



Health Systems & Reform

ISSN: 2328-8604 (Print) 2328-8620 (Online) Journal homepage: http://www.tandfonline.com/loi/khsr20

## One Step Back, Two Steps Forward: An Economic Evaluation of the PEN Program in Indonesia

Waranya Rattanavipapong, Alia Cynthia Gonzales Luz, Suthasinee Kumluang, Nunik Kusumawardani, Yot Teerawattananon, Co-investigators: Dewi Indriani, Priska Apsari Primastuti, Lily Banonah Rivai, Sri Idaiani, Ully Adhie, Thunyarat Anothaisintawee, Sarocha Chootipongchaivat, Kanlaya Teerawattananon, Purvi Paliwal & Devika Singh

**To cite this article:** Waranya Rattanavipapong, Alia Cynthia Gonzales Luz, Suthasinee Kumluang, Nunik Kusumawardani, Yot Teerawattananon, Co-investigators: Dewi Indriani, Priska Apsari Primastuti, Lily Banonah Rivai, Sri Idaiani, Ully Adhie, Thunyarat Anothaisintawee, Sarocha Chootipongchaivat, Kanlaya Teerawattananon, Purvi Paliwal & Devika Singh (2016) One Step Back, Two Steps Forward: An Economic Evaluation of the PEN Program in Indonesia, Health Systems & Reform, 2:1, 84-98, DOI: <u>10.1080/23288604.2015.1124168</u>

To link to this article: <u>http://dx.doi.org/10.1080/23288604.2015.1124168</u>

9	© 2015 The Author(s). Published with license by Taylor & Francis Group, LLC© Waranya Rattanavipapong, Alia Cynthia	+	View supplementary material 🖸
	Gonzales Luz, Suthasinee Kumluang, Nunik Kuତ୍ୟାଙ୍ଗନ୍ଧେଶ୍ୱମିନାର୍ଚ୍ଚ ସ୍ୱୀର୍ପ୍ତ ନହୁମ୍ବିଙ୍କୁ awattananon		Submit your article to this journal 🗹
111	Article views: 402	Q	View related articles 🕑
CrossMark	View Crossmark data 🗹		

Full Terms & Conditions of access and use can be found at http://www.tandfonline.com/action/journalInformation?journalCode=khsr20

### **Research Article**



# **One Step Back, Two Steps Forward: An Economic Evaluation of the PEN Program in Indonesia**

Waranya Rattanavipapong<sup>1</sup>, Alia Cynthia Gonzales Luz<sup>1,\*</sup>, Suthasinee Kumluang<sup>1</sup>, Nunik Kusumawardani<sup>2</sup> and Yot Teerawattananon<sup>1</sup>

Co-investigators: Dewi Indriani<sup>3</sup>, Priska Apsari Primastuti<sup>3</sup>, Lily Banonah Rivai<sup>4</sup>, Sri Idaiani<sup>2</sup>, Ully Adhie<sup>2</sup>, Thunyarat Anothaisintawee<sup>1</sup>, Sarocha Chootipongchaivat<sup>1</sup>, Kanlaya Teerawattananon<sup>1</sup>, Purvi Paliwal<sup>5</sup> and Devika Singh<sup>6</sup>

<sup>1</sup>Health Intervention and Technology Assessment Program (HITAP), Department of Health, Ministry of Public Health, Non-thaburi, Thailand

<sup>2</sup>National Institute of Health Research and Development (NIHRD); Ministry of Health, Jakarta, Indonesia

<sup>3</sup>WHO Indonesia Country Office, Jakarta, Indonesia

<sup>4</sup>Directorate of NCD Control of the Ministry of Health, Jakarta, Indonesia

<sup>5</sup>WHO Regional Office for South East Asia (SEARO), New Delhi, India

<sup>6</sup>Georgia Institute of Technology, Atlanta, GA, USA

#### CONTENTS

Introduction Methods Results Discussion References

Received 8 October 2015; revised 20 November 2015; accepted 20 November 2015.

\*Correspondence to: Alia Cynthia Gonzales Luz; Email: alialuz90@gmail. com

Color versions of one or more of the figures in this article can be found online at www.tandfonline.com/khsr.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-Non-Commercial License (http://creativecommons. org/licenses/by-nc/3.0/), which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited. The moral rights of the named author(s) have been asserted.

Abstract—The economic and health burden of noncommunicable diseases (NCDs) is significant globally. To counteract this problem, the World Health Organization (WHO) introduced the Package of Essential Noncommunicable disease (PEN) interventions. Several countries, including Indonesia, implemented the PEN program. To assess the value of the investment in the current program, an economic evaluation of the program was conducted with collaboration between the Ministry of Health in Indonesia, the WHO, and the International Decision Support Initiative (iDSI). Even in low- and middle-income countries (LMICs) such as Indonesia where there is lack of data and health technology assessment (HTA) expertise, the study aims not only to inform policy but to build HTA capacity in the country through the working partnership between international HTA experts and local partners.

This study evaluated the delivery of screening and treatment for diabetes and hypertension, which are part of NCD interventions in the PEN program. Several screening strategies were compared to explore the options for improving the current PEN program. The findings show that implementing the PEN program is better than a base case of no policy in place, though it can be improved through a targeted screening policy of high-risk groups of population aged 40 and above (as opposed to screening for 15 years old and above as is the current practice). Adopting the recommended policy is a major challenge to policy makers due to a potential negative public perception of the disinvestment from an option that yields higher

<sup>©</sup> Waranya Rattanavipapong, Alia Cynthia Gonzales Luz, Suthasinee Kumluang, Nunik Kusumawardani, and Yot Teerawattananon

health outcomes. However, this study demonstrates that with the same budget currently invested in the program, the changes proposed will result in improvements on the current low uptake and poor coverage, thus yielding cost savings for the government and a possibility to reallocate resources to the country's priority health concerns, consequently leading to better health outcomes.

#### **INTRODUCTION**

The burden and impact of noncommunicable diseases (NCDs) on global mortality and morbidity rates and health care expenditure have increased at an unparalleled rate over the past decade.<sup>1,2</sup> NCDs, or chronic diseases, include ailments such as cardiovascular disease, cancer, chronic respiratory diseases, and diabetes. According to the World Health Organization's (WHO) Global Status Report on Noncommunicable Diseases 2014, NCDs are the leading cause of death globally, accounting for 38 million of 56 million deaths worldwide in 2012.<sup>3</sup> Almost three quarters of those deaths occur in low- and middle-income countries (LMICs), of which nearly half are attributed to "premature deaths" under the age of 70.<sup>4</sup> Due to the significant impact on the workingage population in terms of reduced productivity, loss of life, and increased household costs associated with health care, NCDs have a substantial economic effect in LMICs.

Indonesia's disease profile also reflects the rising number of NCD cases. Data from Indonesia's Basic Health Research (Riset Kesehatan Dasar or RISKESDAS)<sup>5</sup> show that in 2007, NCDs caused 60% of all deaths in the country, compared to 34% for communicable diseases and maternal and perinatal conditions, which have been the main focus of the government's health care resources for the past decade. Higher prevalence is expected in the future, shown in the WHO's 2014 estimate that 71% of total deaths were caused by NCDs in Indonesia,<sup>6</sup> due to an increasingly aging population and unhealthy lifestyles. The Indonesian Ministry of Health's (MoH) commitment to the provision of universal health coverage (UHC) to the populace also implies a higher investment for the government to address the health burden of NCDs.

