FORMALIZING PROCESS: HTA INTRODUCTORY AND TOPIC NOMINATION WORKSHOP

October 18-21, 2016

A HITAP team visited Indonesia to provide two workshops and meet with different partners in their continued goal of assisting Indonesia in developing HTA in the country.

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Disclaimer Page

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List of Acronyms

ADP	Access and Delivery Partnership
Badan POM	Indonesian National Agency of Food and Drug Control
BIA	Budget impact analysis
BPJS	Badan Penyelenggara Jamina Sosial (Agency for the Organization of Social Insurance)
BMGF	Bill and Melinda Gates Foundation
CEA	Cost-effectiveness Analysis
CML	Chronic Myeloid Leukemia
CRC	Colorectal cancer
CUA	Cost utility analysis
CV	Curriculum Vitae
EE	Economic evaluation
DALY	Disability Adjusted Life Years
ESRD	End-stage renal disease
GEAR	Guide to Health Economics Analysis and Research Online Resource
GHD	Global Health and Development Team
HePTA/HTA	Health Technology Assessment Program in the Mahidol University
HITAP	Health Intervention and Technology Assessment Program, Thailand
HTA	Health Technology Assessment
HTAC (InaHTAC)	Health Technology Assessment Committee, Indonesia (or Komite Penilaian Teknologi Kesehatan/KPTK)
IC	Imperial College
IDR	Indonesian Rupiah
iDSI	International Decision Support Initiative
INA CBG	Indonesia Case Based Groups
JKN	Jaminan Kesehatan Nasional, universal healthcare program
MoH	Ministry of Health, Indonesia
MoPH	Ministry of Public Health, Thailand
MoU	Memorandum of Understanding
NIHRD	National Institute of Health and Research Development
PAH	Pulmonary Arterial Hypertension
PEN	Package of Non-Communicable Disease Interventions
PICs	Persons in Charge
PPJK	Pusat Pembiayaan dan Jaminan Kesehatan Centre for Healthcare Financing, Indonesia
QALY	Quality Adjusted Life Years
QoL	Quality of Life
TNP2K	National Program for Poverty Alleviation
TDR	WHO Special Programme for Research and Training in Tropical Diseases
UHC	Universal Health Coverage
UNDP	United Nations Development Programme
WB	World Bank
WHO	World Health Organization

Executive summary

The Indonesian HTA Committee (InaHTAC) was formally renewed and continues its work as a facilitator of national HTA studies as of 2016. Under their oversight, three HTA economic evaluation studies were completed from 2014-2016: the economic evaluation of sildenafil as a first line treatment for pulmonary arterial hypertension (PAH); the economic evaluation of the package of essential non-communicable disease interventions (PEN); and, the economic evaluation of the renal replacement therapy options for Indonesia.

To build up the supply in the country and assist them in conducting these research, HITAP has supported the InaHTAC through capacity building activities and has tried to expand this to other organizations as well such as the BPJS (Badan Penyelanggara Jaminan Sosial or the Agency for the Organization of Social Insurance) Kesehatan. This time, the team provided training to the National Institute of Health and Research Development (NIHRD) during their week-long workshop on health.

HITAP also aimed to help build the HTA process through sharing the Thai experiences in a topic selection workshop with the hopes of helping develop an effective mechanism to determine policy relevant research topics for HTA in Indonesia. The team is also supporting two studies on off-label medicines in an effort to help Indonesian policymakers make the decision on the results of the economic evaluation of sildenafil as a first-line treatment for PAH (given that this is an off-label use of the medication). The two teams conducting the study met with HITAP and PATH, which is also supporting the effort, to discuss the proposal for their study and sign the contract.

Finally, HITAP met with several partners, such as the InaHTAC and PATH to discuss next steps on current activities and collaborations.

Introduction

At the beginning of 2014, Indonesia launched its universal healthcare program, the Jaminan Kesehatan Nasional (JKN), which will cover all Indonesians by 2019. By the end of the year, the Badan Penyelenggara Jamina Sosial (BPJS Health), became the administrator of the largest health insurance scheme in the world with over 133 million people enrolled[1]. In terms of financing, the JKN is a tiered premium-based system supplemented by government subsidies fully covering the poorest. The costs of the program are estimated to be around USD 13-16 billion per year until the JKN is fully rolled out[2]. The ambitious nature of the program, challenges for implementation and high costs associated with bringing healthcare to all brought priority setting to the fore and a Presidential Regulation in 2013 that called for the use of health technology assessment (HTA) in deciding the benefits covered by the scheme[3].

