

MJPHM Official Journal of Malaysian Public Health Physicians' Association

The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference

Embracing the New Era: Advancing Public Health Through AI and Digitalisation

8th - 10th July 2025 The Everly Putrajaya

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TABLE OF CONTENTS

ORAL PRESENTATION: EPIDEMIOLOGY (COMMUNICABLE/NON- COMMUNICABLE DISEASE)

PRESENTATION ID	TITLE	PAGE
EPIDOP01 / 251	Development, Validation and Usability Testing of "Wabak X" Card Game: A Serious Game on Disease X and Outbreak Preparedness for the Orang Asli in Selangor Ameerah Su'ad Abdul Shakor, Mariam Mohamad, Khalid Ibrahim, Izandis Mohamad Sayed	33
EPIDOP02 / 270	A Comparative Study of XGBoost, SVM, and Random Forest for Hypertension Risk Prediction Among Malaysian Adults <u>Ridwan Sanaudi</u> , Muhd Zulfadli Hafiz Ismail, Zamtira Seman, Evi Diana Omar, Hasnah Mat, Asyraf Syahmi Mohd Noor, Yusrina Mohd Yusoff, Anis Syakira Jailani, Munerah Mohamad Zaman, Ainil Zafirah Abd Karim, Nabilah Hanis Zainuddin, Najjah Tohar, Zurina Razalee, Nik Noor Syamimi Ismail, Mohd Azahadi Omar	37
EPIDOP03 / 292	Factors Associated with Tuberculosis Recurrence in Besut, Terengganu - A Case Control Study Mardhiyyah Azmi, Hafizuddin Awang, Mohd Anuar Abd Rahman, Kasemani Embong	41
EPIDOP04 / 299	Depression among Tuberculosis Patients in Sarawak Zulkifli Mohd Nor Faizal, Sahak Noorzilawati, Saimon Rosalia	44
EPIDOP05 / 318	A Competing Risk Analysis of Cardiovascular Events among People Living with HIV - Early Findings from CardHIV Study Hoon Shien Teh, Kim Heng Tay, Yvonne Mei Fong Lim, Su Lan Yang, Wen Yea Hwong	49
EPIDOP06 / 324	Epidemiology of Measles and Factors Associated with Laboratory-Confirmed Measles in Johor Bahru from 2020 until 2024 Md Faizul Abd Razak, Haidar Rizal Toha, Muhammad Saffuan Azli	52
EPIDOP07 / 325	Prevalence and Risk Factors of Cataract Formation in Diabetic Patients in Johor Bahru: A Population-Based Analysis Loganathan Salvaraji, Haidar Rizal Bin Toha, Ng Wei Meng	56
EPIDOP08 / 334	Leading Causes of Death among Children Aged 0-14 Years in Malaysia: A Comparison between 2019 & 2023	61

111d1d 01 1 1 1 1 1 1 1 1	
The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on	
Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putraj	aya

	<u>Tham Sin Wan</u> , Khaw Wan-Fei, Nazirah Alias, Nur Hamizah Nasaruddin, Nur Diyana Rosnan, Wan Kim Sui, Mohd Azmi Suliman, Shubash Shander Ganapathy, Mohd Azahadi Omar	
EPIDOP09 / 342	Modelling Dengue Incidence and Its Association with Temperature in Johor Bahru, Malaysia <u>Nur Sujaihah Hanafi</u> , Akashah Abdullah, Luqmanul Hakim Junaidden, Haidar Rizal Toha	64
EPIDOP10 / 347	Assessing the of accuracy of Artificial Intelligence Diagnostic in Tuberculosis screening: Sensitivity and Specificity in Rural Sarawak Melvin Chung Hsien Liang, Teo Jia Chi, Nurul Amirah Masani, Lai Kah Sheng, Ooi Mann Chek	67
EPIDOP11 / 363	Towards a Mentally Healthier Nation: Expert Consensus on a Depression Intervention for Patients in Primary Care <u>Asma' Khalil</u> , Zahir Izuan Azhar, Chen Xin Wee, Norley Shuib	70
EPIDOP12 / 389	Understanding the Home Tobacco Environment among Non-Tobacco Users in Malaysia: Insights from the National Health and Morbidity Survey 2023 Mohd Ruhaizie Riyadzi, Hamizatul Akmal Abd Hamid, Halizah Mat Rifin, Thamil Arasu Saminathan, Tania Gayle Robert Lourdes, Hasimah Ismail, Wan Kim Sui, Kishwen Kanna Yoga Ratnam, Joan Sonny Limbowoi Saimin, Norhafizah Sahril, Muhammad Fadhli Mohd Yusoff	74
EPIDOP13 / 390	When a Permanent Solution is Taken for a Temporary Problem: Exploring the Demographics of Suicide Mortality <u>Shubash Shander Ganapathy</u> , Wan Kim Sui	78
EPIDOP14 / 391	Antimicrobial Resistance Trends of Gram-Negative Infections in Malaysia: 2018 - 2022. <u>Audrey Huili Lim</u> , Norazida Ab Rahman, Hana Farizah Zamri, Murnihayati Hassan, Rohaidah Hashim, Sheamini Sivasampu, Peter Seah Keng Tok	81
EPIDOP15 / 396	Prevalence of Albuminuria in Malaysia: Early Signs of Kidney Damage in Diabetic and Non-Diabetic Populations <u>Tania Gayle Robert Lourdes</u> , Thamil Arasu Saminathan, Mohd Azmi Suliman	86
EPIDOP16 / 403	Delay In Diagnosis Among Dengue Cases In Perak: A Seven Year Retrospective Analysis Nur Intan Kartiniewatie Kamaruddin, Mohd Fadhli Samsuri	89

The	12th National Public	Health Conferenc	e in conjunc	ction with 26th	NIH Scient	ific Confer	ence on	
Embracing th	ne New Era: Advancin	g Public Health Th	nrough Al an	d Digitalisation	n, 8-10 July	2025, The	Everly Pu	<u>trajaya</u>

EPIDOP17 / 408	Prevalence of Chronic Kidney Disease in Malaysia: Findings from the MyCKD 2024 Study <u>Thamil Arasu Saminathan</u> , Sunita Bavanandan, Loh Chek Loong, Muhammad Fadhli, Mohd Azmi bin Suliman, Tania Gayle Robert Lourdes, Halizah Mat Riffin, Hasimah Ismail, Esther Tan Zhao Zhi, Irene Wong, Hamizatul Akmal Abd Hamid, Noor Ani Ahmad	92
EPIDOP18 / 411	Invisible Exposure: Epidemiologic Clues from a Mucormycosis Outbreak in a Maternal and Child Centre in East Coast of Peninsular Malaysia Noorfariza Nordin, Hasniza Abdullah, Azmani Wahab, Suhaiza Sulaiman, Nor Zubaidah Kadir, Radhiah Abu Bakar	94
EPIDOP19 / 439	Advancing Community-Based Diabetes Self-Screening: A Hypothetical AI-Driven Risk Prediction Model Using National Health Surveillance Data Che Muhammad Nur Hidayat Che Nawi	98
ORAL PRESENT FAMILY HEALTI	ATION: H / HEALTH MANAGEMENT	
FHHMOP01 / 174	Exploring Digitalisation Challenges in Implementing Integrated Care in Langkawi's Healthcare System <u>Devi Shantini A/P Rata Mohan</u> , Nur Azmiah Zainuddin, Tengku Mohamad Iskandar Tengku Mohamad Rosman, Sri Devi A/P Sukumaran, Mohd Suhaili Muhamed Shueib, Adlan Zafrulan Ismail	101
FHHMOP02 / 178	Geographic Information Systems (GIS) Mapping of Primary Care Services: Do Older Adults in Malaysia Have Equitable Access? <u>Suhana Jawahir</u> , Jabrullah Ab Hamid, Nur Elina Abdul Mutalib, Awatef Amer Nordin, Devi Shantini Rata Mohan, Adilius Manual, Iqbal Ab Rahim, Sarah Nurain Mohd Noh	104
FHHMOP03 / 189	Optimising Colorectal Cancer Screening in Malaysia: Are Screening Efforts Aligned with Disease Burden? (2014-2021) <u>Diane Woei-Quan Chong</u> , Vivek Jason Jayaraj, Fathullah Iqbal Ab Rahim, Nurul Athirah Naserrudin, Sharifah Saffinas Syed Soffian, Muhammad Fikri Azmi, Eliana Ahmad, Mohd Yusaini Mohd Yusri, Ahmad Shanwani Mohamed Sidek, Norfarizan Azmi, Rosaida Md Said, Muhammad Firdaus Md Salleh, Norasiah Abu Bakar, Hamiza Shahar, Rima Marhayu Abdul Rashid, Shazimah Abdul Samad, Zanita Ahmad, Mohd Safiee Ismail, Adilah A. Bakar, Nor Mashitah Hj Jobli, Sukumaran Raman, Nurulaisyah Hamzah, Mohd Yasin Raja Abdullah, Sondi Sararaks	108
FHHMOP04 / 229	Gender Disparities in Adolescent Health Risks: A Cross- Sectional Study in Tumpat, Kelantan	111

Malaysian southar of Fabric Health Medicine, vol. 25 (5appr 2) 2025	
The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on	
Embracing the New Era: Advancing Public Health Through Al and Digitalisation, 8-10 July 2025, The Everly Putraja	ıya

	<u>Mohamad Hafiz Harun,</u> Lailatul Nur Noor Azmi, Nabila Balqish Azahar, Aimi Fadilah Shariffuddin, Ahmad Firdaus Mohamed, Hasneezah Hassan	
FHHMOP05 / 231	Development of an Image-based Health Promotion Material to Cultivate Healthy Child Media Habits among Malaysian Toddlers <u>Catherine Thamarai Arumugam</u> , Nik Daliana Nik Farid, Mas Ayu Said	115
FHHMOP06 / 247	Title: Rheumatic Heart Disease Screening Among School Children at Primary Care Level in Tuaran: Task-Shifting Strategy using Hand-held Echocardiography and Risk Factor Analysis Hazeqa Salleh, Nasieha Saquenah binti Ribin	117
FHHMOP07 / 268	Kiambang Merah: Innovating Menstrual Care through Al and Digitalisation in Social Entrepreneurship for Public Health Nor Faiza Mohd. Tohit, Siti Athirah Zafirah Abd Rashid, Wan Farizatul Shima binti Wan Ahmad Fakuradzi, Nur Adnin Ahmad Zaidi	121
FHHMOP08 / 277	Establishing a Cardiac Arrest Registry to Improve Out-of-Hospital Cardiac Arrest (OHCA) Outcomes in Malaysia: A Step Towards Data-Driven Emergency Care Mohd Shahri Bahari, Leong Yuen Chin, Farhana Aminuddin, Sivaraj Raman, Mohd Shaiful Jefri Nor Sham Kunusagaran, Nur Amalina Zaimi, Tan Yui Ping, Ee Vien Low, Marhaini Mostapha, Nor Zam Azihan Mohd Hassan	124
FHHMOP09 / 289	Living in an Obesogenic Environment: Voices of Women of Reproductive Age - A Qualitative Exploration Nurul Farehah Shahrir, Noor Aman Hamid, Nur Nabila Abd Rahim, Zaiton Daud, Siti Harirotul Hamrok Asis, Rohana Abdul Jalil	127
FHHMOP10 / 295	From Policy to Delivery Rooms: Cascade of High-Risk Pregnancy Dynamics and Maternal Outcomes in Ningxia, Northwestern China Yang Xiali, Ning Yanhua, Tian Xiaojuan, He Ying, Nadzratulaiman Wan Nordin, Xin Wee Chen	130
FHHMOP11 / 310	Intimate Partner Violence and Child Maltreatment in Sarawak: Predictive Factors Among Men Siti Romahani Rahman, Md Mizanur Rahman	133
FHHMOP12 / 313	Patients' Perspectives on Good Quality of Care for Managing Diabetes, Hypertension and Dyslipidaemia: A Nominal Group Technique Approach Mohamad Zulfikrie Abas, Norshahiratul Atiqah Mohd Zaidi, Lee Pei Jia, Wan Kim Sui, Azah Abdul Samad, Chan Huan Keat, Sheamini Sivasampu, Ang Swee Hung	136

The 12th National Public Health Conference in	conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Throug	h AI and Digitalisation, 8-10 July 2025, The Everly Putrajay