In an attempt to counteract the rising threat of NCDs by focusing on tools for prevention and control, the WHO created the Package of Essential Noncommunicable disease (PEN) interventions geared toward providing cost-effective NCD interventions for resource-limited settings.<sup>7</sup> Recognizing that cardiovascular disease (CVD) and diabetes account for 31% of the NCD-related deaths in Indonesia,<sup>4</sup> the program uses hypertension and diabetes screening as primary indicators for an integrated system that monitors and assesses cardiovascular health. Early intervention and management of CVD and diabetes have been shown to have significant health and financial benefits,<sup>8-10</sup> which is why the introduction of the PEN program in developing countries, including Indonesia, often targets these particular NCDs.

The MoH adapted parts of the PEN interventions into its public health service at the primary care level in 2011.<sup>11</sup> Trained village health care volunteers or *kader* conduct *Posbindu*, which are community engagement, community-based awareness, monitoring, and screening activities for diabetes and hypertension. These activities take place in various areas within the community, such as designated *Posbindu* facilities, *kader* houses, etc. This arrangement allows the PEN program to be implemented throughout the country despite the large variations in available trained health professionals. After three years of policy implementation, the effectiveness and impact of the program were not known.

With the request from the MoH, an economic evaluation of the PEN package in Indonesia was conducted by departments of the MoH, the WHO country office, and the Health Intervention and Technology Assessment Program (HITAP) of Thailand, the results of which are discussed in this article. The objective of the quantitative assessment is to evaluate the cost-effectiveness of the PEN program compared to a "no screening" policy choice. To assess the potential improvements in the current program, the evaluation also explored the cost and outcomes of modifying the current PEN program through changes in the target population and diabetic screening tests. Two potential amendments to the current policy were proposed based on updated international clinical practice guidelines,<sup>12-14</sup> discussion with collaborators at the MoH, and agreement with stakeholders. Based on the results of this evaluation, Indonesia can take concrete steps to improve their investment in screening programs and make use of the recommendations proposed in the study to inform the implementation of the PEN program.

#### METHODS

The PEN program is implemented primarily through the *Posbindu*, wherein, once a month and on the same day, the *kader* organize the following activities: general health history checkup, weight and height measurements, and screening for hypertension and diabetes mellitus through blood pressure monitoring and random capillary blood glucose (RCBG), respectively. Eligible members of the population aged 15 years or older can come to the *Posbindu* on any screening day.<sup>11</sup> Frequency of screening is unspecified in the WHO PEN program guideline,<sup>7</sup> resulting in differing country adaptations. In addition, because there is no clear recommendation on frequency of screening and each region is responsible for its own implementation of the program, there is high variability in frequency of screening days done in *Posbindu* throughout Indonesia.

Once individuals are diagnosed as positive for diabetes, hypertension, or both, they are referred to the primary health care facilities or *Puskesmas*, where trained health professionals—that is, doctors and nurses—conduct a confirmatory fasting plasma glucose test (FPG, a test with higher accuracy than RCBG). Following this sequence, screening will lead true-positive cases (those with the disease who tested positive) to receive earlier treatment for diabetes and hypertension. On the other hand, false-negatives (those with the disease who tested negative) and nonadherence to *Puskesmas* result in later diagnosis and treatment. Individuals may also screen directly in the *Puskesmas* with the FPG test instead of the *Posbindu*. If these individuals test positive, they receive the confirmatory test.

#### Policy Options for PEN Interventions in Indonesia

The model evaluates a no-screening policy option and the current PEN program, reflecting the reality of the program implementation mentioned above. For no screening, the model assumes that all patients will come to the *Puskesmas* for treatment when they are symptomatic. For the current PEN policy, due to unclear frequency of screening and lack of data on number of screening per individual, the model assumes that individuals screen only once in their lifetime.

In addition to these two policy options, alternative screening strategies policy options 1 and 2 were developed. Similar to the current PEN program, policy option 1 allows a high-risk group of individuals aged 40 years or older to be screened at *Posbindu* by *kader*. Furthermore, the diabetes screening is conducted using fasting capillary blood glucose (fasting CBG) instead of RCBG for higher accuracy.

Population	Screening
------------	-----------

Individuals with positive results, including the false-positive cases, are referred to Puskesmas for further confirmation with FPG. In policy option 2, the screening and confirmatory tests for blood glucose using FPG and blood pressure tests are offered to the targeted population (individuals aged 40 years and above) at Puskesmas. Individuals' positive results or diagnosis of diabetes and hypertension can therefore be verified directly and referral for treatment can be made as necessary. The approach of screening and confirmatory test on the same day as mentioned in option 2 is in line with the American Diabetes Association's standard recommendation.<sup>12</sup>Additional benefits were expected if patients screened at a Puskesmas. Firstly, patients who have a positive test from the Posbindu must travel to the Puskesmas for treatment, whereas screening at a Puskesmas can be performed sequentially on the same day. Secondly, testing at the Puskesmas saves patients the cost of traveling and yields better compliance for treatment (see Table 5 for the difference in follow-up rates between patients' screening and confirmation at the Posbindu and Puskesmas). Finally, there is the training cost for non-health professionals in the Posbindu, which is added on top of the *Puskesmas* costs.

For all options, the model also assumes that the false-positive cases (those who do not have the disease but tested positive) were detected in the confirmation and thus no treatment is provided. All policy options for PEN Indonesia are summarized in **Table 1**.

#### **Model-Based Economic Evaluation**

A hybrid model, with a decision tree and Markov models, was constructed to reflect the current service provision for the PEN interventions, focusing on diabetes and hypertension screening and treatment. The decision tree model (Figure 1) represents the pathway of diabetic and hypertension screenings resulting from current practice of PEN and the aforementioned alternative policy choices. Importantly, when the

	1	U					
	Ag	ge 15–39		Age 40+	Type of Screening	Confirmation and Treatment	
No screening Current policy (PEN)	×	at PBD	×	at PBD	RCBG	Treatment on diagnosis At PKM (FPG)	
Policy option 1 Policy option 2	××		$\checkmark$	at PBD at PKM	CBG FPG	At PKM (FPG) At PKM (FPG)	

PEN = Package of Essential Noncommunicable diseases; PBD = *Posbindu*; RCBG = random capillary blood glucose; PKM = *Puskesmas*; CBG = fasting capillary blood glucose; FPG = fasting plasma glucose.

TABLE 1. Policy Options Evaluated in the Model



FIGURE 1. The Decision Tree Model Showing the Four Strategies of the PEN Program, Focusing on Screening for Diabetes and Hypertension

performance of a screening test is imperfect, the screening test might be positive among those who do not have the disease. In turn, individuals who are incorrectly diagnosed as negative for the diseases would be delayed in receiving their treatment. In the decision tree, the outcome of each policy option can be early and late diagnosis and treatment. Subsequently, the Markov model will be used to predict lifetime treatment cost and outcomes of the early and late treatment groups. The Markov model will run separately between these two groups using different transitional probabilities (probability of moving from one health state to another). Early diagnosis and treatment will result in a lower probability of progressing to complication states compared to the late diagnosis and treatment group.

