



MATHEMATICAL MODELS BASED ON DIFFERENCE AND DIFFERENTIAL EQUATIONS FOR DENGUE DISEASE MAPPING IN BANDUNG, INDONESIA

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THESIS SUBMITTED IN FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

FACULTY OF SCIENCE AND MATHEMATICS SULTAN IDRIS EDUCATION UNIVERSITY

2019



ABSTRACT

This study aimed to introduce a new alternative mathematical model for the discrete space-time compartment models. The study focuses on the development of three new models. The first model is a stochastic model which considers the age-structure based on the difference equation, also known as the ASDE model to estimate the relative risk of dengue disease transmission. This model takes into account the spatial correlation in determining the newly infective number of dengue cases which can be applied to juveniles and adults by using different birth and death probabilities. The second model is the OBDE model which is based on the development of O blood-type differential equation. Lastly, the third model is the WADE model, which is also known as Wolbachia-Aedes mosquito differential equation. The basic reproduction numbers (R_0) of OBDE and WADE models as the threshold of dengue disease transmission are determined, while the stability of the models are analyzed. Results indicate that the ASDE model yielded the best result when it was applied to the juvenile group. Meanwhile, OBDE model analysis shows that the OBDE model was stable for free and endemic states. Additionally, this supports the fact that O blood-type individuals have higher probability to be infected by dengue disease compared to the non-O blood-type people. On the other hand, the analysis of WADE model shows that this model was only stable in the free-state. Based on the form of basic reproduction number of WADE 05.4506 model, the minimum number of Wolbachia-Aedes mosquitoes that must be released in bupst a particular area to reach the free-state condition can be determined. In conclusion, the ASDE model offers better results in estimating the relative risks, especially for the juvenile group. In addition, the other two models with the space-time variables are applied to support the real condition. The implication of the study reveals that the ASDE model can determine the risk areas that need to be treated by the authorities with dengue vaccine as prevention to juveniles as recommended by ASDE model and also to O blood-type people as suggested by OBDE model. Another treatment is by releasing the Wolbachia-Aedes mosquitoes in a certain number as determined by WADE model.









MODEL MATEMATIK BERDASARKAN PERSAMAAN BEZA DAN PEMBEZAAN UNTUK PEMETAAN PENYAKIT DENGGI DI BANDUNG, INDONESIA

ABSTRAK

Tujuan kajian ini adalah memperkenalkan model matematik alternatif baharu bagi model kompatmen ruang-masa diskrit. Kajian ini memberi tumpuan kepada pembangunan tiga model baharu. Pertama ialah model stokastik yang menganggap struktur umur berdasarkan persamaan beza, juga dikenali sebagai model ASDE untuk menganggarkan risiko relatif penyebaran penyakit denggi. Model ini mengambil kira korelasi ruangan dalam menentukan kes jangkitan denggi terbaharu dan digunakan ke atas golongan remaja dan dewasa dengan menggunakan kebarangkalian kelahiran dan kematian yang berbeza. Model kedua adalah model OBDE yang berdasarkan kepada perkembangan persamaan pembezaan darah jenis O. Yang terakhir, model ketiga dikenali sebagai persamaan pembezaan nyamuk Wolbachia-Aedes, iaitu pembangunan model WADE. Bilangan pembiakan asas (R_0) model OBDE dan WADE sebagai ambang batas penyebaran penyakit denggi telah ditentukan, manakala kestabilan model telah dianalisis. Hasil kajian menunjukkan bahawa model ASDE menghasilkan keputusan terbaik apabila digunakan ke atas kumpulan remaja. Sementara itu, analisis OBDE model menunjukkan bahawa model ini adalah stabil dalam keadaan bebas dan endemik. Tambahan itu, ia turut menyokong penyataan bahawa individu berdarah jenis O mempunyai kebarangkalian yang tinggi untuk dijangkiti penyakit denggi berbanding individu berdarah jenis lain. Sebaliknya, analisis model WADE pula menunjukkan bahawa model ini hanya stabil dalam keadaan bebas. Melihat kepada pembentukan bilangan pembiakan asas model WADE, bilangan minimum nyamuk Wolbachia-Aedes yang perlu dilepaskan di kawasan tertentu untuk mencapai keadaan bebas boleh ditentukan. Kesimpulannya, model ASDE menawarkan hasil yang lebih baik dalam menganggar risiko relatif, terutamanya berkaitan kumpulan remaja. Di samping itu, dua model lain dengan pemboleh ubah ruang-masa digunakan untuk menyokong keadaan sebenar. Implikasi kajian mendedahkan bahawa model ASDE boleh menentukan kawasan berisiko yang perlu dirawat oleh pihak berkuasa dengan vaksin denggi sebagai pencegahan kepada golongan remaja seperti yang disarankan oleh model ASDE, dan kepada individu berdarah jenis O seperti yang dicadangkan oleh model OBDE. Rawatan lain adalah dengan cara melepaskan nyamuk Wolbachia-Aedes dalam jumlah tertentu seperti yang ditentukan oleh model WADE.