FHHMOP13 / 319	Development of Public Health Law in Malaysia <u>Justen Han Wei Wong</u> , Tahir Aris, Ismuni Bohari, Mohd Zamre Mohd Zahir	139
FHHMOP14 / 329	Use of Generative Artificial Intelligence among Medical Doctors in Sarawak: An Application of the <i>Theory of Planned Behaviour</i> Wong Siaw Hui, Noorzilawati binti Sahak, Md Mizanur Rahman	142
FHHMOP15 / 362	From Buku Rekod to Mobile: Hajj Health Reimagined <u>Iesza Raihan Ali</u> , Sarah Idayu Mohd Abd Latiff, Vivek Jason Jayaraj, Salmiah Baharudin, Muhammad Shafiq Samsudin, Khairulaizat Mahdin, Maheshwara Rao Appannan	146
FHHMOP16 / 354	The Historical Launch of Virtual Clinic Services at Health Clinics in Ministry of Health Malaysia Kawselyah Juval, Nazrila Hairizan Nasir, Isabel Chung Yin Hooi	149
FHHMOP17 / 412	Unpacking EMR Experiences in Primary Care: A Qualitative Study Ariff Azfarahim Ibrahim , Mohd Rizal Abdul Manaf, Aniza Ismail, Rosnah Ismail, Ahmad Husni Ariffin	153
FHHMOP18 / 326	An Integrated Internal Audit on The Key Benefits of Digital X-Ray Services in Primary Healthcare Clinic <u>Dr. Kisheaan Devarajan</u> , Dr. Amirul Ameer bin Rashidan, Dr. Thava Viknaraj Sivabalan, Ms. Renugah Thevi Murugayah, Ms. Rachael Sharmini Rajendran	156
FHHMOP19 / 425	Advancing Public Health Disaster Management through Al and Digitalisation: Lessons from the Putra Heights Disaster <u>Ahmad Faizul Abd Rahman Sazli</u> , Nur Suhada Ramli, Sharifah Fazlinda Syed Nor, Norain Mansor, Anis Salwa Kamaruddin, Muhammad Fikri Azmi, Mohd Fathulzhafran Mohamed Hanan, Humadevi Sivasamy, Lalitha Malar Maniam, Mas Ahmad Sherzkawee Md Yusoff, Jamiatul Aida Md Sani, Mohd Shahrol Abd Wahil	159
ORAL PRESENT. OCCUPATIONAL HEALTH BEHAV	HEALTH/ ENVIRONMENTAL HEALTH/ SOC	IAL&
OECHODO1 / 190	Ollub 1 0. The Dayslanment of a Centralized Learning	142

OESHOP01 / 180 QHub 1.0: The Development of a Centralised Learning
Hub for Quality Improvement in Malaysia
Nur Ezdiani Mohamed, Samsiah Awang, Muhammad Maziz
Shamsuddin, Muhammad Nur Aiman Abdul Rauf, Izzahtul Afiqah
Kamarullail, Kelly Ngit Khang, Muhammad Izzuddin Abdul Khalid,
Fadzlena A. Rahim, Kavitha Vijayan, Zulqarnain Baharau, Asnida
Abu Bakar

<u>The 1</u>	<u> 2th National Public H</u>	ealth Conference i	n conjunction	n with 26th N	IIH Scientif	fic Conference o	<u>on</u>
Embracing the	New Era: Advancing	Public Health Thro	ugh Al and D	igitalisation,	8-10 July 2	2025, The Everly	<u>Putrajaya</u>

OESHOP02 / 181	The Manifestation of Work-related Fatigue among Scaffolders as Indicated by Physical and Cognitive Dimension: Objective Fatigue Assessment from a One Group Pre-Post Experimental Study Heng Pei Pei, Hanizah Mohd Yusoff, Mohamad Ridza Hj Illias, Saravanan Karrupayah, Muhammad Fadhli Mohd Yusoff, Norizzati binti Amsah Rozita Hod	165
OESHOP03 / 204	Body Weight Perception and Weight Control Behaviours among School-going Adolescents in Malaysia <u>Chan Ying Ying</u> , Norhafizah Shahril, Hamizatul Akmal Abd Hamid, Mohamad Aznuddin Abd Razak, Lim Kuang Kuay, Azli Baharudin, Kee Chee Cheong, Zamtira Seman, Mohd Azahadi Omar, Noor Ani Ahmad	172
OESHOP04 / 215	Spatial Distribution of Dietary Patterns and Its Association with Obesity Among Adults in Malaysia <u>Kimberly Yuin Y'ng Wong</u> , Sanjay Rampal, Foong Ming Moy	177
OESHOP05 / 216	Reimagining Environmental Health in the Digital Age: A Data-Driven Heat Health Warning System (HHWS) for Malaysia Hadita binti Sapari	181
OESHOP06 / 252	Discovering the Health Risks among Healthcare Workers: Prevalence and Its Associated Factors for Obesity in a Major Government Research Institute in Klang Valley, Malaysia Mona Lisa Md Rasi, Mohd Nizam Misran, Azra Abdul Aziz, Wan Afiqah Wan Sabri, Thanuja Narayanan, Rozilawati Jafri, Siti Haslina Othman, S Maria Awaluddin	184
OESHOP07 / 255	Sequential Food Poisoning Outbreaks in a Boarding School: Risk Factors and the Cloud Kitchen Risks Diana Raj, Chew Cheng Hoon, Shakirah binti Jamaludin, Anussa a/p Krishnan, Engku Norma binti Engku Aziz, Mohd Imran bin Mohammed Abdul Wahab, Noriah binti Ismail	190
OESHOP08 / 256	Machine Learning Identifies Autoantibody-defined Systemic Lupus Erythematosus Subgroups and Their Association with Clinical Manifestations Lay-Kim Tan , Ch'ng-Suyin Shereen, Norliza Zainudin, Ravathy Nasadurai, Habibah Mohd-Yusoof, Mollyza Mohd-Zain, Malek Faris Riza Feisal-Jeffrizal, Say-Lee Pok, and Fariz Yahya	193
OESHOP09 / 276	Development and Validation of an Educational Model for Adult with Allergic Rhinitis	

The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putrajaya

OESHOP10 / 290	Spatio-temporal Analysis of Leptospirosis Hotspot Areas and its Association with Hydroclimatic Factors in Selangor (2011-2019) and Developing a Predictive Model Muhammad Akram Ab Kadir, Rosliza Abdul Manaf, Siti Aisah Mokhtar, Luthffi Idzhar Ismail	199
OESHOP11 / 296	Enhancing Ergonomic Risk Prediction: Modifying The National Institute for Occupational Safety and Health (NIOSH) Lifting Equation with Individualised Data Inputs Noor Adillah Dawad, Siti Munira Yasin, Azlan Darus, Ahmad Taufik Jamil, Nyi Nyi Naing	202
OESHOP12 / 303	Validation of the Integrated Palliative Care Outcome Scale (IPOS) - Malay Version Diana Katiman, <u>Wen Jun Wong</u> , Hadhinah Ahmad Puaad, Wen Yea Hwong, Teoh Cy Oun	206
OESHOP13 / 306	Low Back Pain Among Medical Laboratory Technologists: Associating Factors and Ergonomic Risk Assessment Imanul Hassan Abdul Shukor, Mohd Faiz Ibrahim, Siew Wei Fern, Kamal Haikal Mat Rabi, Nurul Farehah Shahrir, Rohaida Ismail	209
OESHOP14 / 322	Modifying Effects of Temperature on PM _{2.5} -Related Hospital Admissions in Klang Valley, Malaysia Mohd Faiz Ibrahim, Rohaida Ismail, Nik Muhammad Nizam Nik Hassan, Nor Zam Azihan Mohd Hassan, Farhana Aminuddin, Sarah Saizan, Fawzi Zaidan Ali, Halmy Sirat	213
OESHOP15 / 330	Translation and Validation of the Motivation Thought Frequency Scales for Alcohol (MTF-A) into an Indigenous Language (Jakun Version) Rifhan Rasuli, Aimi Nadira Mat Ruzlin, Mariam Mohamad	217
OESHOP16 / 338	Exploring Barriers in Anticipatory Guidance Practices on Oral Health for Toddlers Among Dental Therapists <u>Susan Shalani Gnanapragasam</u> , Aznilawati Abdul Aziz, Wan Nadzirah W Pauzi, Nurul Adila Mat Dait, Farhani Md Azizan	221
OESHOP17 / 359	Understanding Service Uptake and Eye Health Inequities in Machang's B40 Community <u>Noor Halilah Buari</u> , Nur Izzah Afifah Shahrir, Nur Suhailah Alias, Sabrina Subri	225
OESHOP18 / 419	Vision impairment among Urban School Children: Socioeconomic Barriers to Eye Health in Kuala Lumpur Naufal Nordin, Mohd Helmi Abu Yahya, Noor Haziq Saliman	227
OESHOP19 / 429	Awareness and Knowledge of Childhood Eye Problems among Special School Teachers in Selangor Sabrina Subri, Nur Suhailah Alias, Noor Halilah Buari	232

E-POSTER PRESENTATION: EPIDEMIOLOGY (COMMUNICABLE/ NON-COMMUNICABLE DISEASE)

EPIDPP01 / 179	Insights for COVID-19 Booster Dose Acceptance in Kolkata, India: A Regional Cross-sectional Study Abhishek Lachyan , Min Fui Wong, Indranil Saha, Vivek Jason Jayaraj	237
EPIDPP02 / 197	Unmasking Susceptibility: HBV in Malaysia's Vaccinated Population, A Cross-Sectional Study from National Health & Morbidity Survey 2020 Filza Noor Asari, Eida Nurhadzira Muhammad, Nurfatehar Ramly, Mohd Hatta Abdul Mutalip, Muhammad Faiz Mohd Hisham, Chong Zhuo Lin	241
EPIDPP03 / 205	Association between cardiovascular disease and cataract: A meta-analysis <u>Jun Fai Yap</u> , Pei Pei Heng, Wan Nur Syamimi Wan Mohamad Darani, Halizah Mat Rifin, Nor Asiah Muhamad, Muhammad Fadhli Mohd Yusoff	246
EPIDPP04 / 209	Multimorbidity among Reproductive-Aged Women: A Nationwide Cross-Sectional Study in Malaysia Siti Hafizah Zulkiply	250
EPIDPP05 / 218	Effectiveness of WhatsApp Messaging Health Education on Uncontrolled Type 2 Diabetes Mellitus Patients - A Cluster Randomized Controlled Trial Alif Ramli, Fredie Robinson, Carol Lim Kai Joo, Nirmal Kaur, Balachandar S. Sayapathi, Anisah Jantim, Ismail Lasa, Norimah Yusof, Mohd Hafizuddin Ahmad, Noriah Mahmud, Mohd Anuar Abd Rahman	259
EPIDPP06 / 219	Depression Among Malaysian Adults: A Sociodemographic Comparison Between NHMS 2019 and NHMS 2023 Mohamad Aznuddin Abd Razak, S Maria Awaluddin, Norlaila Hamid, Wan Sarifah Ainin Wan Jusoh	263
EPIDPP07 / 220	Prevalence and Determinants of Anxiety in Individuals with Type 2 Diabetes Mellitus: Evidence from a Cross-Sectional Study in Southern Malaysia Norizzati Amsah, Zaleha Md Isa, Norfazilah Ahmad, Zaid Kassim	267
EPIDPP08 / 223	Prevalence and Associated Factors of Metabolic Syndrome Among Teachers in Peninsular Malaysia: The CLUSTer Cohort Study Chong Chean Tat, Moy Foong Ming	270
EPIDPP09 / 224	Epidemiology and Predicting Mortality in Melioidosis Patients in Sandakan, Malaysia <u>Mohamad Hafiz Mohamad Nasir</u> , Mohd Faiz Gahamat, Nafsah Dulajis, Aima Bungsu, Saint Alvendy Daraim, Rowena Jamilus, Hafiez Syam Basrin, Muhammad Jikal	274

