vaccination records. Active surveillance for acute febrile illness (AFI) was conducted from November 2017 - October 2023. Those who developed AFI were interviewed and blood drawn for dengue RT-PCR testing.

Results:

Baseline serostatus was determined: 320 (10.7%) dengue naïve, 292 (9.7%) monotypic, 2,384 (79.6%) multitypic. 60% received a single dose of CYD-TDV. Cumulative incidence for VCD was 1.02 cases/100 person-years. Crude and adjusted analyses showed that a single dose of CYD-TDV did not confer protection against VCD in children who were naïve or monotypic at baseline. One dose conferred significant protection against hospitalized VCD among multitypic at baseline: first 3 years, 70% (95%CI 20-88; p=0.017), 5-year follow-up period, 67% (95%CI 19-87; p=0.016).

Conclusion:

No protection was conferred from a single-dose of CYD-TDV with naïve or monotypic profile at baseline against VCD. One dose of CYD-TDV conferred significant protection against dengue hospitalization with multitypic profile.

052 Molecular Epidemiology and Seroprevalence of Dengue Virus in Bangka-Belitung, Sumatra Island, Indonesia within COVID-19 Pandemic

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Background:

Dengue virus infection is a major threat to global health with apparent increase in infections. In Indonesia, the molecular epidemiological study has been limited and mostly in Java Island, leading to insufficient visualizing data of DENV characteristics. Nevertheless, during COVID-19 pandemic, less DENV epidemiological study was conducted, providing a gap of information for this viral circulation. Characterization of DENV such as serotype, genotype and nucleotide substitutions will facilitate appropriate clinical management and vaccine strategy.

Methods:

A cross sectional design with consecutive sampling of DENV suspected patients from a private clinic and hospital in Bangka-Belitung, in 2020 – 2023 was used to determine characteristics of DENV during COVID-19 pandemic. Patients with fever and two or more clinical symptoms of DENV infection were included in this study. DENV infection was confirmed by NS-1 test in which positive samples were further analysed for DENV serotypes by RT-PCR, followed by envelope gene analysis for phylogenetic.

Results:

From a total of 93 suspected dengue infections, we found 57 Positive DENV by RT-PCR. DENV-3 is the most dominant serotype (38.71%) followed by DENV-1 (11.83%) which is concomitant with previous studies in Indonesia for its circulating serotype and hospital-based point of view. In comparison with past DENV in Indonesia, phylogenetic analysis of DENV-1, 2, 3, 4 within COVID-19 pandemic revealed those were clustered in a distinct but still in the same genotypes.

Conclusion:

This molecular epidemiology and seroprevalence data increase an overview of DENV circulating to help future mitigation and disease management in Indonesia.

053 A systematic review of dengue controlled human infection studies from 2000-2024

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Background:

Controlled human infection studies have emerged as key scientific tools for understanding the immunopathogenesis of selected infections and accelerating development of vaccines and therapeutics. There is great potential for a safe dengue controlled human infection model (D-CHIM) to advance the field.

Methods:

A systematic review of contemporary D-CHIMs was performed. A search string of published studies was developed and applied to the Embase and Medline databases on 1-Apr-2024. Studies reporting D-CHIMs were identified, and their methodology, characteristics and safety were compared. Studies solely of fully attenuated dengue vaccine strains were excluded.

Results:

Our search yielded 1034 results and 10 studies of D-CHIMs were identified. Cumulatively these enrolled 228 participants aged 18-50 years. All studies were performed in non-dengue endemic areas and enrolled only individuals with no history of prior dengue infections, confirmed by serological screening. Attenuated dengue strains covering DEN1-4 were utilised as the challenge agents: 6 using strains from the Walter Reed Army Institute of Research (WRAIR) and 4 from the National Institutes of Health (NIH). Participants were seronegative in 6 trials and included vaccinated participants in 4 trials. Viremia with clinical features of dengue were seen in 100% of seronegative participants and 0–83% of previously vaccinated participants and was strain-dependent. There were no serious adverse events or deaths in study participants, and only 9 (3.9%) participants met the protocol criteria for hospitalisation.

Conclusion:

D-CHIMs are a valuable and safe tool. Further work is needed to expand D-CHIMs to an endemic setting and to model secondary infections.

054 Development and validation of an in-house Dengue IgG ELISA to detect past dengue infections

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Background:

To understand the disease burden and plan future vaccine rollouts, it is important to determine the presence of past dengue (DENV) infections in individuals. Therefore, we sought to develop an in-house ELISA to detect past dengue infections.

Methods:

An-inhouse IgG ELISA was developed by coating the wells with DENV virus (DENV1-4) and was validated with the foci reduction neutralization test (FRNT) using 76 samples. Age stratified seroprevalence in 1374 children aged between 4 to 16 years in the Gampaha district in Sri Lanka was performed using the in-house ELISA and compared with the Panbio Dengue Indirect IgG ELISA.

Results:

The in-house ELISA gave a positive response to 35/35 of those who had a multi-typic infection and 13/17 with a monotypic infection, and a negative response in 18/24 (75%) inidviduals identified as negative, when compared with the FRNT (AUC= 0.87). The Panbio ELISA was carried out on 72 of these samples and using the manufacturers cut-off (<9 units) 10/16 of monotypic infections and 30/32 of the muli-typic samples were positive. With a cut-off value of <3 units (as suggested previously), the Panbio ELISA was positive for 14/16 monotypic infections and 32/32 multi-typic infections. The seropositivity rate of the 1374 samples with the in-house ELISA was 76.02% and the Panbio ELISA was 79.3%.