CONTENTS

	Page				
DECLARATION OF ORIGINAL WORK	ii				
DECLARATION OF THESIS FORM	iii				
ACKNOWLEDGEMENT	iv				
ABSTRACT					
ABSTRAK	vi				
CONTENTS	vii				
LIST OF TABLES	xi				
LIST OF FIGURES	xiii				
05-45068 LIST OF ABBREVIATIONS Perpustakaan Tuanku Bainun Kampus Sultan Abdul Jalil Shah	xvii ptbups				
LIST OF APPENDICES	xix				
CHAPTER 1 INTRODUCTION	1				
1.1 Background of the Study	1				
1.2 Problem Statement	8				
1.3 Research Objectives	13				
1.4 Significance of the Study	14				
1.5 Scope and Limitations of the Study	16				
1.6 Research Framework	17				
1.7 Organization of the Report	17				
CHAPTER 2 LITERATURE REVIEW	20				
2.1 Vector Borne Infectious Diseases	20				









Page	
------	--

	2.1.1	Dengue Epidemiology	22	
	2.1.2	Signs and Symptoms	27	
	2.1.3	Cause of Dengue and Transmission of the Dengue Virus	28	
	2.1.4	Treatment and Precaution Development	30	
2.2	Mode for Di	lling and Analysis of Transmission Mechanism sease Mapping	31	
	2.2.1	Modelling Disease Transmission	32	
	2.2.2	Bayesian Modelling	34	
	2.2.3	Analysis of Disease Mapping	37	
	2.2.4	The Existing Relative Risk Estimation Methods	38	
2.3	Differ	rence and Differential Equation Models	45	
9 05-4506832	2.3.1	Deterministic SIR-SI Model	47	
	2.3.2	The Basic Reproduction Number (R_0)	51	
	2.3.3	Stochastic SIR-SI Model	53	
CHAPTER 3 INV	ESTIG	ATION OF DENGUE CASE IN BANDUNG	56	
3.1	3.1 The Data Set			
3.2	Appli Relati Bandu	cation of the Existing Methodologies of ve Risk Estimation to Dengue Case in ang	59	
	3.2.1	Relative Risk Estimation based on Standardized Morbidity Ratio (SMR)	60	
	3.2.2	Relative Risk Estimation based on Poisson- gamma, Log-normal, BYM and Mixture Model	65	
	3.2.3	Model Selection for Existing Models	69	







Page

	3.3	Investigation of Age-group Consideration	71
CHAPTER 4	DE DI HU	VELOPMENT OF AGE-STRUCTURE FFERENCE EQUATION (ASDE) MODEL IN MAN COMPARTMENT	83
	4.1	Background	84
	4.2	Model Development	85
	4.3	Application of ASDE Model to Dengue Cases in Bandung	93
		4.3.1 Parameters Estimation of ASDE Model	93
		4.3.2 Results and Discussion	97
CHAPTER 5	DEV DIF HUN	YELOPMENT OF O BLOOD TYPE FERENTIAL EQUATION (OBDE) MODEL IN MAN COMPARTMENT	107
	5.1	Background	108
🕓 05-4506832 🔮 pustaka	5.2	Model Development Tuanku Bainun	109 ptb
		5.2.1 Basic Reproduction Number of OBDE Model	114
		5.2.2 Stability Analysis of OBDE Model	118
	5.3	Application of OBDE Model to Dengue Cases in Bandung	121
		5.3.1 The Data Set and Parameter Estimation	121
		5.3.2 Results and Discussion	124
CHAPTER 6	DE MC MC	VELOPMENT OF WOLBACHIA-AEDES OSQUITO DIFFERENTIAL EQUATION (WADE) DEL IN MOSQUITO COMPARTMENT	137
	6.1	Background	138
	6.2	Model Development	139
		6.2.1 Basic Reproduction Number of WADE Model	143

O5-4506832 Bustaka.upsi.edu.my Perpustakaan Tuanku Bainun Kampus Sultan Abdul Jalil Shah









Page

		6.2.2	Stability Analysis of WADE Model	147	
	6.3	Applic Bandu	pplication of WADE Model to Dengue Cases in andung		
		6.3.1	The Data Set and Parameter Estimation	151	
		6.3.2	Results and Discussion	151	
CHAPTER 7 CONCLUSION, CONTRIBUTION AND RECOMMENDATIONS				157	
	7.1	Conclu	usion	157	
	7.2	Contri	butions and Significance	163	
	7.3	Recon	nmendations	166	
REFERENCES			168		



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PustakaTBainun O ptbupsi









LIST OF TABLES

Table N	0	Page
2.1	Types of Diseases, The Vector-borne and The Agent	21
3.1	Relative Risk Estimation based on SMR Method and The Observed Dengue Case	62
3.2	Relative Risk Estimation based on some methods other than SMR	66
3.3	Comparison of the Deviance Information Criterion (DIC) from Poisson-gamma, Log-normal, BYM and Mixture Model	70
3.4	Relative Risks Estimation of Juvenile and Adult Groups using Poisson-gamma, BYM and Mixture Models of Dengue Cases in Bandung, 2013	73
3.5 pust	Comparison of DIC Values of Poisson-gamma, BYM and Mixture Models in Juvenile and Adult Group	80 ptbup
4.1	Division area in Bandung	94
4.2	Number of Human Population in 8 Service Sub-Centers in Bandung	96
4.3	The DIC Comparison of Age-structured SIR-SI Model	101
4.4	Juvenile Relative Risk Estimation (<i>θi</i>) of Dengue Disease in Bandung for Week 50	103
5.1	Notation and Description List of OBDE Model	110
5.2	Notations and Initial Values List of OBDE Model	122
5.3	Notations and Initial Values List for Demonstration Purpose of OBDE Model in Setrasari City Sub-center at time 0 (i=6, j=0)	124
5.4	Basic Reproduction Number (R_0^0) of OBDE Model with $Pr(\sigma_0) = 0.6, Pr(\sigma_{\overline{0}}) = 0.4, N_6^{(h)} = 347,024$	127