After the screening pathway, Markov models (see supplementary **Figures S1** and **S2**) were used to follow the natural history of diabetes and hypertension in their progression over time. Three separate Markov models—one for diabetes, one for hypertension, and one for diabetes with hypertension were developed. Each Markov model represents the health states of diabetic and/or hypertensive patients with and without complications. Patients are in each health state for a cycle length of one year. After each cycle, the model allows patients to stay in the same health state, move from one health state of a disease to one of its complications, or transition to death.

The diabetes model consists of six major and severe conditions, which are coronary heart disease, stroke, retinopathy, neuropathy, nephropathy, and death, whereas the hypertension model contains four major conditions, namely, uncontrolled hypertension, controlled hypertension, stroke, and death. For the diabetes with hypertension model, it is possible for the patient to move into any of the complications of either disease. It should be noted that an assumption reflected in the model is that all complications are irreversible.

The economic analysis reflects and captures all of the costs and consequences resulting from both diabetes and hypertension screening and disease progression. A hypothetical cohort of people aged 27 (for the 15- to 39-year-old cohort) and 59 (for the 40-year-old and above cohort) with diabetes and/or hypertension enter and run through the model for the duration of their lifetime. The societal perspective was adopted. The main outcome measures were lifetime costs and disability-adjusted life

#### 88 Health Systems & Reform, Vol. 2 (2016), No. 1

Parameters	Distribution	Mean	SE	Reference	
Aged 15–39				19	
Prevalence of diabetes	Beta	1.5%	0.001		
Prevalence of hypertension	Beta	20.3%	0.003		
Prevalence of diabetes and hypertension	Beta	0.4%	0.001		
Aged $> 40$					
Prevalence of diabetes	Beta	10.6%	0.002		
Prevalence of hypertension	Beta	47.7%	0.004		
Prevalence of diabetes and hypertension	Beta	6.3%	0.002		

TABLE 2. Epidemiological Data Used in the Model

years (DALYs) averted. Future costs and DALYs averted were discounted at a rate of 3% based on the WHO guideline.<sup>15</sup> The results are presented as an incremental cost-effectiveness ratio (ICER) per DALY averted.

Furthermore, budget impact analysis was performed using the perspective of the budget holder to assess the financial impact of the PEN program and the affordability of a new policy option. The size of the eligible population of 245,400,000,<sup>16</sup> the start-up costs for the implementation of the PEN program, the costs of screening and treatment, and the uptake of screening were used to populate budget impact analysis. The budget impact was estimated over a five-yearperiod, focusing on a single cohort with an assumption of 28% uptake, to reflect the current situation of screening coverage in Indonesia.

Uncertainty analyses were conducted to account for the effect of possible variations in parameter values on the results. The values were changed using two methods. The first method, probabilistic sensitivity analysis, is to select 1,000 random values of all model parameters, taking into account parameter distribution and 95% confidence intervals.<sup>17</sup> The second method, one-way sensitivity analysis, which was performed within a Bayesian framework,<sup>18</sup> is to select values based on the upper and lower limits of the 95% credible interval; that is, the 2.5th and 97.5th percentiles of selected model parameters.

#### **Data Input for Decision Models**

The model parameters and the data used for the models are summarized in the following sections:

#### Epidemiological Data

These data are taken mainly from Indonesian databases and are divided by age group. The prevalence of diabetes, hypertension, and diabetes with hypertension was obtained from the 2013 RISKESDAS of Indonesia's National Institute of Health Research and Development (NIHRD), MoH<sup>19</sup> and is summarized in **Table 2**. The estimated prevalence in the younger cohort was derived from data for individuals between the ages of 18 and 34, following the current Joint National Committee.<sup>20</sup> In addition, age-specific mortality rates in the general population were derived from Indonesia's 2010 Global Burden of Disease Study.<sup>21</sup> Due to the lack of data in Indonesia, the mortality rate related to diabetes was obtained from the Thailand Diabetic Registry cohort and set to 0.004 per person per year (95% confidence interval, 0.0033–0.0059).<sup>22</sup>

#### Performance of Screening and Diagnostic Tests

**Table 3** shows the sensitivity and specificity values of the screening tests that were gathered from identified studies with results of head-to-head comparisons between RCBG,<sup>23</sup> fasting CBG,<sup>24</sup> or FPG tests<sup>24</sup> and the two-hour plasma glucose, which is the standard reference for diagnosis. For the confirmatory diabetes test for FPG in policy option 2, the sensitivity and specificity values of sequential testing were calculated using the formula of combined test accuracy.<sup>25</sup> On this basis, the sensitivity and specificity values of sequential testing for FPG are 66% and 100%, respectively.

Based on a meta-analysis conducted by Hodgkinson and colleagues on hypertension,<sup>26</sup> the sensitivity and specificity values of clinical blood pressure monitoring were compared to those for ambulatory blood pressure monitoring.

#### Health State Transitional Probabilities

Transitional probabilities between health states were obtained from multiple sources,  $^{14,22,26-36}$  as shown in **Table 4**. In brief, this is composed of the probabilities of disease occurrence, the probabilities of developing complications, and the probabilities of death. Moreover, data on relative risk reduction of complication or death events from

Parameters	Distribution	Mean	SE	Reference
Sensitivity of random capillary blood glucose	Beta	79%	0.03	23
Specificity of random capillary blood glucose	Beta	84%	0.01	23
Sensitivity of fasting capillary blood glucose	Beta	82%	0.03	24
Specificity of fasting capillary blood glucose	Beta	86%	0.01	24
Sensitivity of fasting plasma glucose	Beta	82%	0.001	24
Specificity of fasting plasma glucose	Beta	100%	0	24
Sensitivity of blood pressure monitoring	Beta	86%	0.02	25
Specificity of blood pressure monitoring	Beta	46%	0.07	25