The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putrajaya

EPIDPP10 / 232	A case study of the implication of World Health Organization (WHO) position on TAK-003 dengue vaccine to Malaysia Chong Zhuo Lin	277
EPIDPP11 / 235	Prevalence And Associated Factors Among Overweight and Obese Adults with Hypertension in Malaysia Nor Azian Mohd Zaki, Khairul Hasnan Amali, Syafinaz Sallehuddin, Kishwen Kanna Yoga Ratnam	281
EPIDPP12 / 237	Assessing Cardiovascular Diseases Mortality in Malaysia, 2023 <u>Nazirah Alias</u> , Nur Hamizah Nasaruddin, Khaw Wan-Fei, Tham Sin Wan, Wan Kim Sui, Shubash Shander Ganapathy, Mohd Azahadi Omar	285
EPIDPP13 / 240	Prevalence and Determinants of Obesity Among Individuals with Diabetes in Malaysia: Findings from the National Health and Morbidity Survey 2023 Hasimah Ismail , Thamil Arasu Saminathan, Zamtira Seman, Halizah Mat Rifin, Tania Gayle Robert Lourdes, Hamizatul Akmal Abd Hamid, Mohd Ruhaizie Riyadzi, Azli Baharudin, Muhammad Fadhli Mohd Yusoff	288
EPIDPP14 / 242	Prevalence of Abdominal Obesity and Its Associated Factors Among Malaysian Adults: Insight from the National Health and Morbidity Survey (NHMS) 2023 Azii Baharudin , Khairul HasnanAmali, Hamizatul Akmal Abd Hamid, Nor Azian Mohd Zaki, Muhammad Fadhli Mohd Yusoff, Thamil Arasu Saminathan, Hasimah Ismail, Syafinaz Mohd Sallehuddin, Lalitha Palaniveloo	292
EPIDPP15 / 243	Ethnic Disparities and Intervention Gaps in Glycemic Control: A Cross-Sectional Study of Known Diabetes Cases Nurul Huda Ibrahim, Halizah Mat Rifin, Wan Kim Sui, Hamizatul Akmal Abd Hamid, Hasimah Ismail, Thamil Arasu Saminathan, Muhammad Fadhli Mohd Yusoff	295
EPIDPP16 / 244	Delayed Dengue Diagnosis in Batang Padang District, Perak: A 2024 Study <u>Muhamad Isa Abdul Aziz</u> , S Maria Awaluddin, Chong Zhuo Lin, Mohd Hatta Abdul Mutalip, Tuan Mohd Amin Tuan Lah, V C Anuratha, Nur Fatihah Shaharuddin	299
EPIDPP17 / 250	Depression and Its Links to Physical Activity, Sedentary Behaviour, and Weight Status in Malaysian Adolescents: A Cross-Sectional Study Norhafizah Sahril, Norliza Shamsuddin, Wan Sarifah Ainin Wan Jusoh, Norlaila Hamid, Ahmad Ali Zainuddin, Noor Ani Ahmad	303

The 12th National Public Health Conference in	conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Throug	h AI and Digitalisation, 8-10 July 2025, The Everly Putrajay

EPIDPP18 / 258	How Age and Employment Status Influence on E-Cigarette Use in Malaysia? <u>Mohd Hazrin Hasim @ Hashim</u> , Mohd Ruhaizie Riyadzi, Tuan Mohd Amin Tuan Lah, Thamil Arasu Saminathan, Muhammad Fadhli Mohd Yusoff, Norliana Ismail, Mohd Hairul Nizam Abd Hamid, Ummi Nadiah Yusoff, Noraryana Hassan, Nizam Baharom	307
EPIDPP19 / 261	User acceptance of the DMOSS Dengue Forecast Model in Malaysia <u>Sarbhan Singh</u> , Lim Mei Cheng, Nuur Hafizah Md. Iderus, Sumarni Mohd Ghazali, Mohd Nadzmi Md Nadzri, Asrul Anuar, Mohd Kamarulariffin Kamarudin, Nur Ar Rabiah Binti Ahmad, ,Chew Cheng Hoon, Balvinder Singh Gill, Chong Zhuo Lin, Wan Ming Keong, Kok Keng Tee, Lokman Hakim Sulaiman, Teh Chien Huey	311
EPIDPP20 / 264	The Prevalence of Hypertension and Its Associated Risk Factors among Indigenous Adults in Malaysia: Findings from the National Health Survey 2022. Kishwen Kanna Yoga Ratnam, Mohd Azmi Suliman, Hamizatul Akmal, Mohammad Aznuddin Abd Razak, Wan Kim Sui, Khairul Hasnan Amali, Thamil Arasu, Tania Gayle, Halizah Mat Rifin	314
EPIDPP21 / 266	Implementation Of Community - Base Rheumatic Heart Disease Screening At Primary Care Facilities in Penampang District: Pilot Project From Sabah, Malaysia Pee Nai Eng, Sam Froze Jiee, Lim Kai Joo, Aini Simon Sumeh, Anisah Jantim, Siva Rao Muniandy, Elron Alpero	317
EPIDPP22 / 278	Predicting Multimorbidity Using Machine Learning: Insights from NHMS 2019 <u>Ainil Zafirah Abd Karim</u> , Ridwan Sanaudi, Muhd Zulfadli Hafiz Ismail, Zamtira Seman, Evi Diana Omar, Hasnah Mat, Munerah Mohamad Zaman, Asyraf Syahmi Mohd Noor, Anis Syakira Jailani, Nabilah Hanis Zainuddin, Mohd Azahadi Omar	320
EPIDPP23 / 280	Mental Health Predictors Among Public Sector Workers at the National Institutes of Health, Selangor <u>Puteri Sofia Nadira Megat Kamaruddin</u> , Mona Lisa Md Rasip, Mohd Nizam Misran, Azra Abdul Aziz, Wan Afiqah Wan Sabri, Thanuja Narayanan, Rozilawati Jafri, Siti Haslina Othman, Mohd Safwan Ibrahim, Shazana Rifham bt Abdullah	323
EPIDPP24 / 304	Multiagency Responses in Managing Leptospirosis Outbreak at A Recreational Site in Perak <u>Abdulloh Mazalan</u> , Hairunnisa Hashami, Husna Maizura Ahmad Mahir, Raja Muhammad Raja Omar, Noor Hidayah Mohd Yasin, Nurul Syariah Shafiin, Ahmad Fahmi Rashid Redza	327
EPIDPP25 / 308	Prevalence and Factors Associated with Pre- Hypertension among Adults in Malaysia <u>Hamizatul Akmal Abd Hamid</u> , Halizah Mat Riffin, Lim Kuang Kuay, Tania Gayle Robert Lourdes, Mohd Ruhaizie Riyadzi, Azli Baharudin, Muhammad Fadhli Mohd Yusoff	329

	The 12th Nation	al Public Health	Conference	in conjunctio	n with 26th	NIH Scien	tific Co	nference o	<u>n</u>
Embraci	ng the New Era:	Advancing Publi	c Health Thr	ough AI and D	igitalisation,	8-10 July	2025,	The Everly	Putrajaya

EPIDPP26 / 311	A Wake-Up Call on Adolescent E-Cigarette Use in Malaysia <u>Muhammad Fadhli Mohd Yusoff</u> , Mohd Ruhaizie Riyadzi, Tania Gayle Robert Lourdes, Hamizatul Akmal Abd Hamid, Thamil Arasu Saminathan	333
EPIDPP27 / 320	Sex Differences in Years of Life Lost in Malaysia, 2023: A Burden of Premature Mortality Khaw Wan-Fei, Nazirah Alias, Tham Sin Wan, Nur Hamizah Nasaruddin, Nur Diyana Rosnan, Wan Kim Sui, Mohd Azmi Suliman, Shubash Shander Ganapathy, Mohd Azahadi Omar	338
EPIDPP28 / 323	Epidemiological Characteristics of Hepatitis B Notifications in Kinta District, Perak, Malaysia, 2024 Lai Yeng Chow, Pathma Reddy, Gregory Xavier	341
EPIDPP29 / 331	Influenza B Outbreak Report at The Hostel of Sekolah Menengah Kebangsaan Tinggi Setapak, Kuala Lumpur <u>Puteri Sofia Nadira Megat Kamaruddin</u> , Shazana Rifham Abdullah, Mohd Safwan Ibrahim	344
EPIDPP30 / 333	Urban-Rural Disparities in Overall Disability among Malaysian Adults: Findings from the National Health and Morbidity Survey 2023 Norliza Shamsuddin, S Maria Awaluddin, Siti Hafizah Zulkiply, Nor'Ain Ab Wahab, Norzawati Yeop, Hashimah Ismail, Halizah Mat Ripin, Muhammad Fadhli Mohd Yusoff	347
EPIDPP31 / 339	The Impact of TB Anatomy on the Duration of Treatment: An ANCOVA Approach Controlling for Age Siti Romaino Mohd Nor, Nyi Nyi Naing, Mat Zuki Mat Jaeb	350
EPIDPP32 / 340	Impact of Diagnostic Delay on Melioidosis Mortality in Sandakan: A Call for Early Detection Strategies Nafsah Dulajis, Mohamad Hafiz Mohamad Nasir, Aizuddin Hidrus, Mohamad Faiz Gahamat	353
EPIDPP33 / 341	Prevalence of Dual Tobacco Users and Sources of Access among Adolescents in Malaysia: Findings from the National Health and Morbidity Survey 2022 Mohd Firdaus Razali, Mohd Ruhaizie Riyadzi, Hamizatul Akmal Abd Hamid, Khaw Wan-Fei, Lim Kuang Kuay	356
EPIDPP35 / 344	Thalassaemia in Sabah: Insights from the Malaysian Thalassaemia Registry Hadhinah Ahmad Puaad, Wen Jun Wong, Gek Bee Ong, Yee Leng Lee, Su Lan Yang, Wen Yea Hwong	360
EPIDPP36 / 346	Systematic Review on Predictors of Smoking Cessation Success Among Adults in Malaysia	364

The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putraja

	Nur Fadzlyanah Khusaini, Chin Ri Wei Andrew, Mohammad Azri Bantalani, <u>Muhammad Aklil Abd Rahim</u>	
EPIDPP37 / 352	Urban-Rural Variation in Predicting Depression Among Elderly Using Naïve Bayes Classifier Nabilah Hanis Zainuddin, Ridwan Sanaudi, Ainil Zafirah Abd Karim, Zamtira Seman	368
EPIDPP38 / 353	The Proportion and Determinants of Incomplete Treatment Among Latent Tuberculosis Infection in Tumpat District, Kelantan, Malaysia <u>Hasneezah Hassan</u> , Ahmad Firdaus Mohamed, Mohamad Hafiz Harun	371
EPIDPP39 / 356	Exploration of Klang's Health District Office Dengue Case Investigations in Relation to Hospital Tengku Ampuan Rahimah Serological Results Hazwa Harith, Nur Nabila Abd Rahim, Gurpreet Kaur Karpal Singh, Suvarna Mohan	375
EPIDPP40 / 358	Tuberculosis Among Orang Asli in Perak: A Cross Sectional Study from 2019-2023 Lau Kin Mun, Afzaninawati Suria Yusof, Adam Prakash Gunaselan, Suntharavalli Vadivalu, Husna Maizura Ahmad Mahir	380
EPIDPP41 / 364	Hypertensive Drug Utilisation and Polypharmacy Among Older Adults in Malaysian Public Primary Care <u>Mohd Shaiful Jefri</u> , Marhaini Mostapha, Rima Marhayu Abdul Rashid, Noor Haslinda Ismail, Sivaraj Raman, Farhana Aminuddin, Mohd Shahri Bahari, Nur Amalina Zaimi, Tan Yui Ping, Ee Vien Low ¹ Nor Zam Azihan Bin Hassan	384
EPIDPP42 / 368	Overweight And Obesity Among Orang Asli Proto Malay Adults In Malaysia <u>Khairul Hasnan Amali</u> , Azli Baharuddin, Ahmad Ali Zainuddin, Muhamad Khairul Nazrin Khalil	388
EPIDPP43 / 370	Determinants of Known Asthma Among Adults in Malaysia: Findings from the National Health and Morbidity Survey (NHMS) 2023 Joan Sonny Limbowoi Saimin, Shubash Shander Ganapathy, Halizah Mat Rifin, Wan Kim Sui, Kishwen Kanna Yoga Ratnam, Lim Kuang Kuay, Mohd Ruhaizie Riyadzi, Mohamad Aznuddin Abd Raza ¹ , Khairul Hasnan Amali, Muhammad Hanafi Bakri, Nurul Haniyah Rosslan, Nur Faraeein Zainal Abidin	394
EPIDPP44 / 375	An Appraisal Of Urban Malaria In Johor Bahru: Gametocyte Cases In 2024 Noor Adillah Dawad, Luqmanul Hakim Junaidden, Akashah Abdullah, Haidar Rizal Toha	398