O5-4506832 V pustaka.upsi.edu.my Perpustakaan Tuanku Bainun Kampus Sultan Abdul Jalil Shah







Stability Analysis of OBDE Model with $Pr(\sigma_0) = 0.6$, $Pr(\sigma_{\overline{0}}) = 0.4$, $N_6^{(h)} = 347,024$ on Condition 2 $\left(N_6^{(m)} = \right)$ 5.5 129 2,639,260)

6.1	Notation and Description List of WADE Model	140
-----	---	-----

6.2 Categories of Wolbachia Simulation 152

- Stability Analysis of WADE with $N_6^{(h)} = 347,024 \left(N_6^{(m)} = \right)$ 6.3 155 7.10^{10}
- Contribution to Knowledge of Dengue Disease Mathematical 7.1 164 Modelling







PustakaTBainun O ptbupsi













LIST OF FIGURES

Figures	Figures No.							
1.1	Number of Dengue Cases in Bandung, 2011-2013	9						
1.2	Juvenile and Adult Dengue Cases in Bandung, 2011-2013	10						
1.3	Research Framework on This Study	17						
2.1	Average Annual Number of DF and DHF cases reported to WHO, and of countries reporting Dengue, 1955-2010 (WHO, 2012)	22						
2.2	Dengue cases of some cities in West Java, 2013	26						
2.3	Aedes Aegypti Mosquito (Updates, 2013)	28						
2.4	Compartmental SIR-SI model for dengue disease transmission (Samat & Percy, 2012a)	48						
05-4506832 3.1	Puskesmas in Bojongloa Kidul sub-district (Jurnal Media, 2018)	57 ptbups						
3.2	Comparison between SMR and Observed Dengue Case in each Sub-district, Bandung, 2013	62						
3.3	Disease Map of Estimated Relative Risk using SMR method in Bandung, 2013	63						
3.4	Disease Map of Estimated Relative Risk based on Poisson- gamma Model in Bandung, 2013	67						
3.5	Disease Map of Estimated Relative Risk based on Log-normal Model in Bandung, 2013	67						
3.6	Disease Map of Estimated Relative Risk based on Mixture Model in Bandung, 2013	68						
3.7	Disease Map of Estimated Relative Risk based on BYM Model in Bandung, 2013	68						
3.8	Dengue Risk Map for Juvenile in Bandung, using the Yearly Data in 2013, based on Poisson-gamma and BYM Models	74						
3.9	Dengue Risk Map for Juvenile in Bandung, using the Yearly Data in 2013, based on Mixture Model	75						









3.10	Dengue Risk Map for Adult in Bandung, using the Yearly Data in 2013, based on Poisson-gamma and BYM	75
3.11	Dengue Risk Map for Adult in Bandung, using the Yearly Data in 2013, based on Mixture Models	76
3.12	Time Series of Weekly Relative Risks Estimation based on Poisson-gamma Model for Juvenile Group	77
3.13	Time Series of Weekly Relative Risks Estimation based on Poisson-gamma Model for Adult Group	77
3.14	Time Series of Weekly Relative Risks Estimation based on BYM Model for Juvenile Group	78
3.15	Time Series of Weekly Relative Risks Estimation based on BYM Model for Adult Group	78
3.16	Time Series of Weekly Relative Risks Estimation based on Mixture Model for Juvenile Group	79
3.17	Time Series of Weekly Relative Risks Estimation based on Mixture Model for Adult Group	79
4.1	Compartment Model for Age-Structure	86
4.2	Time Series of RR Estimations for Juvenile Group under Assumption A(1) with Same Birth and Death Probability	98
4.3	Time Series of RR Estimations for Juvenile Group under Assumption A(1) with Different Birth and Death Probability	98
4.4	Time Series of RR Estimations for Juvenile Group under Assumption A(2) with Same Birth and Death Probability	98
4.5	Time Series of RR Estimations for Juvenile Group under Assumption A(2) with Different Birth and Death Probability	99
4.6	Time Series of RR Estimations for Adult Group under Assumption A(1) with Same Birth and Death Probability	99
4.7	Time Series of RR Estimations for Adult Group under Assumption A(1) with Different Birth and Death Probability	99
4.8	Time Series of RR Estimations for Adult Group under Assumption A(2) with Same Birth and Death Probability	100
4.9	Time Series of RR Estimations for Adult Group under Assumption A(2) with Different Birth and Death Probability	100
4.10	SIR-SI Dengue Disease Mapping for Juvenile Using the Same Life and Death Probability in Bandung, 2013 Based on	104







Assumption A (1)