TABLE 3. Sensitivity and Specificity of the Screening Tests

Parameters	Distribution	Mean	SE	Reference
CAD		·		
Probability of patients developing CAD	Beta	0.009	$1 \times 10^{-5}$	27
Probability of patients developing myocardial infarction	Beta	0.031	0.0004	28
Probability of death due to myocardial infarction	Beta	0.162	0.02	29
Probability of death due to CAD	Beta	0.07	0.0003	22
Risk ratio of developing CAD	Lognormal	0.85	0.09	30
Risk ratio of developing myocardial infarction	Lognormal	0.90	0.06	30
Risk ratio of death due to CAD	Lognormal	1.11	0.13	30
Stroke				
Probability of patients developing stroke	Beta	0.006	0.0001	27
Probability of diabetic patients developing stroke	Beta	0.006	0.0001	28
Probability of death due to stroke	Beta	0.001	$4 \times 10^{-7}$	22
Probability of death due to recurrent stroke	Beta	0.002	$4 \times 10^{-7}$	22
Risk ratio of developing stroke	Lognormal	0.96	0.08	30
Risk ratio of developing previous stroke	Lognormal	0.96	0.08	30
Risk ratio of death due to stroke	Lognormal	1.11	0.13	30
Retinopathy				
Probability of patients developing DR	Beta	0.04	$3 \times 10^{-5}$	27
Probability of progression from nonproliferative DR to proliferative DR	Beta	0.08	0.010	31
Probability of progression from nonproliferative DR to macular edema	Beta	0.03	0.010	31
Probability of progression from DR to blindness	Beta	0.09	0.010	31
Probability of progression from macular edema to blindness	Beta	0.05	0.010	31
Mortality multipliers for nonproliferative DR	Lognormal	1.49	0.08	31
Mortality multipliers for proliferative DR	Lognormal	1.76	0.03	31
Mortality multipliers for macular edema	Lognormal	1.76	0.03	31
Mortality multipliers for blindness	Lognormal	2.34	0.03	31
Risk ratio of patients developing DR	Lognormal	0.85	0.09	32
Risk ratio of blindness	Lognormal	1.0	0.02	32
Neuropathy				
Probability of patients developing amputation	Beta	0.001	$1 \times 10^{-6}$	27
Probability of patients developing foot ulcer	Beta	0.007	$1 \times 10^{-5}$	27
Probability of patients developing peripheral artery disease	Beta	0.004	$4 \times 10^{-6}$	27
Probability of progression from neuropathy to amputation	Beta	0.002	$2 \times 10^{-6}$	33
Probability of death due to neuropathy	Beta	0	0	22
Probability of death due to amputation	Beta	0.10	0.005	34
Risk ratio of developing neuropathy	Lognormal	0.99	0.02	30
Risk ratio of developing amputation	Lognormal	0.84	0.22	33
Risk ratio of death due to amputation	Lognormal	0.84	0.22	30
Nephropathy				

Table 4. Transitional Probabilities Between Health States in the Model (Continued on next page)

Parameters	Distribution	Mean	SE	Reference
Probability of patients developing diabetic nephropathy	Beta	0.08	$4 \times 10^{-5}$	27
Probability of progression from micro-albuminuria to macro-albuminuria	Beta	0.03	0.002	35
Probability of progression from macro-albuminuria to end-stage renal disease	Beta	0.02	0.004	35
Probability of progression from micro-albuminuria to end-stage renal disease	Beta	0.003	0.0008	35
Probability of death due to micro-albuminuria	Beta	0.03	0.002	35
Probability of death due to macro-albuminuria	Beta	0.05	0.005	35
Probability of death due to end-stage renal disease	Beta	0.19	0.03	35
Risk ratio of developing micro-albuminuria	Lognormal	0.86	0.06	32
Risk ratio of developing macro-albuminuria	Lognormal	0.74	0.07	32
Risk ratio of developing end-stage renal disease	Lognormal	0.69	0.21	32
Risk ratio of death due to renal disease	Lognormal	0.99	0.30	32
Hypertension	U			
Probability of progression from uncontrolled hypertension to controlled hypertension	Lognormal	0.73	0.0006	14
Probability of progression from controlled hypertension to uncontrolled hypertension	U	0.05		Assumption
Probability of patients with controlled hypertension developing stroke	Beta	0.007	0.0001	14
Probability of patients with uncontrolled hypertension developing stroke	Beta	0.02	0.0004	14
Probability of death due to controlled hypertension	Beta	0.03	$2 \times 10^{-5}$	36
Probability of death due to uncontrolled hypertension	Beta	0.02	$1 \times 10^{-5}$	36
Probability of death due to stroke	Lognormal	2.72	0.02	26
	1			

CAD = coronary artery disease; DR = diabetic retinopathy.

TABLE 4. Transitional Probabilities Between Health States in the Model (Continued)

patients with diabetes and hypertension who receive medication relied on internationally obtained information.

#### Cost and Resource Use

The information on costs and resource use requires estimates that are relevant to the Indonesian context; as a result, the assembly of these data required locally available sources as explained below. All costs were derived from 2015 values and presented in Indonesian rupiah (IDR), as summarized in **Table 5**. For international comparison, costs can be converted into international dollars using the purchasing power parity (PPP) conversion rate. A PPP 2015 dollar is worth 4,170 IDR.<sup>37</sup>

The breakdown of start-up costs associated with the PEN program includes the cost of materials used in the screening and diagnostic tests, staff salary weighted by their time designated to NCDs work, and the training provided to staff responsible for NCDs prevention and control at all levels of health care. This estimation was based on the approximate number of *Puskesmas* (2,400) and *Posbindu* (3,500) in Indonesia that actively implement the PEN program (up to April 2015). In total, start-up costs require almost 4,300 and 5,300 IDR per person screened for a policy screening from 15 years and above and a policy screening from 40 years and above, respectively.

In taking the societal perspective, both direct medical costs and direct nonmedical costs were included in the analysis. Direct medical costs refers to the screening costs and the annual cost of treating the diseases and their complications, and direct nonmedical costs refers to travel and food, accommodations, and opportunity costs incurred by patients and their relatives or caregivers. There is no consensus in academic circles on whether to include productivity loss for premature mortality in economic evaluation. In this study, these opportunity costs were excluded.<sup>38-40</sup> Overall, screening costs for different types of diabetes tests are similar, valued at about 20,000 IDR per case.<sup>41</sup> In contrast, there is no additional cost for blood pressure monitoring. In the absence of any published Indonesian costing studies, the treatment costs were based on data garnered from Indonesian case base groups in three class C hospitals located in the three regions.<sup>42</sup>

In addition, direct nonmedical costs were obtained from a small community survey (N = 159). Respondents aged 15 years and older who live permanently in the selected area were asked about the out-of-pocket expenses paid by patients and their relatives for the services at *Posbindu*, *Puskesmas*, and hospitals. The total direct nonmedical costs for getting screened and/or treated at various types of health care settings are summarized in **Table 5**.

#### Health State Disability Weights

DALYs were calculated using WHO standard methods<sup>15</sup> without age weighting, where each year of life is given equal

Parameters	Distribution	Mean	SE	Reference
Screening coverage				
Acceptance rate of screening		28.2%		а
Follow-up rate of positive results to		80.0%		Assumption
complete the further investigation/treatment				
at the primary health care level				
Costs				
Screening (per population screened)				
Random capillary blood glucose test		20,000	_	41
Fasting plasma glucose test		20,000	_	41
Blood pressure monitoring		0	_	41
Start-up costs of PEN for population aged 15–39		4,312	_	а
Start-up costs of PEN for population aged $\geq 40$		5,315	—	а
Costs of treating diabetes and follow-up (per year)				
Diabetes				
Without complications	Gamma	6,480,767	1,462,948	42
Coronary artery disease	Gamma	7,397,850	1,344,977	
Stroke	Gamma	7,616,800	1,811,742	
Nephropathy	Gamma	5,574,733	1,179,217	
Retinopathy	Gamma	6,727,333	976,187	
Neuropathy	Gamma	7,192,400	1,507,698	
Hypertension				
Without complications	Gamma	8,353,000	1,411,876	42
Stroke	Gamma	7,616,800	1,811,742	
Direct nonmedical cost (per year)				
Population screened at Posbindu	Gamma	11,920	2,588	а
Population screened at Pukesmas	Gamma	17,426	1,345	а
Patient treated at Pukesmas	Gamma	209,107	1,345	а
Patient treated at hospital	Gamma	2,072,806	54,234	а

PEN = Package of Essential Noncommunicable diseases.