The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putrajaya

EPIDPP45 / 379	Factors Associated with Tuberculosis (TB) Treatment Success among TB Patients in Kelantan; 3 Years Record Review 2021-2023 Siti Romaino Mohd Nor	402
EPIDPP46 / 381	Population-Based Thalassaemia Carrier Mapping in Malaysia: Insights from a Half a Decade of School-Based Screening <u>Don Ismail Mohamad</u> , Radziah Mohamad, Saidatul Norbaya B., Alisahkhairun Rahmat, Mohd Shahriel Mat Daud, Nurul Kausar Izzati Mohd Ghazali, Mardiana Omar	406
EPIDPP47 / 383	The Forgotten Pill? Lipid-Lowering Therapy Adherence at One Year After Acute Myocardial Infarction Hui Li Lim, Wen Jun Wong, Swee Hung Ang, Alan Yean Yip Fong, Gurudevan Mahadevan, Yvonne Mei Fong Lim	409
EPIDPP48 / 384	Concomitant Lymphatic Filariasis in Humans and Animals in Sabah: Findings from the SABAH-VI Baseline Study Mohd Hatta Abdul Mutalip, Khairiah Ibrahim, Rahmah Noordin, Nor Azlin Abdul Aziz, Sajidah Khadijah Meor Azlan, Eida Nurhadzira Muhammad, Faizul Akmal Abdul Rahim, Amierul Fikri Mahmud, Mohammad Ridhuan bin Mohd Ali, Emelia Osman	413
EPIDPP49 / 385	Persistence of Symptoms at 6 months Post COVID-19: A Cohort Study <u>Peter Seah Keng Tok</u> , Norazida Ab Rahman, Sheamini Sivasampu	417
EPIDPP50 / 388	Five-Year Comparative Analysis of Immunochemical Faecal Occult Blood Test Uptake and Its Predictors among Malaysian Average-Risk Population (2019-2023) <u>Wan Nur Syamimi Wan Mohamad Darani</u> , Thamil Arasu Saminathan, Halizah Mat Rifin, Muhammad Fadhli Mohd Yusoff	421
EPIDPP51 / 392	From Therapy to Threat: Legionellosis Outbreak at a Recreational Hot Spring in Melaka <u>Nur Aishah Buang</u> , Khairul Anuar Abdullah, Hafiz Idlan Radzali, Mohd Ridzuan bin Janudin, Siti Nadiah Mohamad Mohsin, Raziah Nordi, Ainur Nafisya Kamarolzaman, Adibah Ibrahim	425
EPIDPP52 / 405	Sociodemographic factors associated with multiple cardiovascular risk factors among adults in Malaysia: A gender-stratified analysis of the National Health and Morbidity Survey (NHMS) 2023 <u>Halizah Mat Rifin</u> , Wan Kim Sui, Hamizatul Akmal Abd Hamid, Tania Gayle Robert Lourdes, Mohd Firdaus Razali, Nurzaime Zulaily, Mohd Hatta Mutalip, Kimberly Wong Yuin Y'ng, Khairul Hasnan Amali	430
EPIDPP53 / 406	Pinpointing Locations And Time For Dengue Preventive Activities In Perak By Exploring Connections Between	434

		IVIGIO Y SIGIT SOGITI	ai oi i abiic ii	icaitii ivicaic	111C, VOI. 23 (3	<u>appi 2) 2023</u>		
	The 12th Natio	nal Public Health	Conference	in conjuncti	on with 26th I	NIH Scientific Co	onference on	1
Embraci	ng the New Era	: Advancing Publi	ic Health Thro	ough Al and	Digitalisation.	8-10 July 2025	. The Everly F	utraiava

	Populations Movements And Previous Dengue Trend Data. <u>Shaffik S</u> , Mohd Fadhli S, Thiruchelvam M, Husna Maizura AM	
EPIDPP54 / 421	Incidence and Factors Associated with Hospital Admission for Hand, Foot, and Mouth Disease (HFMD) in Segamat, Johor Mohamad Fazreen Mohamad Anuar, Mohd Ridzuan Mohd Lutpi, Mohammad Nafis Sahiran, Mohd Khairul Anwar Kamdi, Choo Teck Min, Norjanah binti Johari	436
EPIDPP55 / 427	Tuberculosis Outbreak Investigation at a Workplace in Cheras, Kuala Lumpur, 2024 <u>Mohamad Fazreen Mohamad Anuar</u> , Mohd Ridzuan bin Mohd Lutpi, Mohammad Nafis bin Sahiran, Mohd Khairul Anwar bin Kamdi, Choo Teck Min, Norjanah binti Johari	440
EPIDPP56 / 428	Smokers' Knowledge and Perception of Smoking Norzawati Yoep, Muhammad Faiz Mohd Hisham, Wan Kim Sui	443
EPIDPP57 / 430	The Hidden Epidemic: Leptospirosis Risk and Spread in Kinta District (2022-2024) <u>Zulaikha Abdul Razak, Gregory Joseph Xavier, Mohd Zamri Md Ali, Pathma Sree R, Vinothkumarthevar R</u>	447
EPIDPP58 / 435	Are Men Who Have Sex with Men (MSM) Driving the Shift in HIV Transmission Patterns in Larut, Matang and Selama District, Perak? - A Decade of Insights (2015-2024) Muhammad Naim Ibrahim, Mohd Najimi Ahmad, 'Ammar Amsyar Abdul Haddi, Syahrizal Abdul Halim, Husna Maizura Ahmad Mahir	451
EPIDPP59 / 436	Young, Bold and at Risk: A 10-Year Trend Analysis of Gonorrhoea and Acquired Syphilis in Larut, Matang and Selama District, Perak <u>Muhammad Naim Ibrahim</u> , Mohd Najimi Ahmad, Ammar Amsyar Abdul Haddi, Syahrizal Abdul Halim, Husna Maizura Ahmad Mahir	455
EPIDPP60 / 437	Unseen Chains of Transmission: A Pertussis Outbreak Among Schoolchildren Affecting a High-Risk Infant in Melaka <u>Abdul Ahmad Syafiq Hussein</u> , Ayuzeity Bistari Md Bukhori, Siti Nurbaya Abdul Aziz, Mohd Ridzuan Janudin, Nazirah A Hamid	459
EPIDPP61 / 446	Suppressing Dengue Through Wolbachia-Infected Aedes aegypti: Progress and Impact from a Community-Based Intervention in Melaka Tengah Adibah Ibrahim, Mohd Ridzuan Janudin, Sharifah Nur Shahirah Syed Abdul Halim, Noor Hazmi Noor Hassim, Rabizah Hamzah	463

The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putrajaya

EPIDPP62 / 365	Beyond the Virus: Did COVID-19 Spark a Rise in Autoimmune and Inflammatory Conditions? <u>Masliyana Husin</u> , Swee Hung Ang, Yvonne Mei Fong Lim, Xin Rou Teh, Vivek Jason Jayaraj, Shahanizan Mohd Zin, Santhi Subramaniam, Maheshwara Rao Appanan, Sheamini Sivasampu, Fahd Adeeb, Peter Seah Keng Tok	467
EPIDPP63 / 301	Incidence of Leptospirosis in Segamat District, Johor 2024 and Its Associated Risk Factors Choo Teck Min, Mohd Ridzuan Mohd Lutpi, Mohd Khairul Anwar Kamdi, Mohammad Nafis Sahiran, Nor Alia Nadhirah Ramli, Mohd Serajuddin Mohd Salleh, Ruhaizan Ruwandi	470
EPIDPP64 / 395	Overweight, Obesity, and Hypercholesterolemia Among Adults in Malaysia: Findings from the National Health and Morbidity Survey (NHMS) 2023 (Non-Communicable Disease) Syafinaz Mohd Sallehuddin, Khairul Hasnan Amali, Nor Azian Mohd Zaki, Ruhaya Salleh, Halizah Mat Rifin	473
EPIDPP65 / 401	Improving Diabetes Mellitus Care in Primary Health Clinics in Kuala Lumpur Through Clinical Audit of Diabetes Mellitus Waramlah Ramlan, Jaysina Ayu Jaafar Siddek, Haliza Abd Manaf	476
EPIDPP67 / 424	Dengue Trends in Petaling District, Malaysia: A 2023-2024 Analysis Nor Izyani Bahari, Mas Ahmad Sherzkawee Mohd Yusoff, Jamiatul Aida Md Sani, Junisha Hani Baharudin	480
EPIDPP68 / 433	Dysentery Under the Microscope: A Study from Kuala Krai Sarah Saizan, Siti Salimah Yusoff, Hazura Mat Zubir	484
EPIDPP69 / 434	An episode of food poisoning outbreak: Salmonella, are you the culprit? <u>Mohd Adlan Md Kamal</u> , Anis Nadirah Mohamad Zainudin, Zakiah Othman, Khairul Anwar Jabir, Renuga Devi Kanabalan, Rohaya Ramli	488
EPIDPP70 / 442	Harnessing Artificial Intelligence for Improved Diagnosis and Surveillance of Leptospirosis <u>Murnihayati Hassan</u> , Siti Nur Zawani Rosli, Meruwan Amin Shoib, Mohd Nadzuan Yahaya, Mohammad Ridhuan Mohd Ali	492
EPIDPP71 / 443	Community-Based Weight Management Among KOSPEN community in Malaysia: A Public Health Approach Maizatul Azlina Chee Din, Mohd Tariq Mhd Noor, Ahmad Izzuddin Anuar	495

E-POSTER PRESENTATION: FAMILY HEALTH/ HEALTH MANAGEMENT

FHHMPP01 / 175	Digitalisation in Action: Solutions for Limited-Resource Settings <u>Nur Azmiah Zainuddin</u> , Devi Shantini A/P Rata Mohan, Tengku Mohamad Iskandar Tengku Mohamad Rosman, Sri Devi A/P Sukumaran, Muhammad Suhaili Muhammad Shueib, Adlan Zafrulan Ismail	498
FHHMPP02 / 177	From Concept To Reality: Expert Insights in Content Validation of The Malaysian Diabetic Foot Self-Care Instrument <u>Divya Nair Narayanan</u> , Normaizira Hamidi, Izzatur Rahmi Mohd Ujang, Nurhayati Shaharuddin, Roslina Supadi Samsiah Awang, Nora Hamid, Suhanahani Bastani, Mohammad Luqman Abd Rani, Tengku Mohd Asri Tengku Makhtar, Nurasmilla Md Noor	501
FHHMPP03 / 188	Chronic Ambulatory Care-Sensitive Conditions: A Snapshot of Potentially Preventable Hospitalisations in Ministry of Health Facilities Shakirah Md.Sharif , Hazwa Harith, Ang Zen Yang Melody Soong Yin Yin, Fun Weng Hong	504
FHHMPP04 / 190	Developing Malaysia's Men's Health Report Card: A Tool for Assessing Health Trends <u>Wilfred Mok Kok Hoe</u> , Ang Zen Yang, Chew Cheng Hoon, Mohd Yasin Raja bin Abdullah, Diane Chong Woei Quan, Fun Weng Hong, Wan Mohd Shariffuddin Zainuddin, Zakiah Mohd Said, Sondi Sararaks	508
FHHMPP05 / 192	Do Mental Health Issues Relate to Risky Sexual Behaviour in Adolescents? Findings from the Adolescent Health Survey 2022, Malaysia Noor Aliza Lodz, Mohd Aznuddin Abd Razak	511
FHHMPP06 / 195	Maternal Morbidities (Obesity, Hypertension and Diabetes Mellitus) Influencing Caesarean Delivery Decisions in Malaysia Norlaila Hamid, S Maria Awaluddin, Wan Sarifah Ainin Wan Jusoh, Norliza Shamsuddin, Norhafizah Sahril, Chan Yee Mang, Noor Ani Ahmad	515
FHHMPP07 / 198	Anxiety Symptoms Among Family Caregivers of Persons with Dementia in West Malaysia: Prevalence, Associated Factors and Its Effect on Quality of Life <u>Hashima E Nasreen</u> , Syarifah Amirah binti Syed Ahmad	519
FHHMPP08 / 203	Urban-Rural Disparities in Contraceptive Use Among Women of Reproductive Age in Malaysia: A Cross- Sectional Analysis	523

	The 12th Nation	nal Public Health	Conference	in conjunction	with 26th N	NIH Scientific Co	onference on	
Embraci	ing the New Era:	Advancing Public	c Health Thro	ough AI and Di	gitalisation.	8-10 July 2025	. The Everly P	utraiava