	4.11	SIR-SI Dengue Disease Mapping for Juvenile Using the Same Life and Death Probability in Bandung, 2013 Based on Assumption A(2)	104
	4.12	SIR-SI Dengue Disease Mapping for Juvenile Using the Different Life and Death Probability in Bandung, 2013 Based on Assumption A(1)	105
	4.13	SIR-SI Dengue Disease Mapping for Juvenile Using the Different Life and Death Probability in Bandung, 2013 Based on Assumption A(2)	105
	5.1	Compartment Model for O Blood Type	109
	5.2	Basic Reproduction Number of OBDE with Different Values of $r(\sigma_0)$ and Number of Mosquitoes $(N_6^{(m)})$	125
	5.3	Basic Reproduction Number of OBDE with Different Values of $r(\sigma_0)$ with $N_6^{(m)} = 105,000$	126
	5.4	Numerical Simulation of Proportions for a Disease-Free State for Susceptible Human	130
05-45068	3.5	Numerical Simulation of Proportions for a Disease-Free State for O Blood-type Infected Human	131 ptbur
	5.6	Numerical Simulation of Proportions for a Disease-Free State for Non-O Blood-type Infected Human	131
	5.7	Numerical Simulation of Proportions for a Disease-Free State for Recovery Human	131
	5.8	Numerical Simulation of Proportions for a Disease-Free State for Infected Mosquito	132
	5.9	A Numerical Simulation of Proportions at Disease Endemic State for Susceptible Human	133
	5.10	A Numerical Simulation of Proportions at Disease Endemic State for O Blood-type Infected Human	133
	5.11	A Numerical Simulation of Proportions at Disease Endemic State for Non-O Blood-type Infected Human	134
	5.12	A Numerical Simulation of Proportions at Disease Endemic State for Recovery Human	134
	5.13	A Numerical Simulation of Proportions at Disease Endemic State	134











for Infected Mosquito

6.1	Compartmental Model for Wolbachia-Aedes Mosquitoes	139
6.2	Numerical Simulation of Proportions at Disease-free State for Susceptible Human	153
6.3	Numerical Simulation of Proportions at Disease-free State for Infected Human	153
6.4	Numerical Simulation of Proportions at Disease-free State for Infected Mosquito	153
6.5	Numerical Simulation of Proportions at Disease-free State for Resistant Mosquito	153
6.6	Numerical Simulation of Proportions at Disease-free State for Recovery Human	154







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LIST OF ABBREVIATIONS

ABO Blood-type A, B, AB and O

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- ASDE Age Structure Difference Equations
- BYM Besag, York and Mollie method
- CAR Conditional Auto-regressive
- DEN Dengue virus
- DES Differential Equation System
- DF Dengue Fever

GIS

- DHF Dengue Haemorrhagic Fever
- DIC Deviance Information Criterion
- DSS Dengue Shocked Syndrom
 - Geographical Information System
 - OBDE O Blood-type Differential Equations
 - SEIR Susceptible-Exposed-Infective-Recovery for human populations
 - SEIR-SI Susceptible-Exposed-Infective-Recovery for human populations; Susceptible-Infective for mosquito populations
 - SI Susceptible-Infective for human populations
 - SIR Susceptible-Infective-Recovered for human populations
 - SIR-SI Susceptible-Infective-Recovered for human populations; Susceptible-Infective for mosquito populations
 - SIRS Susceptible-Infective-Recovered-Susceptible for human populations
 - SIRS-SI Susceptible-Infective-Recovered-Susceptible for human populations; Susceptible-Infective for mosquito populations
 - SIS Susceptible-Infective-Susceptible for human populations

05-45068









- Standardized Morbidity or Mortality Ratio SMR
- TBE **Tick-borne Encephalitis**
- Wolbachia-Aedes mosquitoes Differential Equations WADE
- WHO World Health Organization
- Bayesian Inference using Gibbs Sampling running under Windows WinBUGS





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LIST OF APPENDICES

- А **Knowledge Dissemination**
- Poisson-Gamma Code in WINBUGS (Lawson, Browne, & Rodeiro, 2003) B1
- B2 Log-Normal Code in Winbugs (Lawson, Browne, & Rodeiro, 2003)
- Besag, York and Mollie Code in Winbugs (Lawson, Browne, & Rodeiro, **B**3 2003)
- B4 Mixture Code in Winbugs (Lawson, Browne, & Rodeiro, 2003)
- C1 Weekly Dengue Data in Bandung, 2013 for Juvenile
- Weekly Dengue Data in Bandung, 2013 for Adult C2
- 05-450683 Programming Codes of Juvenile ASDE Model

PustakaTBainun O ptbupsi

- D2 Programming Codes of Adult ASDE Model
- Programming Codes of R₀^O Plot E1
- E2 Programming Codes of OBDE Numerical Simulation
- F Programming Codes of WADE Numerical Simulation









CHAPTER 1

INTRODUCTION

This chapter provides the background of the study, followed by problem statement, **O** ptbupsi research objectives and significant of the study. This chapter also elaborate the scope and limitations of the study and brief description of this study is provided in research fremawork. The organization of the report is explained in the last section.

1.1 **Background of the Study**

According to Lawson (2013), disease mapping defined as a collection of disease objects, such as residential locations of individuals or a summary measure or statistic for specified groups of individuals in their geographical association. Disease mapping can be employed to demonstrate the distribution of infectious diseases providing the readers with a clear visualisation of the relationship between the disease and the





geographical location. The impact of the environment on health will be better understood once the maps have been constructed for a wide variety of the diseases.

The spread of a infectious disease has always been our main concerns and threats to the public health. It has caused severe problems for the survival of a human beings and other species, and for the economic and social development of the human society. According to Aregay, Lawson, Faes, & Kirby (2015) and Ma & Li (2009), to prevent and control infectious diseases efficiently, it is essential to fully understand the mechanism of the spread and transmission dynamics of the diseasesto produce useful predictions and guidance for better strategies could be established.