Conclusion:

The in-house ELISA was sensitive in identifying both monotypic and multi-typic dengue infections. The Panbio ELISA is less sensitive in identifying both monotypic and multi-typic infections at the manufacturer's cut-off, while the suggested cut-off is more sensitive.

055 Mosquito control products on the retail market in Gampaha District, Sri Lanka

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Background:

High dengue transmission in Sri Lanka demonstrates a need for new mosquito control products (MCPs). In addition to government dengue-control interventions, Sri Lanka has a considerable retail market for MCPs. Understanding which MCPs people currently use will help successful integration of new tools.

Methods:

This study presents findings from a 2023 retail audit of MCPs available for retail sale in Gampaha District, Sri Lanka. It was conducted as part of a cluster randomized controlled trial testing the efficacy of a spatial repellent (SR) for dengue control. While the SR itself is not currently envisioned as a retail product, the availability and use of other MCPs may affect community perception and acceptance. The study included a stratified random sample of 252 retail outlets drawn from 1,315 that sell or have recently sold MCPs. A structured questionnaire was used to collect data on sales trends, preferences, supply chains, pricing, and retailer views on demand.

Results:

Grocery and hardware stores most commonly sold MCPs. Mosquito coils are the most frequently purchased MCP, available in more than 70% of outlets. Vaporizers, aerosol sprays, and insecticide-treated incense sticks are also common. MCPs without insecticide are available and marketed as a health benefit. Over half of retailers report that consumers buy MCPs while shopping for other products, suggesting that mosquito protection is integrated into routine behavior. Price, seasonality, and advertising are main demand drivers.

Conclusions:

Programs integrating novel vector control tools will benefit by adapting to local preferences and market dynamics to increase acceptability.

056 A Comparison of Study-Based and Regional Surveillance for Dengue Fever in Cebu

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Background:

A robust surveillance system is essential to an effective dengue control program. Dengue surveillance in the Philippines is mainly passive reporting of dengue cases from disease reporting units nationwide. In comparison, disease surveillance from observational studies may be implemented actively through regular phone calls and disease reporting from rural health centers, barangay health stations, private clinics, and hospitals. Our report compared dengue surveillance data from an observational study against regional surveillance data from the Department of Health-Regional and Epidemiological Surveillance Unit 7 (RESU), focusing on Bogo and Balamban, Cebu.

Methods:

We reviewed RESU reports of dengue cases in Bogo and Balamban from 2017 to 2022. We also conducted acute febrile surveillance as part of a cohort study from the same areas and surveillance period. Data were analyzed and compared by age, sex, residence, and trends over time.

Results:

Between 2017 and 2022, the study-based surveillance detected 7,830 dengue cases, while RESU recorded 1,437 cases from Bogo and Balamban. The study-based surveillance revealed there were more dengue cases in Bogo (42.34%) than in Balamban (32.04%), in contrast to the RESU data, where there were more cases in Balamban (61.03%) than in Bogo (39.00%). In both surveillance data, the majority of cases were male children aged 6 to 10 years old. The study-based surveillance consistently captured higher reports of dengue cases during the surveillance period.

Conclusions:

Study-based surveillance identified higher dengue cases than regional surveillance. This affirms that enhanced strategies for dengue surveillance are important to improve case detection and monitoring.

057 TAK-003 Dengue Tetravalent Vaccine: An Integrated Safety Analysis by a Combination of Baseline Dengue Serostatus and Sex

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Background:

The tetravalent dengue vaccine TAK-003 has demonstrated efficacy in an ongoing phase 3 trial in dengue-naïve and -exposed participants. An integrated safety analysis (ISA) from this trial plus four other phase 2/3 placebo-controlled TAK-003 trials was conducted, stratified by the combination of baseline dengue serostatus and sex.

Methods:

This ISA evaluated adverse events (AEs) following TAK-003 or placebo dosing (two doses administered 3 months apart) in healthy participants 4–60 years old. Solicited local/systemic AEs within 7/14 days, respectively, unsolicited AEs within 28 days, and serious AEs (SAEs) up to 57 months post first dose were assessed.

Results:

21,790 participants received TAK-003 (male: seronegative, n=2210; seropositive, n=4928; female: seronegative, n=2262; seropositive, n=4880) or placebo (male: seronegative, n=1032; seropositive, n=2556; female: seronegative, n=1031; seropositive, n=2419); 476 participants had unknown serostatus. Female TAK-003 recipients reported solicited local AEs (seronegative: TAK-003=62.1%, placebo=32.9%; seropositive: TAK-003=43.1%, placebo=25.4%) 47–54% more frequently than their male counterparts (seronegative: TAK-003=40.3%, placebo=26.2%; seropositive: TAK-003=29.4%, placebo=22.3%) and, likewise, solicited systemic events (seronegative: TAK-003=55.2%, placebo=41.8%; seropositive: TAK-003=47.4%, placebo=40.0%) 25% more frequently than their male counterparts (seronegative: TAK-003=44.2%, placebo=42.3%; seropositive: TAK-003=38.0%, placebo=37.5%) after any dose. The most common local event was injection-site pain, whereas headache and myalgia were the most common systemic events. There were no clinically meaningful differences between subgroups for unsolicited AEs and SAEs. The most frequently reported unsolicited AEs and SAEs were in the infections and infestations category.