147	C C - L	4 • •	147	1 1.	_	44	A -	
wan	Sarifah	Ainin	wan	juson,	্	maria	Awa	luaain

FHHMPP09 / 207	Protecting the Future: Vaccine Hesitancy Among Malaysian Mothers of Children Under Two Years Old Norain Ab Wahab, S Maria Awaluddin, Eida Nurhadzira Muhammad, Chong Zhuo Lin, Norliza Shamsuddin, Nazirah Alias, Foong Ming Moy, Noor Ani Ahmad.	526
FHHMPP10 / 210	Streamlining Excellence: A Protocol for Standardising Healthcare Quality Professionals' Roles and Functions in the Ministry of Health Malaysia Normaizira Hamidi, Nurhayati Shaharuddin, Divya Nair Narayanan, Samsiah Awang, Khalidah Maruan, Izzatur Rahmi Mohd Ujang, Nur Ezdiani Mohamed, Roslina Supadi, Mariyah Mohamad	529
FHHMPP11 / 212	The Risk of Health Status of 2024 Pre-Hajj Medical Examination in Malaysia Hajj Pilgrim (MyVAS Outcomes) Khairulaizat Mahdin, Mohd Azmi Suliman, Iesza Raihan Ali, Azah Abdul Samad, Muhammad Shafiq Samsudin, Maheshwara Rao Appannan, Salmiah Baharudin	532
FHHMPP12 / 217	Prevalence and Determinants of Parental Monitoring Among Malaysian Adolescents Noor Syaqilah Shawaluddin, Tuan Mohd Amin Tuan Lah, Maznieda Mahjom, Nur Hamizah Nasaruddin, Nazirah Alias, Mohd Ruhaizie Riyadzi, Thamil Arasu Saminathan, Nur Faraeein Zainal Abidin, Lim Kuang Kuay, S Maria Awaluddin	535
FHHMPP13 / 225	Prevalence of Pre-Pregnancy Comorbidities among Mothers in Malaysia and the Association with Hypertensive Disorder in Pregnancy Maznieda Mahjom, Mohd Shaiful Azlan Kassim, Kishwen Kanna Yoga Ratnam, S Maria Awaluddin, Lim Kuang Kuay, Noor Syaqilah Shawaluddin, Tuan Mohd Amin Tuan Lah, Farah Nabilah Ahmad Zainuddin, Dzarifah Hanis Md Sairi	538
FHHMPP14 / 226	Gross Motor Developmental Delay Among Children Aged 6 To 59 Months in Malaysia, 2022 <u>Nur Hamizah Nasaruddin</u> , S Maria Awaluddin, Noor Syaqilah Shawaluddin, Khaw Wan-Fei, Nazirah Alias, Tham Sin Wan, Sharifah Nazeera Syed Anera, Wan Shakira Rodzlan Hasani, Sulhariza Husni Zain	541
FHHMPP15 / 228	Potentially Preventable Hospitalisations Among Older Adults: Analysis of Hospitalisations in The Ministry of Health Facilities Between 2015 and 2020 Melody Soong Yin Yin, Ang Zen Yang, Tang Kar Foong, Shakirah Md. Sharif, Lim Wern Han, Fun Weng Hong, Alif Haikal Md Razman, Nur Aleeya Syakila Muhamad Subian, Sondi Sararaks	544

The 12th National Public Health Conference in	conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Throug	h AI and Digitalisation, 8-10 July 2025, The Everly Putrajay

FHHMPP16 / 230	Reasons and factors associated with contraceptive non- use among married Orang Asli women: Findings from the Orang Asli Health Survey 2022 <u>Muhamad Khairul Nazrin Khalil</u> , Nurhafizah Sahril, Filza Noor Asari, Noor Syaqilah Shawaluddin, Muhammad Faiz Mohd Hisham	547
FHHMPP17 / 234	Prevalence and Factors Associated with Anaemia among Women of Reproductive Age among Orang Asli in Malaysia Muhammad Azri Adam Adnan, Norizzati Amsah, Norlaila Hamid, Mohd Khairul Nadzrin Khalil	551
FHHMPP18 / 236	Outpatient Healthcare Utilisation Inequalities Among Older Adults in Malaysia - A Multi-Dimensional Analysis <u>Awatef Amer Nordin</u> , Suhana Jawahir, Iqbal Ab Rahim, Adilius Manual, Jabrullah Ab Hamid, Nur Elina Abdul Mutalib, Devi Shantini Rata Mohan, Sarah Nurain Mohd Noh	555
FHHMPP19 / 239	Trends In Glycaemic Control: Evaluating Medical Nutrition Therapy Outcomes Over Time In Public Healthcare Clinics Murnizar Mokhtar, Nurul Huda Ibrahim, Norasima Kassim, Mohammad Zulkarnain Mohammad Ikhram, Rozlinizam Kudori, Aisyah Muhamad, John Kong Jian Pei, Mohd Fauzee Mohd Zaki, Siah Woan Yie	559
FHHMPP20 / 253	Uncovering Gaps in Colorectal Cancer Screening Uptake Among Urban Community-Dwelling Elderly <u>Aidalina Mahmud</u> , Mohd Erfan Edros	562
FHHMPP21 / 257	Incidence and Types of Medication Transcription Errors in Healthcare Facilities in Malaysia Norazida Ab Rahman, Ee Vien Low, Fateha Kamaruddin, Asilah Che Ayub, Sue Chin Chong, Noridayu Tumiran, Norafidah Idris	565
FHHMPP22 / 259	Global Research Trends on Paediatric Obesity: A Bibliometric Analysis from 1994 to 2023 Mohd Azmi Suliman, Tham Sin Wan, Thamil Arasu Saminathan	569
FHHMPP23 / 260	Three Decades of Malnutrition Research Among Older Persons: A Bibliometric Analysis of Contributors and Research Themes Mohd Azmi Suliman, Tham Sin Wan	573
FHHMPP24 / 265	Top-down Costing of Primary Healthcare Services in Malaysian Public Health Clinics <u>Marhaini Mostapha</u> , Mohd Shaiful Jefri, Rima Marhayu Abdul Rashid, Noor Haslinda Ismail, Tan Yui Ping, Mohd Shahri Bahari, Farhana Aminuddin, Sivaraj Raman, Nur Amalina Zaimi, Ee Vien Low, Nor Zam Azihan Mohd Hassan	577

	The 12th National Public H	ealth Conference	in conjunction	with 26th I	NIH Scient	tific Cor	nference c	<u>n</u>
Embracii	ng the New Era: Advancing	Public Health Thr	ough AI and Dig	gitalisation,	8-10 July	2025,	The Everly	Putrajaya

FHHMPP25 / 272	Trends in Equality of Inpatient Care Utilisation for Middle-aged and Older Adults in Malaysia: Findings from the 2011, 2015, and 2019 National Health and Morbidity Surveys <u>Suhana Jawahir</u> , Awatef Amer Nordin, Devi Shantini Rata Mohan, Nur Elina Abdul Mutalib, Iqbal Ab Rahim, Jabrullah Ab Hamid, Adilius Manual, Sarah Nurain Mohd Noh	580
FHHMPP26 / 282	Utilisation of Medical Check-ups Among Older Adults in Malaysia: Findings from the National Health and Morbidity Survey (NHMS) 2023 Nur Hidayati Abdul Halim, Ang Zen Yang	584
FHHMPP27 / 284	Maternal Mortality in Perak: A Decadal Epidemiological Review (2015-2024) Raja Muhammad Raja Omar, Che Wan Ilmiyah, Masliza Mustafa, Khoo Yi Yi, Prem Kumar, Husna Maizura Ahmad Mahir	588
FHHMPP28 / 285	Productivity Impact of Premature Death from Cardiac Arrest Outside Hospitals in Penang Nor Zam Azihan Mohd Hassan, Mohd Shahri Bahari, Leong Yuen Chin, Farhana Aminuddin, Sivaraj Raman, Mohd Shaiful Jefri Nur Sham Kunusegaran, Nur Amalina Zaimi, Tan Yui Ping, Ee Vien Low, Marhaini Mostapha	591
FHHMPP29 / 287	A Review of Antimicrobial Stewardship Program in Primary Healthcare clinics in Perak, Malaysia <u>Hairul Izwan Abdul Rahman</u> , Nur Afini Rozana Mohd Sani, Husna Maizura Ahmad Mahir	595
FHHMPP30 / 288	Association Between Depression and Health Seeking Behaviour Among Women in Malaysia <u>Sharifah Zawani Syed Ahmad Yunus</u> , Mohamad Fuad Mohamad Anuar, Kasturi Manoharan	597
FHHMPP31 / 293	Cost-Minimization Analysis of Kramer's Rule Combined with Transcutaneous Bilirubin Screening versus Kramer's Rule Alone for Neonatal Jaundice in Primary Healthcare Clinics <u>Xin-Jie Lim</u> , Subashini Ambigapathy, E-Li Leong, Nicholas Yee-Liang Hing, Nurul Idayu Mior Azmi, Mary Stella, Sheela Mithra, Ling-Yuin Lee, Mohammad Zawawi Abu Bakar, Paream Kaur, Philip Rajan Devesahayam, Jeyaseelan P. Nachiappan	600
FHHMPP32 / 294	Evaluating the Effect of Equipment Age on Radiographic Service Downtime in Government Primary Healthcare Clinics, Malaysia <u>Huzaifah Hussin</u> , Rajini Sooryanarayana, Asnida Anjang Ab Rahman, Anisah Sariman	604

	The 12th National Public H	ealth Conference	in conjunction	with 26th I	NIH Scient	tific Cor	nference c	<u>n</u>
Embracii	ng the New Era: Advancing	Public Health Thr	ough AI and Dig	gitalisation,	8-10 July	2025,	The Everly	Putrajaya

FHHMPP33 / 298	Strategies Addressing Early Unscheduled Return Visits to Emergency Departments Among Adults in Asia: A Scoping Review <u>Diana Yeo Ing Tieng,</u> Tg Mohamad Iskandar Tg Mohamad Rosman, Nur Khairah Badaruddin, Kavita Jetly Jagjit Kumar Jetly, Fairuz Nadiah Nordin, Nor Asma Musa	608
FHHMPP34 / 307	Cost-Effectiveness Analysis of Nirmatrelvir/Ritonavir Versus Usual Care to Prevent COVID-19 Hospitalization Among Elderly Patients in Malaysia <u>EV Low</u> , NYL Hing, HS Teh, MD Pathmanathan, SK Chidambaram, SMZin, F M.Zin, SB M.Ami, MR Appannan, WR Kim, ZW Teh, WJ Lee, MH Ismail, AA Samad, KM Peariasamy	611
FHHMPP36 / 315	Mapping the Research Landscape on Malnutrition in Older Adults: A Bibliometric Analysis of Trends and Thematic Networks <u>Sin Wan Tham</u> , Mohd Azmi Suliman	614
FHHMPP37 / 316	Analysis of Malaysia's Traditional and Complementary Medicine (T&CM) Policy and Strategies from a Practice Perspective: A Study Protocol Kavita Jetly a/p Jagjit Kumar Jetly, Terence Tan Yew Chin, Tay Yea Lu, Siti Hajar Muhamad Rosli, Teh Li Yin, Teoh Sheh Ki, Gong Jia Ying, Rumana Akhter Saifi, Wong Min Fui @ Esther Wong	617
FHHMPP38 / 327	Improving Maternal Outcomes through Annual Clinical Audit of Pre-pregnancy Care (PPC) in Malaysian Health Clinics Sarah Awang Dahlan, Majdah Mohamed	620
FHHMPP39 / 328	Mapping Patient and Provider Perspectives on Diabetes Control to the Chronic Care Model: Insights from a Review of Qualitative Studies in Malaysia Lee Pei Jia, Norshahiratul Atiqah Mohd Zaidi, Mohamad Zulfikrie Abas, Tan Jie Ne, Wan Kim Sui, Azah Abdul Samad³ Chan Huan Keat, Sheamini Sivasampu, Ang Swee Hung	623
FHHMPP40 / 345	Patient Safety and Medication Errors in Telemedicine: Protocol for a Scoping Review Nor Asma Musa, Mohd Amirul Hariz Aminuddin , Fairuz Nadiah Nordin, Syarifah Nortasya Sayed Muhamad Kamarudin, Zawaniah Brukan Ali	626
FHHMPP41 / 348	Designing a Sustainable Premium Economy Health Service Model in Malaysia Public Hospitals: Insight from Healthcare User Wafaak.E, Natrah.M.S, J.H.W.Wong, W.A.Yap	630