Technically, disease mapping is one of a method to represent the transmission of a particular disease geographically. A good map of disease risk can be beneficial as an important tool for the disease control. This mapping refers to the visual representation of the geographical distributions which useful to identify the risk area that deserves more profound observation and more attention for prevention and accurate treatment (Chaikoolvatana, Singhasivanon, Haddawy, & Saengnill, 2013; Chang, et al., 2009; Eisen & Lozano-Fuentes, 2009).

Lawson (2013) reported that mapping have at least four significant roles for public health specialists. First, it can monitor the spread of infectious diseases to identify the cause of the infection. Second role is to monitor the health service usages such as the uptake of vaccination or the use of community care services. In addition, the third role is for the non-infectious diseases to generate the hypotheses on the disease caution or to identify the clusters of the disease. The last role is mapping the exercises





that could incorporate ecological analysis by adjusting the explanatory variables.

Dengue disease mapping for the whole area in Indonesia is unavailable until now due to the data availability since the only data that available are the aggregate data type. Although prevention and treatment of the disease have been implemented to the society, a large number of dengue cases still reported. Despite an urgent needs for dengue disease mapping of the whole country, they are only available for some areas, such as in Surabaya (Mulyatno, Yamanaka, Yotopranoto, & Konishi, 2012), North Jakarta (Sungkar, Fadli, & Sukmaningsih, 2011), Bantaeng Residence (Munsyir & Amiruddin, 2011), and Bandung (Karina, Sari, Sumardi, & Setiawati, 2015; Supriatna, 2009).

The existing disease mapping research in Bandung focusing on deterministic model by using the existing observed dengue data (Karina, Sari, Sumardi, & Setiawati, 2015; Supriatna, 2009; Supriatna, Soewono, & Gils, 2008). However, in real condition, the random effects cannot be neglected. Hence, the stochastic factor needs to take into account. Some stochastic researches indicated that the stochastic models are more realistic than the deterministic models (Ditlevsen & Samson, 2013; Tango, 2010; Wakefield, 2007; Wakefield & Morris, 2001; Daley & Gani, 1999; Bartlett, 1964).

Currently, the prevention and control strategies in Indonesia for dengue included three important aspects which are environmental, biological and chemical. The strategies involved various concerned stakeholders; starting from the Health Department, Health Services Workers, up to the society. There is a slogan for educating the society known as 3M (Menutup, Menguras, Menimbun), meaning Covering,







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Draining, Burying or Reusing. It means to cover and drain the water storage tank or reservoirs such as bathtubs, buckets of water, drinking water reservoirs and so forth, or to bury or recycle second-hand goods that can be potentially used by the dengue mosquitoes to lay their eggs. Fogging was conducted in the areas that are infected by this disease. The latest is implemented only after dengue cases have occurred in that particular area (Kemenkes RI, 2017; Lestari, 2007).

Indonesia Health Department used the total numbers of dengue cases across the regions to differentiate the high to low risk areas. This practice applied without considered the population or the land size to handle the prevention and control of dengue in Indonesia. This research aims to produce excellence risk map of the highlow risk areas by including the population factor.

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An excellence risk map should consider the relative risk to be mapped for the disease mapping since the excess risk found in relation to that supported purely by the local population, which is 'at risk' (Lawson, 2006). Relative risk is the ratio of the exposed group that will develop disease to the unexposed group that will develop the same disease. In brief, relative risk is usually used to compare the risks of different groups. Samat & Mohd Imam Ma'arof (2013) explained the interpretation of relative risk as the probability that a person within a specified region contracted by the disease which is divided by the probability that a person in the population contracted by the disease.







In addition, the age group is another important factor that has to be considered in disease mapping modelling. The age factor is related to survival capability against a particular disease and specific prevention and treatment in disease transmission. Several studies emphasised the age factor needs to be considered as one of the important factors in disease transmission since the number of dengue cases among juvenile group was significant (Thunguturthi, Reddy, & Kiran, 2013; Tahir, Hafeez, & Chaudhry, 2010; Supriatna, 2009; Lawson, 2006; Pongsumpun & Tang, 2003; Lawson & Williams, 2001). WHO (2012) and WHO (2009) mentioned that the greatest burden of dengue in most countries is among children, although in some areas older age groups are also significantly affected. The number of weekly dengue cases for particular age group for all sub-districts in Indonesia undetermined precisely due to unavailability data since some researches reported the yearly data or monthly data and only covered particular areas (Lestari, 2007). However, detailed dengue cases by age group for Bandung, West Java, Indonesia have been classified and made available and ready to be used in this study.

Furthermore, age factor has relation to different treatment of vaccine. However, it is not absolutely related to the medical treatment of the disease. Even though there is dengue vaccine which is known as Dengvaxia that can be clinically used, vaccine allocation, provided for particular age group will minimise the incidence of dengue transmission (WHO, 2016; Wilder-Smith & Massad, 2016; Mbah, Durham, Medlock, & Galvani, 2014) as this vaccine is allocated to people of age 9-45 years (Constenla & Clark, 2016). However, vaccinating children will be more effective in cost (Constenla & Clark, 2016; Johansson, Hombach, & Cummings, 2011; Suaya, et al., 2009; Cruz-Pacheco, Esteva, & Vargas, 2005; Shepard, et al., 2004).