Conclusion:

TAK-003 was well-tolerated, with no clinically significant safety risks, irrespective of participants' baseline serostatus and sex.

Funding: Takeda.

058 Immunogenicity and Safety Following Co-administration of a Live, Attenuated Tetravalent Dengue Vaccine and a Recombinant 9-Valent Human Papillomavirus Vaccine in Healthy Participants Aged ≥9 to <15 Years in a Dengue Endemic Country

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Background:

The tetravalent dengue vaccine TAK-003 and the 9-valent human papillomavirus (9vHPV) vaccine regimens are complementary, with overlapping target age groups, potentially facilitating inclusion of TAK-003 into established immunization programs.

Methods:

This phase 3, open-label, clinical trial (NCT04313244), conducted in Thailand, investigated the immunogenicity and safety of co-administration of TAK-003 with 9vHPV in healthy participants aged ≥9 to <15 years. Participants were randomized 1:1 to Group 1 (9vHPV+TAK-003 Day 1, TAK-003 Day 90, 9vHPV Day 180) or Group 2 (9vHPV Days 1 and 180) and followed for 6 months after last vaccination. The primary objective was non-inferiority of the immune response to 9vHPV co-administered with TAK-003 compared with 9vHPV alone, assessed by immunoglobulin G for HPV Types 6, 11, 16, 18, 31, 33, 45, 52, and 58 at Day 210. The frequency and severity of solicited local/systemic adverse events (AEs) (within 7/14 days), unsolicited AEs (within 28 days), and serious AEs (throughout) were recorded.

Results:

Of 614 enrolled participants, 606 (98.7%) completed the trial and 477 (77.7%) were included in the per-protocol set (Group 1, n=242; Group 2, n=235). Non-inferiority (upper bound of 95% CI for the geometric mean titer [GMT] ratio [Group 2/Group 1] <1.5) was demonstrated for all HPV types. GMTs for HPV types ranged from 504.0-7777.7 in Group 1 and 561.0-7822.6 in Group 2 at Day 210. Most participants (99.6%) showed dengue tetravalent seropositivity at Day 120. No clinically relevant differences in AEs were observed between groups.

Conclusion:

These findings support the co-administration of the TAK-003 and 9vHPV vaccines.

Funding: Takeda.

059 A Methodological Approach to Measuring the Impact of TAK-003 in Dourados, Brazil: Optimizing Strategies for Public Health

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Background:

Takeda's tetravalent dengue vaccine TAK-003 has been approved by the Brazilian regulatory agency ANVISA, for the prevention of dengue disease in individuals aged 4–60 years. After approval, Dourados, in the state of Mato Grosso do Sul became the world's first city to implement a mass vaccination campaign targeting ~120,000 individuals between 4–60 years old. Aiming to measure the impact of the vaccine in reducing dengue incidence, an ongoing collaborative, observational, population-based study using national surveillance and vaccination data was planned. Here, we describe the study's methodology, including its programmatic steps and public health relevance.

Methods:

We conducted a collaborative assessment with multi-disciplinary researchers in Brazil to identify key programmatic areas for the successful implementation of the study.

These areas included: feasibility and site selection assessment, methodology selection, vaccination program implementation, and public health importance.

Results:

Identifying the public health problem, understanding the disease burden, local healthcare infrastructure, and strategic partnerships were crucial for a robust feasibility assessment. The selection of the analytical methods, such as time series analysis, was dependent on the national and local structure of the databases and data availability. Effective communication strategies and distribution channels were essential for increasing vaccination adoption and coverage, community mobilization, and sensitization.

Conclusion:

Implementing a vaccine impact study within an ongoing vaccination program requires thorough planning, execution, and analysis. Feasibility assessment, selection of analytical methods, having an early multi-stakeholder collaboration, and public health relevance are critical considerations during the planning stages of a study collecting real world data.

Funding:

This study was funded by Takeda Vaccines Inc. Medical writing support was provided by Excel Medical Affairs, and funded by Takeda.

060 Development of Single Round Infectious Pseudovirus of DENV-2 (Cosmopolitan strain) for a rapid Antibody-Dependent Enhancement evaluation.

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Background:

Antibody-dependent enhancement (ADE) has been hypothesized to be one of the factors for severe dengue development and is a possible hurdle dengue vaccine development. Previous study in Malaysia reported that patients infected by DENV-2 Cosmopolitan genotype significantly manifests severe dengue compared to other genotypes. Most reference lab uses DENV-2 New Guinea C (NGC) in their test for ADE. Thus, we try to examine the difference between DENV2 Cosmopolitan and NGC in their ADE profile by using a rapid ADE evaluation method using single-round infectious particles (SRIPs) in place of live dengue virus.

Methods:

SRIPs were generated by transfection of HEK293FT cells with plasmid encoding premembrane and envelope (prME) proteins from DENV2 Cosmopolitan or NGC, plasmid carrying yellow fever virus replicon containing luciferase gene, and plasmid expressing DENV1 capsid. Serum samples were incubated with the SRIPs to form immunocomplex before co-incubation with our in-house immortalized myeloid cell lines (referred to as Mylc cell lines).