<sup>a</sup>Analysis of community survey and primary data by the authors.

#### TABLE 5. Input Data on Costs and Resource Use

value. DALY is a combination of the years of life lost due to premature mortality and the years lost due to disability of patients with diabetes, hypertension, and their resulting complications. Years lost due to disability are calculated using a disability weight for each health condition. The disability weight reflects the severity of the disease ranging from zero (perfect health) to one (death). The disability weights of diabetes, hypertension, and their resulting complications were identified by the Global Burden of Disease Project.<sup>43,44</sup> A standard life table with average life expectancies for different age groups was applied. The disability weights employed in the model are presented in **Table 6**.

#### **Model Transparency and Validation**

Face and predictive validity were assessed. For face validity, the model's structure, parameter values, and assumptions were presented to the local research partners and then a broader range of stakeholders with approximately 40 local officials and/or representatives from various relevant agencies, offices, and organizations.<sup>45</sup> They provided comments on the relevance to the local context. For predictive validity, estimates of life expectancy of individuals without the disease and individuals with either hypertension or diabetes were used as a proxy to compare data derived from the model and other local and internationally relevant

Parameters	Distribution	Mean	SE	Reference
Diabetes	Beta	0.015	0.002	43
Hypertension	Beta	0	0	43
Blindness	Beta	0.552	0.021	43
Nephropathy	Beta	0.091	0.006	43
End-stage renal disease	Beta	0.098	0.005	44
Neuropathy	Beta	0.072	0.003	44
Amputation	Beta	0.102	0.017	43
Coronary artery disease	Beta	0.246	0.025	43
Myocardial infarction	Beta	0.439	0.018	44
Stroke	Beta	0.920	0.092	43
Previous stroke	Beta	0.266	0.017	43

TABLE 6. Disability Weights

information. The results showed that the model predicted that the cohorts without the disease will live until an average age of 73 and 77 for the first cohort representing the younger cohort with an average age of 27 and the second cohort representing the older cohort with an average age of 59, respectively. These estimations are reasonably comparable to the Indonesian life table developed by the WHO,<sup>46</sup> which revealed that life expectancy at age 27 is 76 and at age 59 it is 79.

#### **Ethical Considerations**

Ethical clearance was not obtained because the interviews conducted for the community survey did not involve sensitive queries that would be physically, psychologically, or mentally harmful to the respondents. Interviews were also undertaken with consent, because respondents were well informed about the study through written and oral consent obtained before the interview process. Additionally, the name and identity of each interviewee are kept confidential. All of them remain anonymous in the report.

#### RESULTS

#### **Cost-Effectiveness Results**

The total lifetime costs and DALYs lost from diabetes and/or hypertension per Indonesian individual in the population (with and without screening) are presented in **Table 7**. All screening programs have dominance over a no-screening policy because they incurred lower lifetime costs and higher health gains. Without screening is associated with 7.14 DALYs lost, the current PEN program with 7.10 DALYs lost, policy option 1 with 7.12 DALYs lost, and policy option 2 with 7.11 DALYs lost. Providing the current PEN policy had the greatest health benefits in terms of the lowest DALYs lost or highest DALYs averted compared to no screening; that is, 7.14 less 7.10 equals 0.04. The average lifetime cost of the current policy, which is approximately 57.86 million IDR, is slightly lower than policy option 1, which is 57.88 million IDR, though current PEN policy has higher health gains. In this case, current PEN dominates over policy option 1. The average lifetime cost of policy option 2 is 57.66 million IDR; as such, when compared to the current policy, it saves cost though with less health benefit.

The results show that the current policy of screening for diabetes and hypertension is cost-saving compared to no screening at the ICER of -14.22 million IDR per DALY averted; that is, 14.22 million savings for every DALY averted. This means that investing in screening and early treatment interventions is less costly than late-stage treatment interventions and has more health gains. Moreover, compared to the current policy, policy option 1 is cost-ineffective—that is, more costly and with less health gains—whereas policy option 2 saves costs with only a small loss in health benefit. The ICER of policy option 2 compared to current PEN is 52.14 million IDR per DALY averted or, in other words, with reference to policy option 2, the current PEN program costs 52.14 million IDR more for every DALY averted.

Currently, Indonesia does not have an explicit cost-effectiveness threshold, which is the government's willingness to pay for funding public health interventions. Based on probabilistic sensitivity analysis, the cost-effectiveness frontier (Figure 2) shows the probability at which each screening program is cost-effective (represented in the *v*-axis) given the different willingness-to-pay values (represented in the xaxis). Policy option 2 is therefore most likely to be costeffective, unless the Indonesian government has a willingness-to-pay per DALY averted above 51.5 million IDR, which is equivalent to 1.1 times the gross domestic product per capita in Indonesia.<sup>37</sup> The results showed that policy option 2 is the best option compared to all others, given that the value of one DALY averted is higher than 51.5 million IDR. On the other hand, no screening and policy option 1 do not appear to be cost-effective.

For one-way sensitivity analysis of parameter values, the results are outlined as follows. First, a screening policy is found to be a preferable option to a no-screening strategy, unless the disease prevalence is extremely low; for example,

	Total Costs (Million IDR)	Total DALYs Lost	ICER Compared to No Screening (Million IDR per DALY Averted)	ICER Compared to Current Policy (Million IDR per DALY Averted)	
No screening	58.33	7.14			
Current policy (PEN)	57.86	7.10	Dominance		
Policy option 1	57.88	7.12	Dominance	Dominated	
Policy option 2	57.66	7.11	Dominance	Saves cost, less effective	52.14

IDR = Indonesian rupiah; DALYs = disability-adjusted life years; ICER = incremental cost-effectiveness ratio; PEN = Package of Essential Noncommunicable diseases. All costs can be converted into international dollars using the purchasing power parity (PPP) conversion rate. A PPP 2015 dollar is worth 4,170 IDR.<sup>37</sup>

TABLE 7. Cost and Health Outcomes per Individual Population (With and Without Screening) of Each Policy Option in Base-Case Analysis



FIGURE 2. The Cost-Effectiveness Frontier

close to 0 or 0.15 and 2.03 per 100,000 population for diabetes and hypertension among population aged 15–39, respectively. Unsurprisingly, an increase in coverage can lead to an increase in the value for money of policy option 2 compared to the current PEN. In addition, discount rate, relative risk of death due to renal disease, and relative risk of death due to controlled and uncontrolled hypertension are the main influential parameters to the cost-effectiveness results (**Table 8**). For instance, discount rate significantly affects the ICER of policy option 2 compared to the current PEN. The higher the discount rate (6%), the greater the decrease in savings. Moreover, the higher the relative risk of deaths, with the exception of relative risk of death due to uncontrolled hypertension, the higher the corresponding increase in savings and decrease in health outcomes for current PEN compared to no screening. On the other hand, the higher the relative risk of death, with the exception of relative risk of death due to controlled