The 12th Nation	al Public Health Cor				nference on
Embracing the New Era:	Advancing Public He	ealth Through AI a	nd Digitalisation,	8-10 July 2025,	The Everly Putrajay

FHHMPP42 / 357	Determinants of Period Poverty Among Women in a Malaysian Low-Income Housing Community <u>S A Zafirah</u> , Nor Faiza Mohd Tohit, Wan Farizatul Shima Wan Ahmad Fakurazi, Badrul Hisham Abdul Samad, Nur Adnin binti Ahmad Zaidi	633
FHHMPP43 / 360	Primary Healthcare Utilization and Cost Among Older Adults with Diabetes Mellitus: Insights from TPC-OHCIS 2022 <u>Hazwa Harith</u> , Weng Hong Fun, Zen Yang Ang, Shakirah Md.Sharif, Su Fen Chia, Wern Han Lim, Alif Haikal Md Razman, Kar Foong Tang, Noraliza Noordin Merican, Sheleaswani Inche Zainal Abidin, Siti Raidah Mohamad Azman, Muhammad Amiruldin Bin Harun	636
FHHMPP44 / 374	Knowledge and Attitudes on Contraception Among an Underprivileged Community in Sungai Besi Nur Adnin Ahmad Zaidi, Siti Athirah Zafirah Abdul Rashid, Nor Faiza Mohd Tohit, Wan Farizatul Shima Wan Ahmad Fakuradzi, Badrul Hisham Abd Samad	640
FHHMPP45 / 382	Evolution Of HPV Vaccination Strategies Over 15 Years In Malaysia Mardiana Omar, Radziah Mohamad, Saidatul Norbaya B., Noorhaire Sumarlie Nordin, Don Ismail Mohamed	643
FHHMPP46 / 393	Client Dissatisfaction At Public Health Facilities In Perak: A Cross Sectional Descriptive Study From Sistem Pengurusan Aduan Awam, Ministry Of Health Malaysia, 2019-2024 Lau Kin Mun, Husna Maizura Ahmad Mahir	646
FHHMPP47 / 394	From Paper Trails to Digital Tales: A Mixed-Methods Implementation Study of CCMS Rollout in Rural Primary Care Karen Christelle, Tong Yung Hung, Abby Chan Kai Ern, Mohd. Azzahi Mohamed Kamel, Mohd. Farid Abd. Hamid	649
FHHMPP48 / 399	Silent Burden: Insights into α-Thalassaemia Carrier Status from a Nationwide Adolescent Screening in Malaysia <u>Don Ismail Mohamed</u> , Alisahkhairun Rahmat, Mohd Shahriel Mat Daud, Nurul Kausar Izzati Mohd Ghazali, Radziah Mohamad, Saidatul Norbaya Buang	653
FHHMPP49 / 416	Expanding the Role of Community Nurses in Rural Clinics for Elderly Care: Malaysia's Community-Based Ageing Initiative <u>Sheleaswani Inche Zainal Abidin, Noraliza Nordin Merican, Nurhayati Mardiah Manut, Nor Hasimawati Shaari, Shamsol Lot, Saidatul Norbaya Buang</u>	656

<u>The 1</u>	2th National Public I	lealth Conference	in conjunction	with 26th N	IH Scientifi	c Conference o	<u>n</u>
Embracing the	New Era: Advancing	Public Health Thro	ough Al and Di	gitalisation, 8	8-10 July 20	25, The Everly	<u>Putrajaya</u>

FHHMPP50 / 441	Psychological Distress among Malaysian Infertile Individuals: A Comparison Between First Visit and Recurrent Fertility Clinic Visits Noor Izni Mohamed Shapie, Nik Daliana Nik Farid, Rafdzah Ahmad Zaki	660
FHHMPP51 / 444	Maternal Mortality: A Situational Analysis from 2020 to 2024 in an East Coast State of Peninsular Malaysia Nur Akmal Ismail, Nurnajayati Omar, Yazreen Najihah Mohd Nor, Siti Nor Shuhada Mustfar	663
FHHMPP52 / 350	Evaluating the Effectiveness of an Antimicrobial Stewardship Program in Malaysian Primary Health Care Noraini M Yusof, Hazirah M Noor, Bee Kiau, Mardhiyah Kamal, Marziaty Shazreena Mohd Shah, Durga Murugia, Wan Noor Azlin Wan Idris, AF Azam Abd Rahman, Izwan Effendy	666
FHHMPP53 / 407	Integrating Primary Care and Public Health in Malaysia: A Path Forward for Primary Healthcare Reform <u>Rima Marhayu Abdul Rashid</u> , Noor Haslinda Ismail, Saidatul Nurbaya Buang, Mohd Safiee Ismail	669
FHHMPP54 / 420	Seamless Healthcare, Digitally Delivered: Malaysia's Patient Summary Initiative Chin Yangxin, Vivek Jason Jayaraj, Maheshwara Rao Appannan	673
FHHMPP55 / 426	Reaching the Unreachable: A Review of Malaysia's Mobile Clinic Services in Advancing Primary Health Care and Universal Health Coverage <u>Hidayatul Fariha Sulaiman</u> , Mohamad Hafizan Abd Hadi, Mastura Mohamad Tahir, Juriati Ismail, Azah Abdul Samad, Christina Baun Lian, Abdul Shukor Salha Azlie Ismail [,] Wan Mohd Izuadi Wan Mahmud	676
FHHMPP56 / 432	Alcohol Consumption Patterns among Urban Residents in Malaysia <u>Fazila Haryati Ahmad</u> , Mohd Hatta Abd Mutalip, Halizah Mat Rifin	681
FHHMPP57 / 445	A Simulation-Based Cost-Effectiveness Analysis of Reflex DNA Versus Multi-Sample Adolescent Screening for Thalassaemia in East Malaysian Schools <u>Azrin Syahida Abd Rahim</u> , Don Ismail Mohamed, Nour El Huda Abd Rahim	684

E-POSTER PRESENTATION: OCCUPATIONAL HEALTH/ ENVIRONMENTAL HEALTH/ SOCIAL& HEALTH BEHAVIOUR/ OTHERS

OESHPP01 / 183	Effect Of Employer-Sponsored Health Coverage on Oral Healthcare Utilisation: Findings from National Health and Morbidity Survey (NHMS) 2019 Nur Elina Abdul Mutalib, Suhana Jawahir, Jabrullah Ab Hamid, Devi Shantini Rata Mohan, Adilius Manual, Iqbal Ab Rahim, Sarah Nurain Mohd Noh, Awatef Amer Nordin	689
OESHPP02 / 184	The Efficacy Of Anthelmintics Against Sth Infection In Population-Based Studies In Malaysia - Results Of A Scoping Review Analysis Muhammad Faiz Mohd Hisham, Fazila Haryati Ahmad, Filza Noor Asari, Noor Aliza Lodz, Norzawati Yoep, Eida Nurhadzira Muhammad, Nor Asiah Muhamad	693
OESHPP03 / 186	Developing and Validating Instruments to Identify Preferred Features of Systematic Grey Literature Review Automation Tools <u>Ang Zen Yang</u> , Shakirah Md Sharif, Melody Soong Yin Yin, Fun Weng Hong, Shaun Lee Wen Huey	699
OESHPP04 / 193	Effectiveness of KOSPEN Plus Mental Health Promotion Activity at Workplace: Findings from the KOSPEN-Plus Program in Malaysia <u>Lim Kuang Kuay</u> , Maznieda Mahjom, S Maria Awaluddin, Noor Syaqilah Shawaluddin, Tuan Mohd Amin Tuan Lah, Chan Ying Ying, Hamizatul Akmal Abd Hamid, Muhammad Fadhli Mohd Yusoff, Mohd Azahadi Omar	704
OESHPP05 / 194	The Role of Strained Family Relationships and Economic Hardship During COVID-19 Pandemic in Determining Adolescent Depression Based on Patient Health Questionnaire (PHQ-9) scores S. Maria Awaluddin, Muhamad Khairul Nazrin Khalil, Lim Kuang Kuay, Noor Syaqilah Shawaluddin, Tuan Mohd Amin Tuan Lah, Maznieda Mahjom, Noor Ani Ahmad	708
OESHPP06 / 196	Healthcare Without Hardship: Are we are Financially Protected? <u>Adilius Manual</u> , Jabrullah Ab Hamid, Suhana Jawahir, Awatef Amer Nordin, Iqbal Ab Rahim, Sarah Nurain Mohd Noh, Nur Elina Abdul Mutalib, Devi Shantini Rata Mohan	712
OESHPP07 / 200	Do Our Adolescents Eat an Adequate Healthier Diet During The COVID-19 Pandemic? <u>Eida Nurhadzira Muhammad</u> , Filza Noor Asari, Muhammad Faiz Mohd Hisham, Ruhaya Salleh, Chong Zhuo Lin	716

	The 12th National Public H	ealth Conference	in conjunction	with 26th I	NIH Scient	tific Cor	nference c	<u>n</u>
Embracii	ng the New Era: Advancing	Public Health Thr	ough AI and Dig	gitalisation,	8-10 July	2025,	The Everly	Putrajaya

OESHPP08 / 201	Tracking Lymphatic Filariasis Transmission Through Molecular Surveillance of <i>Brugia</i> Species in Sabah's Mosquito Vectors <u>Faizul Akmal Abdul Rahim</u> , Mohd Amierul Fikri Mahmud, Mohd Hatta Abdul Mutalip, Tanrang Yusin, Mohd Azrool Rizal Mohd Azahari, Izhan Shahrin Jaafar	720
OESHPP09 / 202	Targeting Dengue at Its Source: Spatial and Principal Component Analyses on Aedes Breeding Sites. Mohd Amierul Fikri Mahmud, Faizul Akmal Abdul Rahim, Eida Nurhadzira Muhammad, Mohd Hazrin Hashim, Mohd Hatta Abdul Mutalip, Hanipah Shahar, Izfa Riza Hazmi	723
OESHPP10 / 206	Primary Water Sources in Remote Communities: A Descriptive Study <u>Tuan Mohd Amin Tuan Lah</u> , Lim Kuang Kuay, Maznieda Mahjom, S Maria Awaluddin, Noor Syaqilah Shawaluddin	727
OESHPP11 / 211	The Influence of Temperature on Dengue Transmission Dynamics in Kuantan, Pahang <u>Mohd Amiru Hariz Aminuddin</u> , Muhammad Al Azim Baharudin, Muhamad Isa Abdul Aziz, Khairul Aizat Mahdin	730
OESHPP12 / 213	Determinants for Injury Among Healthcare Workers Involved in Occupational Accidents and Dangerous Occurrence in Terengganu Hafizuddin Awang, Noriah Mahmud, Mohd Anuar Abd Rahman, Kasemani Embong	734
OESHPP13 / 214	Predictors of Delayed Healthcare Seeking Among Dengue Patients in Klang District: A Logistic Regression Approach <u>Nur Nabila Abd Rahim</u> , Hazwa Harith, Nurul Farehah Shahrir, Gurpreet Kaur Karpal Singh	738
OESHPP14 / 222	Insufficient Water Intake and Its Association with Nutritional Status: Findings From The Adult Population Survey <u>Sulhariza Husni Zain,</u> Nurzaime Zulaily, Khairul Hasnan Amali, Halizah Mat Rifin	743
OESHPP15 / 227	Breaking the Barrier: What's Keeping Malaysians from Eating Fruits and Veggies? Noorhayati Kassim, Teh Wai Siew, Rosnani Kassim, Nadia Amirudin, Siti Nurhanim Mohamed Aimanan, Nurashma Juatan, Manimaran Krishnan	746
OESHPP16 / 233	Bridging Spatial And Temporal Gaps in Dengue Prediction: A Deep Learning Approach <u>Sakshaleni Rajendiran</u> , Noraishah Mohd Sham, Sarbhan Singh Lakha Singh, Yuvaneswary Veloo, Syahidiah Syed Abu Thahir, Nurulhusna Ab Hamid, Wan Ming Keong, Siti Morni Umor, Md Nazri Safar,	750

ividiaysian southar of rabile freath ividalence, vol. 25 (5appl 2) 2025
The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10 July 2025, The Everly Putrajaya

Noriman	iah /	Mazlan,	Siti	Masayu	Yahaya,	, Nor	Atika	Abd	Manap,
Imanul F	lassa	n Abdul	Shuk	kor, Jey	ranthi Su	ppiah	, Roza	inane	e Mohd
Zain, M	ohd	Khairud	ddin	Che II	orahim,	Radi	Mohai	mad,	Uswah
Khairuda	din, A	\hmad `.	Athif	Mohd F	Faudzi, R	ohaid	a Ismai	il	