Results:

Sequence analysing results revealed that there is a difference of 6.5% in the prME gene between the genotypes. We tested serum from healthy donor with dengue history, against DENV-2 Cosmopolitan or NGC SRIPs. ADE was observed when both SRIPs were used in experiments. Further analysis will be performed to determine if there is a difference in the magnitude of ADE between the two strains.

Conclusion:

We established SRIPs of DENV-2 Cosmopolitan and NGC genotype for ADE profiling. This is helpful for dengue surveillance, preparation for dengue outbreak and dengue vaccine development.

061 A Comprehensive Overview of Developing the Live-attenuated Dengue Vaccine, TAK-003

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Background:

Dengue cases are increasing, necessitating an urgent need for a safe and effective vaccine. However, developing a live-attenuated dengue vaccine has faced several challenges, such as inducing multi-faceted tetravalent immune responses, balancing safety/immunogenicity through optimal viral attenuation, and obtaining enough serotype-level data through long-term efficacy and safety analyses from different countries. We present an overview of Takeda's live-attenuated tetravalent dengue vaccine (TAK-003) development program and share approaches for overcoming key challenges.

Methods:

Extensive pre-clinical investigations and 19 clinical trials (28,175 participants, 1.5-60-years-old from 13 countries) supported TAK-003 development. Studies included analysis of vaccine formulation, dosing schedule, safety, and immunogenicity, ultimately leading to the pivotal phase III DEN-301 (NCT02747927) trial.

Results:

Initial studies confirmed genetic stability, optimal attenuation with acceptable reactogenicity, and balanced immunogenicity. The DEN-204 (NCT02302066) trial supported the two-dose schedule to maximize multivalent seroconversion in TAK-003 recipients. The DEN-301 trial showed that vaccine efficacy (VE) was 80.2% (95%CI:73.3-85.3) against virologically confirmed dengue (VCD) after 12 months (primary endpoint) and after 18 months 90.4% (95%CI: 82.6-94.7) against hospitalization. VE against VCD and hospitalization was comparable among dengue-naive and dengue-exposed vaccinees. Cumulative VE over 54 months was 61.2% (95%CI: 56.0-65.8) against VCD and 84.1% (95%CI: 77.8-88.6) against hospitalization, though variable by serotype. No clinically important safety signals, irrespective of baseline serostatus/age, were observed by integrated safety analysis.

Conclusion:

TAK-003, developed through extensive studies, showed acceptable reactogenicity, balanced immunogenicity, and prolonged efficacy and safety, addressing an unmet need for a dengue vaccine with no identified clinically important safety risks.

Funding: Takeda.

062 Design and Implementation of a Post-authorization Study of TAK-003: Vaccine Effectiveness Against Hospitalized Virologically Confirmed Dengue in a Pediatric Population (DEN-401)

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6. Takeda Pharmaceuticals (Asia Pacific) Pte, Ltd, Singapore
7. P95 Pharmacovigilance and Epidemiology Services, Leuven, Belgium

Background:

Dengue vaccine trials face challenges in obtaining sufficient data for all clinical endpoints for each serotype and serostatus. The tetravalent dengue vaccine TAK-003 has demonstrated safety and efficacy in the TIDES Phase 3 trial. Despite 4.5 years of follow-up with >20,000 participants, a knowledge gap remains on the efficacy against DENV-3 and DENV-4 in dengue-naïve participants due to the low circulation of these strains during the study. DEN-401, a multi-country study, has been designed to provide additional data in a post-authorization setting.

Methods:

DEN-401 will utilize a nested case-control design to evaluate the effectiveness of TAK-003 as part of a public vaccination programme on hospitalization due to virologically confirmed dengue (VCD), including severe dengue. Secondary objectives include evaluation of the effect of TAK-003 on hospitalized VCD by serotype and baseline serostatus. A cohort of 70,000 participants, age-eligible to be vaccinated with TAK-003 as part of a planned dengue public vaccination program, will be recruited, and baseline blood samples will be collected. Hospital-based active surveillance will ascertain hospitalized VCD. This study can only be implemented in strong collaboration with Ministries of Health and provincial health authorities in participating Southeast Asian countries.

Results:

Data collection is scheduled to begin by 2025 with a three-year study period. Results will be reported in 2029 following the formal end of data collection.

Conclusion:

The DEN-401 study, designed to address an important research question, will further expand our knowledge of the effectiveness of TAK-003 in preventing hospitalized dengue in the real-world setting.

Funding: Takeda.

063 Arbovirus seroprevalence and environmental risk factors amongst children living in informal urban settlements in Indonesia and Fiji

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Background:

Transmission of dengue, chikungunya, and Zika, viruses transmitted by *Aedes* aegypti and *Aedes* albopictus, have been increasing globally at alarming rates. Increasing temperatures, extreme weather events, and water insecurity increase *Aedes* spp. habitat suitability. The built environment and under-resourced water and trash management systems can further exacerbate the risk of *Aedes*-transmitted arboviruses.

Methods:

We conducted baseline dengue seroprevalence testing amongst children under 5 years old living in 24 informal settlements in Suva, Fiji tand Makassar, Indonesia hat were enrolled in a randomized control trial of a community-level water infrastructure intervention. Blood samples were collected in 2018 and 2019 and evaluated for dengue IgG using a commercial Abcam ELISA kit. Baseline individual and household survey data was evaluated as potential risk factors using univariate and multivariable regression models.