Parameters (Min–Max value)	Intervention	No Screening Versus Current PEN	Current PEN Versus Policy Option 2
Discount rate (0%–6%)	Minimum ICER per DALY averted (million IDR)	-10.21	30.03
	Maximum ICER per DALY averted (million IDR)	-14.22	537.62
Relative risk of death due to renal disease (0.531–1.835)	Minimum ICER per DALY averted (million IDR)	-10.61	36.74
	Maximum ICER per DALY averted (million IDR)	-22.15	102.55
RR of death due to controlled hypertension (1.099–1.304)	Minimum ICER per DALY averted (million IDR)	-7.57	41.85
	Maximum ICER per DALY averted (million IDR)	-28.99	70.19
RR of death due to uncontrolled hypertension (1.317–1.546)	Minimum ICER per DALY averted (million IDR)	-29.55	75.80
	Maximum ICER per DALY averted (million IDR)	-7.44	37.87

PEN = Package of Essential Noncommunicable diseases; ICER = incremental cost-effectiveness ratio; DALY = disability-adjusted life year; IDR = Indonesian rupiah; RR = relative risk.

All costs can be converted into international dollars using the purchasing power parity (PPP) conversion rate. A PPP 2015 dollar is worth 4,170 IDR.<sup>37</sup>

**TABLE 8.** One-Way Sensitivity Analysis Results for Comparison of the Current PEN and No-Screening as Reference Case and Policy Option 2 and the Current PEN as Reference Case

hypertension, the greater the decrease in savings and increase in DALYs lost for policy option 2 compared to current policy.

#### **Budget Impact Analysis**

The results indicate that annual total budget impact for the current PEN program is approximately 565 trillion IDR for the first year and 2,750 trillion IDR over a five-year period. Adopting policy option 2 requires a slightly lower budget for the first year compared to the current policy because of a smaller proportion of the population being screened. However, over a five-year period, the annual total budget impact of all screening strategies does not differ significantly, which is approximately 2,750 trillion IDR.

Table 9 presents the estimated patient numbers and treatment costs for each policy option. The estimated budget for the current policy amounts to 1.3 trillion IDR with a screening coverage of 28%. If this budget is reallocated to the targeted screening in policy option 2, the screening coverage can be increased to 63% because the eligible population (denominator) is smaller with a similar number of people screened (numerator). More people are likely to be diagnosed and treated at the early stage of diabetes and hypertension for policy option 2 compared to current PEN policy; therefore, policy option 2 has the potential for budget savings because individuals are less likely to require treatment costs for advanced stages of their diseases. In terms of health benefits, Table 10 shows that patients who are diagnosed and treated late would lead to higher DALYs lost compared to those diagnosed and treated early. As a result, additional DALYs averted can be observed for policy option 2 that benefits from a higher number of patients screened and fewer patients diagnosed and treated late.

#### DISCUSSION

All strategies for diabetes and hypertension screening, including the current PEN program, are more cost-effective

than a no-screening strategy because they not only saved costs but also yielded more life years gained and DALYs averted. This implies that the value of health resources investment avoided through prevented late-stage illness related to diabetes and hypertension exceeds the value of resources required to implement the PEN program. Though the DALYs averted seem small because they are calculated per individual in the eligible population, with and without screening, the aggregated health gains are high from a societal perspective if the screening program is implemented on a nationwide level in Indonesia, where the total eligible population is 173 million.

In evaluating the various policy strategies, current PEN policy yields the highest health benefit. Policy option 1 is inferior to both the current PEN program and policy option 2 due to relatively high costs but less health benefit. Policy option 2 saves costs with only a small loss in health benefit due to exclusion of the younger generation with a low disease prevalence from screening. However, comparing the current PEN program and policy option 2 is challenging because they offer two different benefits. If the government reallocates the same investment on the current PEN program (28% screening coverage) to policy option 2, screening coverage can be increased to 63% of the eligible population. Moreover, the higher number of patients detected at the early stage of the disease can receive early treatment, averting later stages and saving on total treatment costs. Despite these benefits, improving the coverage may be difficult because the screening program depends not only on financing but also on demand from the population. Addressing this issue may require additional investment in activities such as public awareness or community engagement. These costs are not considered in this study.

Should policy option 2 prove more favorable to the national goals and strategies, the investment in the current program poses a challenge. Adopting policy option 2 will be

	_	Earl	y Diagnosis	Late	e Diagnosis		Total
Policy Options	Screening Cost (Trillion IDR)	Patients (Million)	Treatment Costs (Trillion IDR)	Patients (Million)	Treatment Costs (Trillion IDR)	Patients (Million)	Treatment Costs (Trillion IDR) <sup>b</sup>
No screening				70.90	564.29	70.90	564.29
Current policy (28% coverage)	1.3	11.42	91.34	59.48	472.94	70.90	564.28
Policy option 2 (63% coverage)	1.3	25.27	200.81	45.63	363.30	70.90	564.11

IDR = Indonesian rupiah.

aAll costs can be converted into international dollars using the purchasing power parity (PPP) conversion rate. A PPP 2015 dollar is worth 4,170 IDR.<sup>37</sup>

bWe assume a situation in which a total of 1.3 Trillion IDR is invested for PEN program. Coverage figures are based on projected patients reached in each intervention's target population.

**TABLE 9.** Estimated Patient Numbers and Treatment Costs for Current PEN Program and for the Targeted Screening Option of Policy 2 in the Case of Spending the Same Amount for Screening Costs

			Early Dia	Ignosis					Late Dia	gnosis		
Policy Options	Diabet	es	Hyperte	nsion	Diabetes Hyperte	With nsion	Diabe	tes	Hyperter	asion	Diabetes Hyperte	With 1sion
	Patients (Million)	DALYs <sup>a</sup> (Years)										
Current policy (28% coverage) Aged 15–39	0.21	15.57	3.18	6.48	0.06	15.58	1.21	16.31	16.06	7.10	0.36	16.31
Aged $\ge 40$	1.18	9.95	6.08	8.27	0.71	9.92	6.99	10.15	30.67	8.77	4.18	10.15
Policy option 2 (63% coverage)							141	1071	30.01		ç	16.21
Aged 12-39							1.41	10.01	C2.4I	/.10	0.42	16.01
Aged $\ge 40$	3.42	9.95	19.82	8.27	2.04	9.92	4.76	10.15	16.93	8.77	2.84	10.15
DALYs = disability-adjusted life years. <sup>a</sup> DALYs lost per patient.												

TABLE 10. Comparison Between the Health Benefit From the Current PEN Policy (28.2% Coverage) and the Health Benefit From Policy Option 2 (63% Coverage)

a disinvestment from the current PEN, which is a change from a more expensive and higher benefit policy option to one that is less expensive and has lower health outcomes. Policy option 2 is likely to be unacceptable to stakeholders due to the perception of the government intending only to save on costs. Decision makers must decide once they have evidence that the resources released are used for appropriate purposes; for example, funding new cost-effective interventions or expanding coverage of existing cost-effective interventions—for example, the screening of high-risk populations. This study demonstrates how modeling can be used to justify disinvestment.