Another factor that associated with dengue transmission besides the age factor, is the ABO groups or blood type groups (Khode, Kabbin, & Ruikar, 2013; Thunguturthi, Reddy, & Kiran, 2013; Orsi, et al., 2013; Young, et al., 2013; Kalayanarooj, et al., 2007). They found that the relationship between ABO groups and dengue disease is limited due to data on the frequency distribution of ABO blood group in dengue patients unavailable. The term of blood type has been used instead of ABO group, due to the regularities in previous studies (Khode, Kabbin, & Ruikar, 2013; Kalayanarooj, et al., 2007).

According to Khode, et al. (2013), blood type group system is a part of the innate or congenital immune system. Therefore, humans with different types of blood have different risk of being infected by certain viral or bacterial infections and diseases. Therefore, blood type can be considered as one important factor in disease transmission since less previous studies considered the relevance of blood type group and the severity of dengue disease.

Moreover, Khode, et al. (2013), Thunguturthi, et al. (2013), and Young, et al. (2013) emphasised that O blood type patients have higher risk to be infected by dengue disease in the transmission dynamics. Thus, based on these researches, this study concerns with O blood type to consider in the transmission dynamics.

Another fact should be considered in dengue disease transmission are human and mosquito factors. Therefore, it is important to consider the treatment in vector population as well. Recently, there is a natural treatment to control the transmission of





dengue disease by infecting Aedes mosquitoes as the vector with Wolbachia bacteria. The Wolbachia-Aedes mosquitoes unable to transmit dengue virus to human being even it has been infected by Dengue virus because it becomes resistant towards dengue virus. This bacterium also decreases the lifespan of Aedes mosquitoes (Joubert & O'Neill, 2017; Ndii, Hickson, Allingham, & Mercer, 2015; Afizah & Lee, 2013).

The deterministic compartment SIR-SI (Susceptible-Infective-Recovered for human populations and Susceptible-Infective for mosquito populations) model is discussed. The discussion is continued with deterministic compartmental SIR-SI with the age structure model. The models proposed by Pongsumpun (2012), Pongsumpun (2008), Pongsumpun & Tang (2003) have been developed with the stochastic approach for the real condition. This research is continued by improving the compartment model including the O blood type factor in human compartment with the last compartment model developed is the SIR-SI model considering Wolbachia-Aedes mosquitoes in mosquito compartment.

This study primarily concerned on the mathematical models based on difference and differential equations of dengue disease in Bandung, West Java, Indonesia. If the transmission can be mapped, the particular areas that required serious treatment, therefore, will be visible. Thus, the Indonesia Health Department will be able to determine the right policies that enable all stakeholders to implement the prevention and treatment of dengue disease more effectively and efficiently.







1.2 Problem Statement

Dengue disease is the most rapidly spreading mosquito-borne viral disease in the world. Dengue disease outbreaks will cause not only death, but also economic losses. The economic losses are imposed by treating dengue occurrence that causes substantial costs (WHO, 2016; Constenla & Clark, 2016; Gubler, Ooi, Vasudevan, & Farrar, 2014; WHO, 2009). There are two economic impacts which are direct and indirect form. The direct economic impact is the costs of the treatment or cure, for ambulatory case or hospitalisation case. Meanwhile, the examples of indirect economic impact is the lost of productivity, school absenteeism, and unpaid time of caregivers. Other losses are social losses, those are panic in the family or mortality in the family (Widiyani, 2013; Suaya, et al., 2009). In average, the costs that required for the purposes of dengue treatment in the world was reported around USD 6 Billion, while the annual cost for Indonesia was estimated around USD 300 Million in 2014 (Maharani & Dewi, 2015).

Widiyani (2013) reported that the number of dengue cases continues to increase every year. WHO (2009) mentioned that 150,000 dengue cases in Indonesia were reported in 2007 and Jakarta and West Java recorded over 25,000 dengue cases. According to Indonesia Health Department , the total number of dengue case in 2012, reported to World Health Organization (WHO), was 90,245 cases. This number increased to 112,511 cases in 2013. Bandung as the most populous city in the West Java, Indonesia also has significant number of dengue cases. Figure 1.1 illustrates the number of dengue cases in Bandung that increased significantly over years (Bandung, 2011; Bandung, 2012).



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Figure 1.1. Number of Dengue Cases in Bandung, 2011-2013

Compared to Singapore, for instance, treatment and prevention for the transmission of dengue have been anticipated this disease since years ago. The number of dengue cases in 2004 is 9,459 and in 2005 is 13,817. If it is divided by the area of the country, that is 697 km^2 , then, in 2004, averagely, that would be 13.571 cases per km^2 . This ratio became higher in 2005, which was 19.824 cases per km^2 . With such ratio, it is obvious that this country has started to apply the research findings to manage dengue transmission (Burattini, et al., 2008). In Bandung, the ratio of case number compared to the area in 2013 was 5,749 cases divided by 167,31 km^2 equals to 34.36 cases per km^2 . Therefore, the transmission of this disease transmission should be executed immediately by community, health department and government.

As stated in Fong (2013), it is affirmed that it is time to fight against this disease, and there is an additional alternative that can be done by using a research approach. The researches against dengue transmission must be well organized and implemented to make a good policy of prevention. Thus, this research is intended to support that purpose. From the theories that are discussed, it would be beneficial to choose the method to estimate the relative risk and determine the basic reproduction





number that suits dengue disease in Bandung, West Java, Indonesia.