Results:

In Indonesia, dengue, chikungunya, and Zika seropositivity in children under 5 years old was 33%, 3%, and 2% respectively; in Fiji rate were moistest higher at 46%, 3%, and 9%. Dengue seropositivity was significantly associated with increased age in both Indonesia [OR 2.0; 95% CI 1.4-3.1] and Fiji [OR 2.9; 95% CI 2.1-4.2]. Trash collection was protective against dengue infection in Indonesia [OR 0.4, 95% CI 0.2-0.8] but not in Fiji [OR 1.1, 95% CI 0.5-2.5] Household flooding and housing construction were not found to be significant risk factors for infection.

Conclusion:

Arbovirus transmission is high in Indonesia and Fiji. Modifications to the build environment, such as improved trash disposal, may offer some opportunity to mitigate risk.

064 Spatial analysis and modelling of risk factors for dengue infection in the urban and semi-urban areas in Colombo, Sri Lanka.

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Background:

Many factors influence dengue transmission and infection rates, with significant variation in seroprevalence in different locations within the same geographical region. Therefore, we carried out a spatial analysis and modelling to identify risk factors associated with dengue infection, between an urban and semi-urban area in Colombo.

Method:

Dengue seropositivity rates were assessed by ELISA in 1298 individuals living in 492 households (263 urban and 229 semi-urban). Socioeconomic and household characteristics and anthropometric measurements of the individuals were recorded at the time of recruitment. Local spatial analysis was performed using the Getis-Ord statistic Gi*(d) in ArcGIS Pro version 3.2 at household level and socio-demographic and household variables were used for risk factor analysis.

Results:

Spatial statistics identified 11 hot spots, 4 within urban and 7 in semi-urban areas. 29/587 (4.94%) individuals from semi-urban and 31/680 (4.55%) individuals from urban areas were living within a hot spot household. Risk factors associated with living in a hot spot household were individuals aged 36-45 years ($p<0.001$), female gender ($p<0.001$), those who only had completed primary education ($p<0.001$), individuals with a formal job ($p<0.001$), and those who had central obesity ($p=0.01$). Household risk factors associated with being in a hotspot included using cement as floor material ($p<0.001$), clay roof tiles ($p<0.001$) and presence of sanitary sewer ($p<0.001$) as the drainage method.

Conclusion:

Individual and household risk factors associated with high dengue transmission show the complex dynamics of dengue transmission, which would help in designing targeted surveillance and dengue control programs.

065 Expressions of NFκB and TNF-α on Dengue Virus Serotype-1 Infected-PBMC Treated with Cassia alata Leaves Butanol Fraction

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Background:

The NFκB pathway activation during dengue virus (DENV) infection has been reported to induce the transcription of pro-inflammatory cytokines, including the regulation of TNF-α expressions. TNF-α emerges as a primary cytokine linked to blood vessel leakage, with its levels correlating with infection severity. Our previous study indicates that Cassia alata (CA) leaves butanol fraction holds promise as an antiviral agent (SI value of 18.67), but the anti-inflammatory activity has not been explored.

Methods:

This research investigates the anti-inflammatory effects of CA on DENV-1 infected PBMCs by quantifying mRNA expression through real-time PCR. The study employs DENV-1 IDS 11/2010 and PBMCs obtained from healthy donors, with testing conducted at two-time points (2 hours and 24 hours post-CA treatment).

Results:

NFκB expression showed stability at both 2 and 24-hour intervals, while TNF-a levels notably increased significantly after 24 hours. This implies that NFκB acts as an early responder, primarily functioning as a transcription factor during infection, whereas TNF-α expression persists for up to 24 hours post-infection. The administration of CA leaves butanol fraction 10.92 µg/mL 2 hours after infection downregulates the expression of transcription factor NFκB and cytokines TNF-α, 0.084-fold changes (7.85%) and 0.528-fold changes (22.61%), respectively. After 24 hours of CA treatment, NFκB downregulation was observed at 0.092-fold (8.54%), while TNF-α showed upregulation at 0.075-fold (1.32%). However, this downregulation/upregulation was not statistically significant.

Conclusions:

This study demonstrates that the C. *alata* leaves butanol fraction exhibits promising anti-inflammatory properties, suggesting its potential development as a therapeutic agent for inflammation associated to DENV-1 infection.

066 Pregnancy outcomes following unintentional exposure to TAK-003, a live-attenuated tetravalent dengue vaccine

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Background:

During development of a live-attenuated, tetravalent dengue vaccine (TAK-003), participants who were confirmed as pregnant prior to vaccination were excluded from all clinical studies, and despite measures to avoid pregnancy in the clinical studies, some participants became pregnant. We report pregnancy outcomes and neonatal adverse events following unintentional TAK-003 exposure during pregnancy.

Methods:

This post-hoc analysis comprised integrated data (cutoff: Aug-18-2023) from phase 2 and 3 TAK-003 clinical studies. Participants were considered "exposed" if their last menstrual period (LMP) date was within 6 weeks before vaccination up to the outcome of pregnancy. Pregnancies with unknown LMP date were excluded. Outcomes were summarized by vaccine administered (TAK-003 or placebo) and exposure status.