A study was performed to evaluate the cost-effectiveness of the PEN program in Bhutan.<sup>14</sup> Although the policy options in the decision tree model are different in order to reflect real practices in each country, both studies show that diabetes and hypertension screening interventions represent good value for money and improve health outcomes at a reasonable cost. In Bhutan, for example, a universal screening program is still more cost-saving than a no-screening policy. Additionally, the study in Bhutan found that universal screening (of the targeted population of overweight, obese, or those aged 40 years and above) is likely more cost-effective than opportunistic screening of only a portion of the targeted population. In comparison with other studies done in the Indonesian context, this study supports prior research findings conducted by Mihardja and colleagues<sup>20</sup> that early detection interventions such as screening programs should be expanded greatly due to the high prevalence of diabetes among Indonesians, especially undiagnosed diabetes.

The major limitation of the Indonesian study is lack of good local data, for example, the mortality rate and the relative risk of death, which the uncertainty analyses show have a significant effect on the ICER. This study also does not include costs related to public awareness, which should be part of the screening program. This model assumes that in the no-screening policy, all patients come to health facilities only when they are symptomatic, which means late treatment. Opportunistic screening is therefore not taken into account due to lack of data on its coverage. These limitations can be addressed once more and/or better quality data are generated within the country.

Going forward, data should be collected on the program coverage at national and local levels in Indonesia. Records should also be kept about the percentage of patients who have positive screening results and proceed for a follow-up confirmation test and treatment in order to evaluate areas of the program that could be improved. Similarly, in the future, the evaluation of the PEN program can be improved by collecting data on annual incidence of the disease to determine the frequency of the screening, which can have an impact on the cost-effectiveness of the PEN program. Finally, some quality of care and treatment success data should be monitored, such as the rate of development of complications from the disorders. As an indicator of the quality of diabetes treatment, fasting plasma glucose and/or hemoglobin A1C should be checked at least once a year; to measure hypertension care, the level of controlled blood pressure should be noted.

Despite these limitations, there are clear strengths and advantages to this study. This study can be used as a model for evaluating the cost-effectiveness and sustainability of health care programs in Indonesia and other LMICs. Notably, the quantitative nature of this study provides policy makers with a meaningful framework, particularly in terms of determining the average life expectancy of Indonesians with diabetes and hypertension, calculating the life years saved and DALYs averted from different interventions, and detailing present and future costs of each policy option. The information that is presented can be useful for public education, program management, future modeling and evaluations, and allocating resources across other public health programs (e.g., investment in better early treatment for diabetes and hypertension and/or public awareness or community engagement programs to promote PEN). The study has also promoted collaboration among many agencies, including stakeholders, which promotes involvement and transparency in health policy.

### DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST

The authors have no conflict of interest.

#### ACKNOWLEDGMENTS

The authors acknowledge the WHO country office and SEARO as well as the Indonesian MOH for their assistance and support for this project. We are grateful to Saudamini Dabak for her comments on the article.

#### FUNDING

The World Health Organization (WHO) and the International Decision Support Initiative (iDSI) funded the health technology assessment (economic evaluation) for the PEN program; the authors did not receive any financial support for writing the article. HITAP is funded by the National Health Security Office, the Health System Research Institute, and the Bureau of Health Policy and Strategy, Ministry of Public Health. HITAP's International Unit was established with support from the Thai Health–Global Link Initiative Project (TGLIP), iDSI (funded by the Bill & Melinda Gates Foundation and the Department for International Development, UK), and the Rockefeller Foundation to provide technical assistance on health intervention and technology assessment for governments of low- and middle-income countries. The findings, interpretations, and conclusions expressed in this article do not necessarily reflect the views of the aforementioned funding agencies.

#### SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

#### REFERENCES

- [1] Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, Abraham J, Adair T, Aggarwal R, Ahn SY, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet 2012; 380 (9859): 2095-2128.
- [2] Muka T, Imo D, Jaspers L, Colpani V, Chaker L, van der Lee SJ, Mendis S, Chowdhury R, Bramer WM, Falla A, et al. The global impact of non-communicable diseases on healthcare spending and national income: a systematic review. Eur J Epidemiol 2015; 30(4): 251-277.
- [3] World Health Organization. Global status report on noncommunicable diseases 2014. Geneva: World Health Organization; 2014.
- [4] Bloom DE, Chen S, McGovern M, Prettner K, Candeias V, Bernaert A, Cristin S. Economics of non-communicable diseases in Indonesia. April 2015. Available at http://www3.wefo rum.org/docs/WEF\_The\_Economics\_of\_non\_Disease\_Indone sia\_2015.pdf (accessed 17 August 2015)
- [5] National Institute of Health Research and Development. Indonesia basic health research. Jakarta, Indonesia: Ministry of Health; 2010.
- [6] Riley L, Cowan M. Noncommunicable diseases country profiles 2014. Geneva: World Health Organization; 2014.
- [7] World Health Organization. Package of Essential Noncommunicable (PEN) disease interventions for primary health care in lowresource settings. Geneva: World Health Organization; 2010.
- [8] Furie KL, Kasner SE, Adams RJ, Albers GW, Bush RL, Fagan SC, Halperin JL, Johnston C, Katzan I, Kernan WN, et al. Guidelines for the prevention of stroke in patients with stroke or transient ischemic attack: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011; 42(1): 227-276.
- [9] Qaseem A, Fihn SD, Dallas P, Williams S, Owens DK, Shekelle P. Management of stable ischemic heart disease: summary of a

clinical practice guideline from the American College of Physicians/American College of Cardiology Foundation/American Heart Association/American Association for Thoracic Surgery/ Preventive Cardiovascular Nurses Association/Society of Thoracic Surgeons. Ann Intern Med 2012; 157(10): 735-743.