- OESHPP17 / 238 Knowledge of Antibiotic Resistance among The General 753
 Population in Malaysia
 Chong Zhuo Lin, Noor Aliza Lodz
- OESHPP18 / 241 Comparing Urban-Rural Disparities in Travel-Related 757
 Physical Inactivity: A Nationwide Study of the Malaysian
 Population
 Nurfatehar Ramly, Nor Izzati Amsah, Hasimah Ismail, Halizah Mat
 Riffin, Kishwen Kanna Yoga Ratnam, Syafinaz Mohd Sallehudin,
 Tuan Mohd Amin Tuan Lah, Sulhariza Husni Zain, Mohd Aznudin,
 Abdul Razak, Lim Kuang Kay
- OESHPP19 / 245 It Takes Two to Tango Understanding Perspectives on 760 Indicators in Ministry of Health Malaysia

 Iqbal Ab Rahim, Muna Zahira Mohd Yusof, Awatef Amer Nordin, Devi Shantini Rata Mohan, Nur Elina Abdul Mutalib, Suhana Jawahir, Sarah Nurain Mohd Noh, Adilius Manual
- OESHPP20 / 246 Breaking the Burnout Cycle: A Modified Delphi Protocol 763 on the Development of a Psychoeducation Intervention Package for Nurses

 Norehan Jinah, Pangie Bakit, Ili Abdullah Sharin, Nor Haniza Zakaria, Siti Zubaidah Ahmad Subki, Izzuan Khirman Adnan, Nursyahda Zakaria, Lee Kun Yun
- OESHPP21 / 248 Factors Influencing Cigarette Smoking Initiation Among 766
 Children: A Systematic Review And Meta-Analysis
 Nor Asiah Muhamad, Izzah Athirah Rosli, Nur Hasnah Ma'amor, Fatin
 Norhasny Leman, Tengku Puteri Nadiah Tengku Baharudin Shah, Nik
 Athirah Farhana Nik Azhan, Nurul Hidayah Jamalluddin, Nazihah
 Nazri, Normi Mustapha, Zulkarnain Abd Karim, Norliza Chemi, Nor
 Fariza Ngah, Muhammad Radzi Abu Hassan
- OESHPP22 / 249 Antibiotic Use Among Children Under Five Years with Cough or Fever in Malaysia: A National Representative Study

 <u>Chan Yee Mang</u>, Khaw Wan-Fei
- OESHPP23 / 254 Pufferfish Pandemonium: Public Perception and 776 Awareness of Pufferfish in Kota Marudu, Sabah Ahmad Syukri Radzran, Mohamad Zulfikri Rusdi, Mohd Helmi Abdul Hamid, Sheila Miriam Mujin
- OESHPP24 / 262 Emergency Department (ED) Overcrowding in MOH 779 hospitals: Workload Disparities and Contributing Factors

ividia y sidit southar of t ablic ficaltit ivicalcine, vol. 25 (suppl 2) 2025
The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Through Al and Digitalisation, 8-10 July 2025, The Everly Putrajay

Jabrullah Ab Hamid, Adilius Manual, <u>N</u>	<u>lur Elina Abdul Mutalib</u> , Iqbal
Ab Rahim, Devi Shantini Rata Mohan, S	Suhana Jawahir, Sarah Nurain
Mohd Noh, Awatef Amer Nordin	

OESHPP25 / 267	Prevalence and Predictors of Depression Among 7 Healthcare Workers in a Rural District Health Office in	783
	Terengganu	
	Norhafizah Mohd Noor, Syahrul Faiz Zakari @ Zakaria, Nadhirah	
	Ramli ¹ , Mohamad Zen Zakaria	

OESHPP26 / 269 Mental Health Challenges of Healthcare Workers in 786
Selangor Amid a National Health Crisis

Nadia Mohamad, Siti Sara Yaacob, Mohd Faiz Ibrahim, Imanul
Hassan Abdul Shukor, Mohd Zulfinainie Mohamad, Muhammad
Farhan Mahmud, Rohaida Ismail

OESHPP27 / 273 Title: Urban-Rural Perspectives on Socioeconomic 790 Inequalities in Oral Healthcare Utilisation in Malaysia: Insights from a National Survey

Sarah Nurain Mohd Noh, Suhana Jawahir, Devi Shantini Rata Mohan, Iqbal Ab Rahim, Adilius Manual, Nur Elina Abdul Mutalib, Jabrullah Ab Hamid, Awatef Amer Nordin

OESHPP28 / 279 From Policy to Practice: Uncovering Gaps in Virtual 793
Consultation Implementation in Malaysian Public Health
Clinics
Yea Lu Tay, Zalilah Abdullah, Min Fui Wong, Nur Hidayati Abdul
Halim, Noor Hasidah Ab Rahman, Nur Khairah Badaruddin, Nurul

Iman Jamalul-lail

OESHPP30 / 283 Low Birth Weight Among Children Below 5 Years and Its 796
Associated Factors: Findings from a Nationwide Study
Ruhaya Salleh, Sulhariza Husni Zain, Shubash Shander Ganapathy,
Mohamad Aznuddin Abd Razak, Nurzaime Zulaily

OESHPP31 / 297 Predicting Adolescent Obesity from Meal Patterns using 800 Machine Learning
Nur Liana Ab Majid, Syahid Anuar, Kimberly Wong

OESHPP32 / 300 Comparative Performance of Machine Learning 803
Algorithms for Possible Sarcopenia Screening in Older
Malaysian Adults
Kee Chee Cheong, Ng Chai Chen, Tay Chai Li, Kong Sie Zin, Ding Ai
Lee, Nor Faizah Ghazali, Kiew Lee Boon, Lorna Chin Kin Tze,
Thenmoli Palaniyappan, Srinevasarao Ramanaidu, Khalilati Barizah
Binti Md Salimun, Zaleha binti Jusoh

OESHPP33 / 302 Urine Iodine Status in Malaysia: A National Study in 808
Adults
Noor ul-Aziha Muhammad, Ahmad Ali Zainuddin, Lalitha
Palaniveloo, Ruhaya Salleh, Filza Noor Asari, Lim Kuang Kay, Chan
Yee Mang

	The 12th National Pub	lic Health Conference	ce in conjunctio	n with 26th I	NIH Scienti	fic Conference c	<u>on</u>
Embracii	ng the New Era: Advan	cing Public Health T	hrough AI and D	igitalisation,	8-10 July 2	2025, The Everly	Putrajaya

OESHPP34 / 305	Lost in Translation: How Coding Errors in Ophthalmology Undermine MyDRG-Based Hospital Reimbursement <u>Jin Ziang Tok</u> , Deying Yu, Maznah Dahlui, Nazirah Hasnan, Tengku Ain Fathlun Tengku Kamalden, Amirah Azzeri, Mohd Hafiz Jaafar	812
OESHPP35 / 309	Leveraging AI in Evaluation of Community Outreach Program for Detection of Prevalence and Causes of Abnormal Chest Radiography in Rural Areas of Sarawak Melvin Chung Hsien Liang, Lai Kah Sheng, Nurul Amirah Masani, Teo Jia Chi, Rawa Anak Bau	814
OESHPP36 / 314	Potential and Feasibility of Red Blood Cells Spectra for the Detection of Blood Disorders: A Proof-of-Concept Study (MOSTHA@POC) <u>William Kian Boon Law</u> , Royan Hian Lee Ong, Nurul Atiqah Zulazmi, Lai Hui Pang, Siew Lian Chong, Kar Ying Yong	817
OESHPP37 / 332	Designing and Developing a Game-based Learning Intervention Program (VAPGAMO) to Prevent Vaping Intention among Adolescent <u>Muhamad Zulhilmie Saruddin</u> , Rosliza Abdul Manaf, Ahmad Zaid Fattah Azman, Farah Nadia Azman	820
OESHPP38 / 335	Digital Lifelines: A Public Health Lens on Tech-Driven Disaster Response - A Narrative Review <u>Muhammad Zulhilmie Saruddin</u> , Muhammad Izmanuddin Fitri Abdul Razak, Khadijahtul Qubra Amizah Hamzah, Syafiq Ameerul Ibtisyam Zulkiflee, Aidalina Mahmud	822
OESHPP39 / 336	Prevalence and Factors Associated with Children Who Have Never Attended a Dental Clinic: Findings from a National Survey Nur Faraeein Zainal Abidin, Khaw Wan-Fei, Hasimah Ismail, Shubash Shander	825
OESHPP40 / 351	What Drives the Public to Seek Care at the Emergency Department's Green Zone? A Cross-Sectional Study at Hospital Tengku Ampuan Rahimah Klang Norbaidurah Ithnain, Saiful Adli Suhaimi, Evi Diana Omar, Hasnah Mat, Manimaran Krishnan	829
OESHPP41 / 361	Bridging the Gaps: Factors of Eye Care Utilisation Among Malaysia's Low-Income Groups Using Andersen Behavioural's Model Nur Suhailah Alias, Noor Halilah Buari, Sabrina Subri	832
OESHPP42 / 367	Knowledge of Rational Use of Medicines Among Know Your Medicine (KYM) Ambassadors in Malaysia: A National Cross-Sectional Study	836

The 12th National Public Health Conference in	conjunction with 26th NIH Scientific Conference on	
Embracing the New Era: Advancing Public Health Through	h AI and Digitalisation, 8-10 July 2025, The Everly Putrajay	٧

<u>Nurashma</u>	<u>Juatan,</u>	Noorhayati	Kassim,	Rosnani	Kassim,	Nadia
Amirudin,	Siti Nurh	anim Mohan	ned Aima	ınan, Nur	syazwani	Jabir,
Munira Mu	hammad,	Maisara Abo	l Rahman	, Atika M	ahfuza M	ahbub,
Mohd Shah	iri Abd G	hapar				

OESHPP43 / 369	Prevalence of Caregivers' Disciplinary Practices Among Malaysian Children Aged 12 to 59 Months: Findings from the National Health and Morbidity Survey 2022 <u>Nurul Haniyah Rosslan</u> , Shubash Shander Ganapathy, Muhammad Hanafi Bakri, Norzawati Yeop	839
OESHPP44 / 372	Harnessing Artificial Intelligence and Ultraportable X-ray for Chest Screening in rural Bintulu: Detection Rates and Locality Variation Melvin Chung Hsien Liang, Nurul Amirah Masani, Lai Kah Sheng	842
OESHPP45 / 376	Urban-Rural Disparities in Inpatient Healthcare Utilisation in Malaysia: Insights from a National Survey Noor Hasidah Ab Rahman, Tay Yea Lu, Nurul Salwana Abu Bakar, Tan Yui Ping, Mohd Shahri Bahari	845
OESHPP46 / 378	Prevalence and Predictors of Self-Harm among Adolescents in Malaysia Rimah Melati Ab Ghani, Nor Asiah Muhamad, Suria Husin, Nur Hasnah Maamor, Izzah Athirah Rosli, Nik Athirah Farhana Nik Azhan, Tengku Puteri Nadiah Tengku Baharuddin Shah, Nor Hidayah Jamalluddin, Fatin Norhasny Leman, Norli Abdul Jabbar, Ling Shiao Ling, Normi Mustapha, Norliza Chemi, Norni Abdullah, Nurashikin Ibrahim	850
OESHPP47 / 380	Factors Associated with Beliefs in Physical Punishment Towards Children Aged 12-59 Months Among Malaysian Caregivers: Findings from the National Health and Morbidity Survey 2022 <u>Muhammad Hanafi Bakri, Shubash Shander Ganapathy, Nurul</u> Haniyah Rosslan, Norzawati Yeop	854
OESHPP48 / 387	Too Tight to Work Right: Back Pain in Data Entry Among Laboratory Workers <u>Imanul Hassan Abdul Shukor</u> , Nurul Farehah Shahrir, Siew Wei Fern	857
OESHPP49 / 402	How Far Is Too Far? Comparing Straight-Line and Road-Network Travel Burdens for Low-Income Cancer Patients in Malaysia Farhana Aminuddin, Marhaini Mostapha, Tan Yui Ping, Nur Amalina Zaimi, Mohd Shahri Bahari, Mohd Shaiful Jefri, Sivaraj Raman, Nor Zam Azihan Mohd Hassan	861