Results:

A total 375 and 182 pregnancies were reported by 344 TAK-003 recipients and 159 placebo recipients, respectively; 52 participants had >1 pregnancy. Most pregnancies occurred in the long-term follow-up period (up to 54 months) after vaccination in the DEN-301 study, and were considered not exposed. Of the 28 and 10 exposed pregnancies for TAK-003 and placebo recipients, respectively, 23 (82.1%) and 5 (50.0%) were live births, 2 (7.1%) and 2 (20.0%) were elective terminations, 3 (10.7%) and 2 (20.0%) were spontaneous abortions (unrelated to TAK-003 exposure), and 1 (10.0%, placebo) was an unknown outcome. No neonatal adverse events were attributable to TAK-003 exposure.

Conclusion:

The post-hoc integrated analysis did not reveal any evidence of increased adverse pregnancy or neonatal outcomes following inadvertent TAK-003 exposure.

Funded by Takeda.

067 Identification of asymptomatic secondary dengue infection rates in a cohort of individuals in urban and semi-urban areas Colombo, Sri Lanka

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Background:

While most primary dengue infections are asymptomatic, the risk of symptomatic infection is higher with secondary dengue infections (SDI). However, the factors leading to symptomatic SDI are not fully understood. Therefore, we sought to identify possible risk factors that contribute to asymptomatic and symptomatic SDIs.

Methods:

Paired serum samples collected in 2022 and 2023, from individuals 5 to 80 years, who tested positive for the presence of DENV-IgG (n=356) at the time of recruitment were included in the study. 142 individuals resided in urban areas and 214 in semi-urban areas. Serum was tested by an in-house DENV inhibition ELISA (iELISA) and a secondary infection was defined as a ≥ 4 fold rise in antibody titres between the samples.

Results:

28/356 individuals were identified as having had SDI during the year, with 18/142 (12.68%) of those from the urban area and 10/214 (4.67%) from the semi-urban area. In the urban areas 7/18 SDIs were identified in children aged 5 to 19, whereas in the semi-urban area, only 1/10 had evidence of a SDI. 6/10 identified SDIs were seen in adults >50 years of age in the semi-urban areas. 2/18 SDI in the urban areas and 1/10 SDIs resulted in symptomatic infections. Those who experienced SDI during the year had significantly lower baseline titres ($p<0.0001$) than individuals who were uninfected.

Conclusion:

A higher incidence of SDI were seen in urban areas in Colombo, especially in children. Lower antibody levels appeared to be associated with an increased risk of infection with DENV.

069 Spatial Analysis of *Aedes* Mosquitoes as Dengue Fever Disease Spread in Java Island Indonesia: Indonesia Vectora Special Research Report

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Abstract:

Dengue fever remains a significant health problem in Indonesia, especially in Java. One of the main factors contributing to the spread of DHF is the *Aedes* mosquito as the vector of the disease. Spatial analysis plays an important role in understanding the distribution pattern of *Aedes* mosquitoes and determining high-risk areas for DHF. This study aims to conduct a spatial analysis of *Aedes* mosquitoes that cause dengue in Java, Indonesia. The method involved spatial mapping of *Aedes* mosquito capture data, DHF incidence data, and environmental factors such as vegetation type, rainfall, and population density. The analysis showed a clear spatial pattern in the distribution of *Aedes* mosquitoes in Java. Areas with dense vegetation, high rainfall, and high population density tend to have a higher risk of *Aedes* mosquito spread and DHF incidence. This study makes an important contribution to understanding the distribution pattern of *Aedes* mosquitoes and the potential spread of DHF in Java. The findings can serve as a basis for more effective prevention policies and dengue control programs at the local and national levels.

Keywords : *Aedes*, Dengue, Spatial Analysis, Distribution Pattern, Risk Factor

070 Alert of possible Zika transmission triggered by wastewater and mosquito signals

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Background:

Since the first Zika outbreak in 2016 in Singapore, there had been no sustained transmission until June 2023, where a cluster of 15 cases was reported in Northeastern Singapore. To monitor the situation and mitigate further transmission, enhanced Zika virus (ZIKV) surveillance comprising case, mosquito and wastewater testing was implemented.

Methods:

Zika cases were monitored through the Ministry of Health. *Aedes* mosquitoes collected from the National Gravitrap surveillance system, and wastewater samples from the case locations and surrounding areas were screened for ZIKV RNA.

Results:

At the reported cluster, ZIKV was detected in mosquito pools (3/43; 7%), individual mosquitoes (3/82; 3.7%), and wastewater samples (13/503; 2.6%) collected from the vicinity; samples from other sites across the country were negative. The peak detection of signals in wastewater and mosquitoes coincided temporally with the peak in the number of cases. The subsequent waning of signals suggested effectiveness of control measures.

In February 2024, persistent ZIKV signals were similarly detected in a neighbourhood in Western Singapore, after a single case was reported. This prompted an alert to caution the public of potential Zika transmission in the area, and vector control efforts were intensified. ZIKV RNA was detected in mosquito pools (10/871; 1.1%) and wastewater samples (28/490; 5.71%) collected from the neighbourhood over 10 weeks before signals turned negative.

Conclusion:

Wastewater and mosquito surveillance of ZIKV provides non-intrusive situational monitoring. This is particularly useful for diseases such as Zika, which generally causes mild infections, but may cause severe outcomes including congenital Zika syndrome.