- [10] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003; 289(19): 2560-2572.
- [11] Rivai LB. Presentation of historical development of PEN program in Indonesia Training Course for PEN evaluation in Indonesia. Jakarta, Indonesia: Ministry of Health; 2015.
- [12] American Diabetes Association. Standards of medical care in diabetes 2014. Diabetes Care 2014; 37(Suppl 1): S14-S80.
- [13] National Health and Medical Research Council. National evidence based guideline for case detection and diagnosis of type 2 diabetes. Canberra, Australia: National Health and Medical Research Council; 2009.
- [14] Dukpa W, Teerawattananon Y, Rattanavipapong W, Srinonprasert V, Tongsri W, Kingkaew P, Yothasamut J, Wangchuk D, Dorji T, Wangmo K. Is diabetes and hypertension screening worthwhile in resource-limited settings? An economic evaluation based on a pilot of a Package of Essential Noncommunicable disease interventions in Bhutan. Health Policy Plann 2014; 8: 1–12.
- [15] Edejer TT-T, Baltussen R, Adam T, Hutubessy R, Acharya A, Evans D, Murray CJL. WHO guide to cost-effectiveness analysis. Geneva: World Health Organization; 2012.
- [16] Statistics Indonesia. Estimated population of selected countries (million), 2000–2013 statistics Indonesia. 2012. Available at http://www.bps.go.id/linkTabelStatis/view/id/1284 (accessed 3 April 2015)
- [17] Briggs A. Handling uncertainty in cost-effectiveness models. Pharmacoeconomics 2000; 17: 479-500.
- [18] Ades AE, Claxton K, Sculpher M. Evidence synthesis, parameter correlation and probabilistic sensitivity analysis. Health Econ 2006; 15(4): 373-381.
- [19] National Institute of Health Research and Development. An unpublished report of Indonesia National Health Survey (RIS-KESDAS). Jakarta, Indonesia: Ministry of Health; 2013.
- [20] Mihardja L, Soetrisno U, Soegondo S. Prevalence and clinical profile of diabetes mellitus in productive aged urban Indonesians. J Diabetes Investig 2014; 5(5): 507-512.
- [21] Salomon JA, Wang H, Freeman MK, Vos T, Flaxman AD, Lopez AD, Murray CJL. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden Disease Study 2010. The Lancet 2013; 380(9859): 2144-2162.
- [22] Pratipanawatr T, Rawdaree P, Chetthakul T, Bunnag P, Ngarmukos C, Benjasuratwong Y, Leelawatana R, Kosachunhanun N, Plengvidhya N, Deerochanawong C, et al. Thailand Diabetic Registry cohort: predicting death in Thai diabetic patients and causes of death. J Med Assoc Thai 2010; 93(Suppl 3): S12-S20.
- [23] Somannavar S, Ganesan A, Deepa M, Datta M, Mohan V. Random capillary blood glucose cut points for diabetes and pre-diabetes derived from community-based opportunistic screening in India. Diabetes Care 2009; 32(4): 641-643.

- [24] Rolka DB, Narayan KMV, Thompson TJ, Goldman D, Lindenmayer J, Alich K, Bacall D, Benjamin EM, Lamb B, Stuart DO, et al. Performance of recommended screening tests for undiagnosed diabetes and dysglycemia. Diabetes Care 2001; 24(11): 1899-1903.
- [25] Praditsitthikorn N. Economic evaluation of screening for disease. J Med Assoc Thai 2014; 97(Suppl 5): S94-S101.
- [26] Lovibond K, Jowett S, Barton P, Caulfield M, Heneghan C, Hobbs FDR, Hodgkinson J, Mant J, Martin U, Williams B, et al. Cost-effectiveness of options for the diagnosis of high blood pressure in primary care: a modelling study. The Lancet 2011; 378(9798): 1219-1230.
- [27] Leelawattana R, Pratipanawatr T, Bunnag P, Kosachunhanun N, Suwanwalaikorn S, Krittiyawong S, Chetthakul T, Plengvidhya N, Benjasuratwong Y, Deerochanawong C, et al. Thailand Diabetes Registry project: prevalence of vascular complications in long-standing type 2 diabetes. J Med Assoc Thai 2006; 89(Suppl 1): S54-S59.
- [28] UK ProspectiveDiabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). The Lancet 1998; 352(9131): 854-865.
- [29] Srimahachota S, Boonyaratavej S, Kanjanavanit R, Sritara P, Krittayaphong R, Kunjara-Na-ayudhya R, Tatsanavivat P. Thai Registry in Acute Coronary Syndrome (TRACS)—an extension of Thai Acute Coronary Syndrome Registry (TACS) group: lower in-hospital but still high mortality at one-year. J Med Assoc Thai 2012; 95(4): 508-518.
- [30] Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, Lafont S, Bergeonneau C, Kassai B, Erpeldinger S, Wright JM, Gueyffier F, Cornu C. Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: meta-analysis of randomised controlled trials. BMJ 2011; 343(7817): d4169.
- [31] Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. JAMA 2000; 283(7): 889-896.
- [32] Coca SG, Ismail-Beigi F, Haq N, Krumholz HM, Parikh CR. Role of intensive glucose control in development of renal end points in type 2 diabetes mellitus: systematic review and meta-analysis intensive glucose control in type 2 diabetes. Arch Intern Med 2012; 172(10): 761-769.
- [33] Krittiyawong S, Ngarmukos C, Benjasuratwong Y, Rawdaree P, Leelawatana R, Kosachunhanun N, Plengvidhya N, Deerochanawong C, Suwanwalaikorn S, Pratipanawatr T, et al. Thailand Diabetes registry project: prevalence and risk factors associated with lower extremity amputation in Thai diabetics. J Med Assoc Thai 2006; 89(Suppl 1): S43-S48.

- [34] Junrungsee S, Kosachunhanun N, Wongthanee A, Rerkasem K. History of foot ulcers increases mortality among patients with diabetes in northern Thailand. Diabet Med 2011; 28(5): 608-611.
- [35] Adler AI, Stevens RJ, Manley SE, Bilous RW, Cull CA, Holman RR. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). Kidney Int 2003; 63(1): 225-232.
- [36] Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of ACE inhibitors, calcium antagonists, and other blood-pressure-lowering drugs: results of prospectively designed overviews of randomised trials. The Lancet 2000; 356(9246): 1955-1964.
- [37] International Monetary Fund. The World Economic Outlook Database. April 2015. Available at https://www.imf.org/exter nal/pubs/ft/weo/2015/01/weodata/index.aspx (accessed 2 April 2015)
- [38] Brouwer WB, Koopmanschap MA, Rutten FF. Productivity costs in cost-effectiveness analysis: numerator or denominator: a further discussion. Health Econ 1997; 6(5): 511-514.
- [39] Liljas B, Karlsson GS, Stalhammar NO. On future non-medical costs in economic evaluations. Health Econ 2008; 17(5): 579-591.
- [40] Weinstein MC, Siegel JE, Garber AM, Lipscomb J, Luce BR, Manning WG Jr, Torrance GW. Productivity costs, time costs and health-related quality of life: a response to the Erasmus Group. Health Econ 1997; 6(5): 505-510.
- [41] Ministry of Health, Indonesia. An unpublished data of start-up costs for PEN program in Indonesia. Jakarta, Indonesia: Ministry of Health; 2015.
- [42] Ministry of Health, Indonesia. Indonesia case base groups (INA-CBGs). Jakarta, Indonesia: Ministry of Health; 2015.
- [43] World Health Organization. Global burden of disease 2004 update: disability weights for diseases and conditions. Geneva: World Health Organization; 2004.
- [44] Murray CJL, Vos T, Lozano R, Naghavi M, Flaxman AD, Michaud C, Ezzati M, Shibuya K, Salomon JA, Abdalla S, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet 2012; 380(9859): 2197-2223.
- [45] Rattanavipapong W, Kumluang S, Luz ACG, Singh D, Teerawattananon Y. Economic evaluation of the WHO Package of Essential Non-communicable disease (PEN) interventions in Indonesia. Nonthaburi, Thailand: Health Intervention and Technology Assessment Program; 2015.
- [46] World Health Organization. Global Health Observatory (GHO) data. 2012. Available at http://apps.who.int/gho/data/ view.main.60750?lang=en (accessed 3 April 2015)