The 12th National Public Health Conference in conjunction with 26th NIH So	cientific Conference on
Embracing the New Era: Advancing Public Health Through AI and Digitalisation, 8-10	July 2025, The Everly Putrajaya

OESHPP50 / 409	Association between HbA1c and Optical Coherence Tomography Angiography (OCTA) Parameters in Type 2 Diabetes Mellitus without Retinopathy <u>Abdallah Naqaweh</u> , Shelina Oli Mohamed, Noor Haziq Saliman	865
OESHPP51 / 414	Prevalence Of Refractive Error Among Malay Primary Schoolchildren In Denai Alam, Selangor <u>Fatin Nur Najwa Norazman</u> , Nurul Syahidah Jasmi	868
OESHPP52 / 415	Digital Transformation of COMBI in Dengue Prevention: Development and Evaluation of the eCOMBI-Denggi Mobile Application Ahmad Farid Nazmi Abdul Halim, Mohd Rohaizat Hassan, Rozita Hod, Khaironi Yatim Sharif, Muhammad Luqman Mahamad Zakaria, Noor Khalili Mohd Ali, Rozita Ab Rahman, Mohd Fauzy Samsudin, Nur Faezah Che Mat, Karthik Sundram A/L Mohanasundram, Roslinda Aziz	871
OESHPP53 / 417	Correlation Between HBA1c and Intra-Retinal Layers in Type 2 Diabetes Mellitus Without Retinopathy Noor Haziq Saliman, Nasrul Rasydan Faizal, Abdallah Naqaweh, Shelina Oli Mohamed	876
OESHPP54 / 422	Vitamin D Levels Among Female Adults and Factors Associated: Findings from National Health & Morbidity Survey (NHMS) 2024 Lalitha Palaniveloo, Fazila Haryati Ahmad, Ahmad Ali Zainuddin	879
OESHPP55 / 431	Development of a School-based Aedes Breeding Search and Destroy Online Checklist and Collaborative Dengue Transmission Risk Stratification of School Compounds in Wilayah Persekutuan Putrajaya, Malaysia Mohd Fauzy Samsudin, Ahmad Farid Nazmi Abdul Halim, Nur Faezah Che Mat, Karthik Sundram Mohana Sundram, Roslinda Aziz, Rozita Ab Rahman	882
OESHPP56 / 438	Expanding MyVAS for HIV Screening: A Case Report on Integrating Public Health Services into Malaysia's National Provider Platform Nurain Amirah Zolkefli, Nurul Zariffa Saat, Siti Aishah Iskandar, Lee Wei Jia, Maheshwara Rao Appannan, Vivek Jason Jayaraj	885
OESHPP57 / 440	Evaluation of the Chance2Act Behavioural Intervention (Chance2act) for Weight Loss Readiness among Adults with Type 2 Diabetes and Obesity Noraini Mohd Saad, Mariam Mohamad, Aimi Nadira Mat Ruzlin, Mohd Hafeez Intiaz Hussein	888
OESHPP58 / 274	Tobacco Advertising Exposure Among Malaysian Adults: Key Findings from GATS 2023	892

Manaysian south at the after the aft
The 12th National Public Health Conference in conjunction with 26th NIH Scientific Conference on
Embracing the New Era: Advancing Public Health Through Al and Digitalisation, 8-10 July 2025, The Everly Putrajay

	<u>Nurzaime Zulaily</u> , Hamizatul Akmal Abd Hamid, Thamil Arasu Saminathan, Tania Gayle Robert Lourdes, Muhammad Fadhli Mohd Yusoff	
OESHPP59 / 349	The Impact of Air Pollution-Related Mortality in Malaysia: Assessing the Burden of Disease and Economic Consequences Mohamad Iqbal M, Nor Zam Azihan MH, Mohd Azahadi Omar	896
OESHPP60 / 355	Sexual and Reproductive Health Knowledge, Attitudes, and Practices Among Men in an Economically Disadvantaged Community in Kuala Lumpur, Malaysia Wan Farizatul Shima Wan Ahmad Fakuradzi, Nor Faiza Mohd. Tohit, Siti Athirah Zafirah Abdul Rashid, Nur 'Adnin Ahmad Zaidi.	899
OESHPP61 / 366	Healthy Malaysia in Progress: Evaluating Agenda Nasional Malaysia Sihat (ANMS) for a Sustainable Future Logeswary Krisnan, Affendi Isa, Vanitha Subramaniam	902
OESHPP62 / 377	Parental Knowledge and Gaps: A Cross-Sectional Study on Benzene Exposure Awareness in Johor Nabihah Ali, Shamsul Bahari Shamsudin, Haidar Rizal Toha	905
OESHPP63 / 398	Prevalence of Food insecurity among adult in Malaysia: Findings from the National Health and Morbidity Surveys 2024 <u>Ahmad Ali Zainuddin</u> , Mohd Azmi Suliman, Ruhaya Saleh, Murnizar Mokhtar, Hasimah Ismail, Teh Wai Siew Norashikin Ramlan Khairul Zarina Mohd Yusop	909
OESHPP64 / 413	Emergency or Not? Public Knowledge and Misuse of the Emergency Department Green Zone in Malaysia Khairulnissa Abdul Kadir, Nurbaidurah Ithnain, Saiful Adli Suhaimi, Gunasundari Marimuthu, Elniee Melson, Logeswary Krishnan	913

FHHMPP57 / 445

A Simulation-Based Cost-Effectiveness Analysis of Reflex DNA Versus Multi-Sample Adolescent Screening for Thalassaemia in East Malaysian Schools

Azrin Syahida Abd Rahim¹, Don Ismail Mohamed², Nour El Huda Abd Rahim³

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Summary

This study compares the cost-effectiveness of two school-based thalassemia screening protocols—multi-sample (P1) and Single-sample Reflex DNA (P2)—in Sabah and Sarawak using 2018 National Thalassaemia Screening (NTSP) data. Although P2 was 9-11% costlier upfront, it eliminated dropouts and improved carrier detection. Sabah, a high-prevalence state, demonstrated superior cost-effectiveness with P2 (RM379.95 per carrier detected) compared to Sarawak (RM821.85). Lifetime treatment cost savings for avoided births with thalassemia major were substantial. The findings support the phased implementation of P2, starting with high-prevalence states, to reduce the economic burden on Malaysia's healthcare system.

Keywords

Thalassemia, school-based screening, simulation-based analysis, Reflex DNA, dropout rates

Introduction

Thalassemia remains a significant public health concern in Malaysia, with an estimated lifetime treatment cost of RM2.66 million per transfusion-dependent patient¹. Since 2016, the Ministry of Health Malaysia has implemented the National Thalassemia Screening Programme (NTSP), targeting Form Four students through a school-based multi-sample approach (P1)². However, the multi-stage workflow contributes to significant dropout rates. In 2018 alone, 2,950 students in Sabah and 2,836 in Sarawak discontinued the screening, resulting in missed carrier detection and a preventable disease burden. To address this, an alternative strategy Single-sample Reflex DNA approach (P2) was retrospectively modelled using 2018 data. This study aims to compare the cost-effectiveness of P1 and P2 in Sabah and Sarawak and evaluate the potential national impact of adopting P2.

Materials and Methods

A retrospective, simulation-based cost-effectiveness analysis used 2018 NTSP data involving 36,860 students from Sabah and 35,161 from Sarawak. Two protocols were compared as shown in Table 1.

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Table 1: Comparing P1 and P2 steps involved

Step	Conventional Multi-Sample (P1)	Single-Sample Reflex DNA (P2)
Enrolment	Form 4 students enrolled	Form 4 students enrolled
Consent	Consent obtained	Consent obtained
Sample	3 separate samples (Full Blood	Single blood sample collected
Collection	Count (FBC), Haemoglobin	
	Analysis (HbA), DNA testing)	
Suspected	Identified after HbA	Identified after same sample
Carrier		tested
DNA	Requires return visit	DNA test done reflexively from
Confirmation		same sample
Dropout Risk	At 3 stages: FBC-Hb, Hb-DNA,	Zero dropout risk
	before post-test	
Time to	6-12 months	<3 months
Completion		

As P2 was not implemented in 2018, a hypothetical simulation was applied assuming full compliance, zero dropout, and equivalent diagnostic sensitivity. Direct medical costs from a provider perspective were included, with no discounting due to the single group of students.

The effectiveness of Incremental Cost-Effectiveness Ratio (ICER)³ was measured by comparing the cost difference and dropout reduction between P2 and P1, reflecting the additional cost per dropout averted using this calculation:

ICER = (Cost of P2 - Cost of P1) / (Dropouts averted by P2 - Dropouts averted by P1) Cost per carrier and lifetime savings from prevented births were estimated using inter-carrier marriage rates of 2%, 4%, and 6% with a 25% inheritance risk⁴. Sensitivity analysis benchmarked P2's ICER against the WHO threshold (RM25,000-75,000)⁵. Crucially, nationwide scale-up requires real-world pilot studies to assess operational feasibility.

Results and Discussion

While P2 incurred higher upfront costs (Sabah: RM793,326; Sarawak: RM485,716) compared to P1, it proved cost-effective. The ICER per averted dropout was RM25.14 (Sabah) and RM22.19 (Sarawak), which is well below the WHO threshold of RM25,000-75,000 (1-3 times the GDP per capita), indicating excellent economic value. Additionally, the cost per carrier detected was lower in Sabah (RM379.95) than in Sarawak (RM821.85), reflecting greater efficiency in high-prevalence settings.

The P2 eliminated all dropouts, compared to 2,950 in Sabah and 2,836 in Sarawak under P1, and increased diagnostic yield. Further analysis estimated 286 and 57 additional carriers detected, respectively. This translates to a 12% increase in detection in Sabah and 5% in Sarawak. Fisher's Exact Test confirmed the statistical significance of dropout elimination (p < 0.001) (Figure 1).

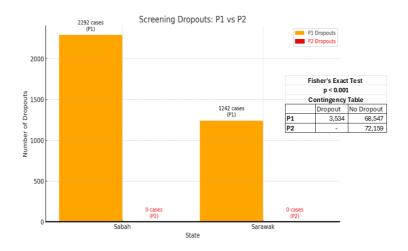


Figure 1: Dropout Comparison for P1 vs P2 Protocols using Fisher's Exact Test

Projected long-term savings were substantial. If the missed carriers under P1 entered inter-carrier marriages (2%-6%) (Figure 2), the lifetime treatment cost potentially avoided ranged from RM3.8 million to RM11.4 million in Sabah, and RM758,000 to RM2.3 million in Sarawak. These estimates were modelled using intercarrier marriage probabilities and a 25% Mendelian inheritance risk⁴.

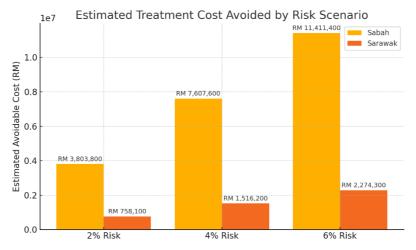


Figure 2: Estimated Avoidable Cost by Risk Scenario Under P1 Enter Inter-Marriages

With each thalassaemia major case costing RM2.66 million in lifetime treatment, the case for P2 is reinforced by both short-term diagnostic gains and long-term healthcare savings. Table 2 summarises the comparative performance of P1 and P2.

Table 2: Comparative Performance of Conventional (P1) vs. Reflex DNA (P2)

Screenings

Item	Conventional Multi-Sample (P1)	Single-Sample Reflex DNA (P2)	Gains with P2
Dropouts	2,950 (Sabah)	0	100% dropout
	2,836 (Sarawak)		elimination
Carriers	~1,500 (Sabah)	286 (Sabah)	12% (Sabah),
Detected (Est.)	~1,100 (Sarawak)	57 (Sarawak)	5% (Sarawak)
Cost per	Not available	RM379.95 (Sabah)	Lower in high-
Carrier		RM821.85 (5wk)	prevalence
Detected			areas
ICER per	Not available	RM25.14 (Sabah)	Highly cost-
Dropout		RM22.19 (Sarawak)	effective
Averted			
Preventable	Not available	RM3.8M-11.4M (Sabah)	Significant
Treatment		RM758K-2.3M (Sarawak)	long-term
Costs			savings

Conclusion

The P2 approach demonstrates superior cost-effectiveness and operational efficiency compared to the P1 strategy, particularly in high-prevalence states such as Sabah. While based on modelled projections using retrospective data, these findings justify phased implementation, preceded by pilot studies, to reduce thalassaemia births and generate long-term savings across Malaysia's healthcare system.

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