As mentioned previously, the stochastic researches indicated that stochastic models are more realistic than deterministic ones. According to Lawson (2013) and Daley & Gani (1999), the spread of an infectious disease is a random process. If the number of individuals is very large, it is customary to represent the infection process deterministically. However, deterministic models are unsuitable for small populations, while in the larger populations, the mean number of infective in a stochastic model may not always be approximated satisfactorily by the equivalent deterministic model. Figure 1.2 depicts the dengue case of juvenile and adult in Bandung. It informs that the juvenile cases increased in significant number from 2011 to 2013.



Figure 1.2. Juvenile and Adult Dengue Cases in Bandung, 2011-2013

In the analysis for mosquitoes-borne diseases, especially in malaria and dengue disease with age structure, many studies only consider deterministic models (Addawe & Lope, 2012; Pongsumpun, 2012; Pongsumpun, 2008; Supriatna, Soewono, & Gils, 2008; Pongsumpun & Tang, 2003). Therefore, the first aim of this



research is to develop the new stochastic model to estimate the relative risk of the SIR-SI compartmental model which considers the age factor for dengue disease transmission in Bandung, West Java, Indonesia. The extension will include the basic age-structure for the SIR-SI model as proposed by (Pongsumpun, 2012; Pongsumpun, 2009; Pongsumpun & Tang, 2003). This model includes not only the interactions between mosquito and human host but also the space-time factor. The stochastic approach is formerly based on the stochastic SIR-SI models which suggested by Samat & Percy (2012a).

In some studies that consider the SIR-SI compartmental model, usually the birth and mortality rate for humans are assumed constant in each compartment (Esteva & Vargas, 1998). This assumption was due to data unavailability. In this thesis, the birth and mortality rate will be distinguished based on particular life table of Indonesians because this assumption is closer to the real condition. This rate could be used to assume the related rate of population in certain critical areas of Bandung.

Furthermore, the immune system of human influenced on the risk of human infected by a particular disease. Khode, Kabbin, & Ruikar (2013) explained that the blood type group system is a part of the congenital immune system. Consequently, the humans with the different type of blood have the different risk of being infected by certain viral or bacterial infections and diseases. It also stated that there are less research that considered the relevance of the blood type group and the severity of dengue disease. Therefore, this study discusses the influenced of the blood type group system in the transmission factor.







Sari , et al. (2018), Sjafaraenan, Alvionita, Agus, & Sabran (2018), Khode, et al. (2013), Thunguturthi, et al. (2013), and Young, et al. (2013) emphasized the blood type O patients have higher risk to be infected by dengue disease. Thus, from these finding, this study concerns with the O blood type as one of factors that is considered in developing mathematical models.

Another fact should be considered is that dengue disease transmission involves host and vector factors. The government programs have focused to the host treatments, such as maintaining stamina, maintaining environmental hygiene, preventing mosquito bites; and to the vector treatments, such as fogging, using temephos in the water reservoirs so that Aedes mosquitoes can be eradicated.

Another alternative prevention of dengue spread by using dengue vaccine. However, the use of dengue vaccine is less effective to be applied to the community due to the cost that is quite expensive and unsubsidised by the government (Attikah, 2018; Kinanti, 2016; Sativa, 2016). Therefore, another alternative could be encouraging community to execute a treatment for Aedes mosquitoes as a vector in the spread of this disease. One eco-friendly way is to infect Aedes mosquitoes with Wolbachia bacteria. Whereby the Aedes mosquitoes are infected by Wolbachia bacteria, they are unable to spread the Dengue virus to other humans since the bacteria detain the virus replication in infected mosquitoes. It has been proven that this method was able to reduce the spread of Dengue virus from infected mosquitoes to the susceptible human (Joubert & O'Neill, 2017; Ndii, Hickson, Allingham, & Mercer, 2015; Afizah & Lee, 2013).







Several models of mathematical transmission associated with this phenomenon have been widely discussed. Ndii, Hickson, Allingham, & Mercer (2015) and Supriatna, (2016) developed the mathematical modelling that considered the Wolbachia effect in Aedes mosquitoes. However, the study considered the time variable; while in fact, dengue disease transmission was affected by spatial effect. Moreover, they unconsidered to analyze the stability of the difference equations dynamical model for Bandung condition.

However, due to the data unavailability for the blood type group and Wolbachia cases, the relative risk based on blood-type group and Wolbachia effect unable to be estimated. Therefore, this study will focus on determining the R_0 as the threshold for dengue disease transmission together with the blood type group and Wolbachia effect. R_0 is the basic reproduction number defined as the average number of new infections generated by a single infectious individual in a fully susceptible population (Supriatna, 2016; Nishiura, 2006).

1.3 **Research Objectives**

The objectives of this research are:

To develop a new discrete time, discrete space, and stochastic model based on 1. difference equations in the form of a SIR-SI model for mosquito-borne dengue disease transmission with the effect of age group which takes into account different birth and death probability.







- To estimate the relative risk for dengue disease mapping based on the SIR-SI 2. compartmental models with age-structure using dengue data from Bandung, Indonesia.
- To develop a new discrete time, discrete space model based on differential 3. equations in the form of a compartmental SIR-SI model for mosquito-borne dengue disease transmission with the effect of O blood type group.
- To develop a new discrete time, discrete space model based on differential 4. equations in the form of a compartment SIR-SI model for mosquito-borne dengue disease transmission with the effect of the Wolbachia- Aedes mosquitoes.