071 Long-term circulation of Dengue virus lineages causing successive outbreaks in Singapore

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Background:

Dengue virus (DENV) populations undergo constant lineage fluctuations, especially in hyperendemic settings, where four DENV serotypes co-circulate. Even though lineage replacements have been attributed to outbreaks, there is limited data on the contribution of pre-circulating, long-established virus lineages in a country to such replacement events.

Methods:

DENV genomic surveillance data from 2013 to 2023 were analyzed to determine the diversity, temporal dynamics and survival of the most common virus lineages associated with outbreaks in Singapore. Lineages were defined based on the genetic similarity and phylogenetic analyses.

Results:

Over 20,000 envelope gene sequences of four DENV serotypes were analysed. Lineages belonging to DENV-1 (genotype V), DENV-2 (cosmopolitan genotype) and DENV-3 (genotype III), but not DENV-4 were dominant during successive outbreaks in the study period. A lineage of DENV-2 cosmopolitan genotype demonstrated the longest period of survival (11 years) and was dominant during two major outbreaks in 2016 and 2019-2020. Even though DENV-3 (8 years) and DENV-1 (4 yrs) lineages demonstrated long-term survival, they could not sustain transmission long after the outbreaks primarily caused by respective lineages. High genetic diversity of each lineage suggested in-situ evolution and potential re-introductions.

Conclusions:

The findings showed that certain DENV lineages have the potential to maintain persistent transmission, and cause periodic and repetitive outbreaks. It is worth investigating whether the genetic diversity within such lineages drives vector and host transmissibility. Besides introductions, replacements may also occur among existing lineages, highlighting the importance of their regular monitoring.

072 Evaluation of a multiplex RT-PCR assay for the detection of Dengue, Zika and Chikungunya in clinical specimens

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Background:

Differential clinical diagnosis of Dengue (DENV), Chikungunya (CHIKV), and Zika (ZIKV) infection is challenging as they cause similar symptoms including fever, rashes, and myalgia. Effective diagnostic tests are therefore needed to differentiate the infections for accurate patient management and public health response. This study assessed the performance of the multiplex TaqMan™ Arbovirus Triplex Kit for the detection of DENV, CHIKV and ZIKV, using single-plex virus specific assays as a reference.

Methods:

Limits of detection (LOD) for the assays were first determined using serially diluted DENV-1 to -4, CHIKV, and ZIKV virus isolates. Positive (PPA) and negative percent agreement (NPA) between the tests were then calculated using 99 positive sera samples (85 DENV, 4 ZIKV and 10 CHIKV) and 29 febrile samples (tested negative for all 3 viruses).

Results:

Despite showing high concordance, the multiplex assay yielded a higher LOD than the virus-specific assay for all isolates except for DENV-2 and -4. The assay yielded 100% PPA and 100% NPA for CHIKV, DENV-1, -2 and -4 detection; 98% PPA and 100% NPA for DENV-3 detection; and 75% PPA and 100% NPA, for ZIKV, albeit based on a small sample size.

Conclusion:

The multiplex assay showed high specificity in detecting all six viruses but was 1-log less sensitive than the virus specific assays for DENV-1, -3, CHIKV and ZIKV. The kit has similar sensitivity for DENV-2 and -4. These results suggest potential use of the multiplex assay in differential laboratory diagnosis of Dengue, Chikungunya and Zika, although its utility would depend on the epidemiological backdrop of the population.

073 Impact of pre-existing cross-reactive antibodies on cyclic dengue outbreaks in the hyperendemic region of Bali, Indonesia

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Background:

The four serotypes of the dengue virus (DENV) cause a range of diseases ranging from mild fever to severe conditions. Understanding the immunological interactions among the four serotypes is crucial in comprehending the dynamics of serotype shifting during outbreaks in areas where all four serotypes co-circulate.

Methods:

Hence, we evaluated the neutralizing antibody and antibody-dependent enhancement responses against the four DENV serotypes using acute-phase plasma samples collected from 48 laboratory-confirmed dengue patients during a dengue outbreak in Bali, Indonesia in 2022. We employed single-round infectious particles to exclusively investigate immunogenicity to the structural surface proteins of DENV, which are the targets of antibodies.

Results:

We found that individuals with previous DENV-1 infection exhibited increased susceptibility to secondary DENV-3 infection, attributed to cross-reactive antibodies with limited neutralizing activity against DENV-3 (geometric mean 50% neutralization titer ($GMNT_{50}$) = 47.6 ± 11.5). This susceptibility was evident in vitro, with a mean fold enhancement of 28.4 ± 33.9. Neutralization titers against DENV-3 were significantly lower compared to other serotypes (DENV-1 $GMNT_{50}$ = 678.1 ± 9.0; DENV-2 $GMNT_{50}$ = 210.5 ± 8.7; DENV-4 $GMNT_{50}$ = 95.14 ± 7.0).

Conclusions:

We demonstrate that prior immunity to one serotype provides limited cross-protection against the other serotypes, influencing the dominant serotype in subsequent outbreaks. These findings underscore the complexity of dengue immunity and its implications for vaccine design and transmission dynamics in hyperendemic regions.

075 Climate-driven variation in mosquito density predicts the spatiotemporal dynamics of dengue

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Background:
Dengue is a climate-sensitive mosquito-borne disease with increasing geographic extent and human incidence. Although the climate–epidemic association and outbreak risks have been assessed using both statistical and mathematical models, local mosquito population dynamics have not been incorporated in a unified predictive framework.

Methods:
Here, we use mosquito surveillance data from 2005 to 2015 in China to integrate a generalized additive model of mosquito dynamics with a susceptible–infected–recovered (SIR) compartmental model of viral transmission to establish a predictive model linking climate and seasonal dengue risk.

Results:
We found a significant association between mosquito density and local climate conditions in the previous month. Our climate-driven models thus accurately characterize human risk across a range of magnitudes indifferent years and cities, including the large outbreak in Guangzhou in 2014. Seasonal variation in R0 shows that the epidemic season lasts for 4–5 mo, typically starting in May and ending in the middle of September to October.

Conclusion:
The findings illustrate that spatiotemporal dynamics of dengue are predictable from the local vector dynamics, which in turn, can be predicted by climate conditions. Therefore, our integrated modeling approach improves inference on dengue transmission at the climate–epidemic interface.

076 Evolution of automated systems for large-scale rearing of male *Wolbachia-Aedes* mosquitoes for Project *Wolbachia*-Singapore

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Background:

Project *Wolbachia*-Singapore utilizes male *Wolbachia*-infected *Aedes aegypti* mosquitoes to suppress urban *Aedes aegypti* populations, the primary dengue vector in Singapore. Demonstrating promising results, residents staying at areas with at least one year of releases were up to 77% less likely to acquire dengue, while Ae. *aegypti* populations decreased by over 90%. To achieve wider coverage and sustain this feat, efficient and sustainable large-scale mosquito production is necessary.

Methods:

Nine automated modules were developed for various stages of mosquito production and release, including egg counting, hatching, larval rearing, feeding, pupal separation, counting, and adult mosquito release. Their uses were assessed for efficiency and productivity.

Results:

These modules significantly enhanced efficiency and productivity compared to manual methods. The hatching system reduced space usage by 15 times, water usage by 90%, and labor requirements by 80%. The automated larval counter enhanced productivity by 80 times, and the high-density rearing racks yielded a tenfold increase in yield with faster production cycles. Similarly, the automated feeding system increased productivity by 80 times while reducing labor by 90%. The pupal separation system achieved a high male pupae recovery rate (90%) with minimal female contamination (<0.1%). With the the pupae counter, a further 20-fold increase in productivity was obtained.

Conclusion:

These modules resulted in an 8-10 fold increase in production efficiency and productivity. Project *Wolbachia*-Singapore has developed and implemented innovative, automated mosquito production modules that significantly improved efficiency, productivity, and sustainability, enabling project expansion to benefit more residents. This achievement highlights the importance of interdisciplinary collaboration and innovation in tackling public health challenges.

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ADVA JA DENGUE SLAYERS CHALLENGE ABSTRACT

ADVA:*NexGen* Community Outreach & Education - Dengue Slayers Challenge

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Introduction:

The Asia Dengue Voice and Action (ADVA) Dengue Slayers Challenge, initiated following the ADVA Task Force Workshop during the 5th Asia Dengue Summit in 2020, aimed to enhance community participation and outreach in the fight against dengue. Collaborating with Junior Achievement (JA), this educational competition engaged students aged 16-19 from Indonesia, Malaysia, the Philippines, Singapore, and Thailand.

Challenge Methodology:

From January 2024 to May 2024, a total of 459 students the five countries, organized into 153 teams, participated in the challenge, which comprised preparatory workshops on Design Thinking and Pitching & Presentation, as well as mentorship to support their projects.

The challenge focused on three key areas: Outreach, Surveillance and Epidemiology, and Vector Control: Prophylaxis/ Prevention. The Design Thinking workshop provided students with a comprehensive understanding of the dengue epidemic, the competition's framework, and the necessary skills and tools. The Pitching & Presentation workshop aimed to enhance their presentation abilities.

Outcomes:

The desired outcomes of the ADVA-JA Dengue Slayers Challenge included raising awareness about the escalating dengue epidemic, reaching a vast youth audience through the ADVA and JA networks, and fostering a network of youths committed to ongoing engagement in dengue-related activities. Additionally, the challenge sought to collect extensive data on behavioural attitudes towards dengue in Asia for future longitudinal studies, emphasizing the collective effort required from students, healthcare professionals, and policymakers to control dengue's spread. The initiative also aimed to inspire participants to pursue careers in dengue-related fields and generate scalable, locally relevant solutions with demonstrable impacts on dengue prevention and control.

The challenge aspired to generate significant public relations opportunities to increase awareness of the event and its sponsors. Furthermore, it aimed to harness the learnings from dengue education to explore the potential for creating school-based dengue awareness programs.

In conclusion, the ADVA-JA Dengue Slayers Challenge 2024 successfully engaged students across multiple countries, fostering community participation and generating innovative solutions to combat dengue. The insights and experiences gained from this initiative will be instrumental in developing future community outreach and educational programs aimed at dengue prevention and control.

Acknowledgment:

We thank ADVA steering committee and advisors for their support and help with giving Dengue 101 to the youths, colleagues from JA Malaysia, Indonesia, Philippines, Singapore and Thailand in organising the country workshop and finals, mentors to guide the students and our sponsor Takeda for supporting this education initiative.

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