Dengue is one of the most dangerous vector-borne infectious diseases in the world which are fatal in many cases due to inefficient treatment. The disease is difficult to be eradicated because it is influenced by many factors, such as unhealthy lifestyle of the society, for example: littering, keeping empty containers or cans in an open place that forms the habitat for the mosquitoes; and environment factors, i.e. climate and rainfall especially in the tropical country. Other factors that accelerate to the spread of this disease are population density and high rates of urbanization in an area (Fong, 2013; WHO, 2012; Pongsumpun, Patanarapelert, Sriprom, Varamit, & Tang, 2004).

A real medicine to cure dengue disease still becomes a question to many researchers (WHO, 2012). Therefore, it is necessary to plan strategic steps to prevent







dengue from quick spreading by understanding the transmission process. The mathematical model could helps to estimate the transmission relative risk as one of the prevention strategies (Fong, 2013; Ma & Li, 2009).

This study takes the stochastic factor into account in modelling dengue to obtain the best result to represents the real condition. Meanwhile, the random effects that are usually neglected in deterministic models included in this stochastic approach to estimate the relative risk of dengue disease transmission to produce better depiction of high-low risk areas. A good maps of disease risk can be useful as an important tool for disease control and can be used to identify the risk area that deserves deeper observation and more attention for prevention and accurate treatment. If the dengue transmission can be mapped very well, the particular areas that needs serious treatment could be arise, hence the prevention and treatment could handle effectively and efficiently.

Since there are many juvenile cases in the spread of dengue disease, hence, it is important to consider the juvenile age group in some prevention and treatment strategies. The age factor is, therefore, included in this estimation model. Moreover, the blood-type factor in human population and Wolbachia-Aedes mosquitoes in mosquito population play important role in dengue transmission dynamics. However, due to the unavailability of the data, the relative risk of dengue transmission related to these factors is unable to estimate. Nevertheless, supported by more realistic modelling and computer simulations, this study significantly provides improvement in terms of dengue transmission dynamics with the knowledge which are beneficial to control the dengue disease transmission.







The findings of this study are expected to be advantageous for the authorities to prepare prevention and control the disease before it occurs; and for medication purposes. This analysis can be applied to Bandung, Indonesia, specifically, and broader area, such as provinces, countries or continents, generally.

1.5 Scope and Limitations of the Study

This study is discussing about dengue disease transmission which includes human as the host and mosquitoes as the vector. The factors that must be considered in building the compartment models are age and blood type of human population and Wolbachia-Aedes mosquitoes since they affect the deployment. The location of Bandung municipality is chosen as the critical area. The weekly data dengue cases in Bandung in 2013 are from seven hospitals.

The limitations of this study are the severity levels of this disease are not considered in this study since there was limitation in data documentation in some hospitals and the number of hospitals is limited only seven reputable hospitals since there are limitations in time, fund and license issues from some hospitals. The study is also limited because of some conditions, such as the critical area is limited only in Bandung municipality and the case considered in the compartment models is limited only on one type of DEN virus because there is no documentation of DEN virus type of patients. It is assumed that one a human is infected by one type of DEN virus, he or she becomes resistant to that particular type.







1.6 Research Framework

The purpose of this study is to introduce new discrete space-time mathematical models of dengue disease transmission. This utilizes the quantitative research in modeling the dengue transmission focusing on treatment to human and mosquito. The findings of this study can be applied by the authorities to make more effective and efficient strategies in preventing and controlling the disease before it occurs. The framework of this research is displayed in Figure 1.3.



Figure 1.3. Research Framework on This Study

1.7 Organization of the Report

This thesis is organised into seven chapters. Chapter 1 introduces the background of the study and the problem statement. Then, in the next subsections, the research objectives and questions, significance of the study, scope and limitation of the



study and research framework are elaborated. In the last subsection in this chapter, the design of the research is explained.

Chapter 2 discusses about dengue disease that becomes the main topic in this research. The explanation includes the condition of prevention and control strategies worldwide and specifically in Indonesia. This topic is narrowed down into the more specific condition in Bandung, West Java, Indonesia. The next section presents the modelling and analysis of transmission mechanism for the disease mapping presented by previous researchers.

Chapter 3 presents the number of dengue cases in Bandung. The description on the aggregated data of dengue cases and weekly data needed in this study was elaborated. This study uses the weekly data from Bandung in 2013. The next section discusses the application of the existing models to estimate the relative risk in Bandung. Preliminary investigation of dengue condition in Bandung as a critical area discussed in the next section. The last section elaborates the existing models to estimate the relative risk of dengue transmission by considering the age group factor. The frequentist and Bayesian approach are discussed and applied in the weekly data.

Chapter 4 elaborates the development of stochastic discrete space and time SIR-SI compartmental model which consider the age factor. The implementation of the different approach in the compartment model is discussed and the result is analysed.

Chapter 5 discusses the consideration of O blood-type factor in the dynamic system of dengue transmission in human compartment. The deterministic





compartment model is introduced and the differential equation system is produced to determine the basic reproduction number of this model. The stability of free and endemic state is analysed and discussed.

Chapter 6 introduces the dynamic system of dengue transmission which considers the influence of Wolbachia-Aedes mosquitoes. The differential equation system is determined based on the compartmental model described in this Chapter to build the basic reproduction number. Furthermore, the stability of free and endemic state is also analysed and discussed.

Finally, Chapter 7 discusses the conclusion of the study, the contribution to the knowledge and the recommendation of further research.



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