The Health Technology Assessment Committee (InaHTAC) was set up in the Ministry of Health (MoH) to serve as the secretariat for HTA activities. It has received support from various international partners including the International Decision Support Initiative (iDSI) through which the Health Intervention and Technology Assessment Program (HITAP) has been providing technical assistance. To date, three HTA studies have been completed as part of this collaboration, one on the treatment of End Stage Renal Disease (ESRD), another on the use of sildenafil as treatment of Pulmonary Arterial Hypertension (PAH) and the third, an economic evaluation of the Package for Non-Communicable Disease Interventions (PEN) in Indonesia.

Of the three, the economic evaluation of sildenafil as a first-line treatment for PAH has drawn much attention domestically. Sildenafil (Viagra) is registered for another indication, which means using it as a treatment for PAH is an off-label medicine use. Potential legal options are being considered to include sildenafil as a reimbursable drug. During this process, however, to connect the study for policy, HITAP supports the conduct of the review of laws, regulations, and use of off-label medicines in Indonesia locally as well as drawing from the experiences of other countries.

This visit is part of HITAP's ongoing efforts to assist the development of HTA in the country through support for the PAH study as well as discussing the next steps for HITAP's assistance to establish HTA in the country. HITAP also met with several partners to share the Thai experience on topic nomination as the Indonesian HTA process develops.

Objectives:

1. To provide an introductory HTA workshop to the NIHRD staff.
2. To support the development of HTA in Indonesia and plan next steps through meetings and the topic nomination workshop.
3. To support the conduct of the off-label medicines studies.
4. To explore opportunities and avenues to introduce HTA and collaborate with local and international partners on future activities.

[1] Official figure from "Indonesia Economic Quarterly In times of global volatility", The World Bank Group, October 2015. Available at: http://www.worldbank.org/en/news/feature/2015/10/22/indonesia-economic-quarterly-october-2015

[2] "Indonesia's universal health care goals", Oxford Business Group, 2015, Available at: http://www.oxfordbusinessgroup.com/overview/indonesias-universal-health-care-goals

[3] "Regulation Of President Of The Republic Of Indonesia No. 12 Year 2013 Concerning Health Care Benefits", Translation – Presidential Regulation No. 12/2013 Social Protection Team, The World Bank, Jakarta Office. Available at: www.social-protection.org

Summary of Meetings

Introductory HTA Workshop

HITAP conducted a pre-conference workshop on HTA and economic evaluations for the International Symposium on Health Research and Development organized by the National Institute of Health Research and Development (NIHRD), one of the InaHTAC's (Indonesia Health Technology Assessment Committee) research partners. HITAP provided a full day workshop on October 18, 2017, and attended the symposium on October 19, 2017.

On the first day, HITAP introduced the process and methods of HTA, the overview of economic evaluation, model-based economic evaluation, an exercise on model planning and conceptualization, an exercise on decision tree model, and the policy implication and implementation of HTA. Some of the discussions during the group work are outlined below. Groups were asked to think about a model planning and conceptualization for cost effectiveness of extending the current vaccination program against influenza to include healthy 50–64 year olds. The discussion among team members include the following components:

- Deciding on the health outcome of interest, the type of economic evaluation that would reflect the outcome of interest, the perspective to be used (societal or payer's perspective), costs to be included based on this, and the time horizon. They also discussed the source of the input parameters.
- The participants discussed which important events and factors that should be included in the model, such as infections, complications (e.g. pneumonia, side effects of the vaccine), the socio-economic status subgroups, patients' reliance on family members for care, higher risk for elderly patients, and death.
- For one group, there was confusion between cost-effectiveness and cost-utility analysis (CUA). Participants agreed to have QALY as their outcome; however, after discussing the type of economic evaluation (EE) later, they needed clarification on whether it was a CUA or cost-effectiveness analysis (CEA). HITAP explained that these two terms (CEA and CUA) may use QALY as the outcome.

HITAP attended the NIHRD symposium, during which Dr. Yot Teerawattananon also promoted on the process of developing health quality indicators for the Thai Universal Health Coverage (UHC); the notes from this event are in *Introductory HTA Workshop Notes* and *NIHRD Seminar Notes*.

After Action Review

HITAP staff appreciated the chance to teach and explain concepts to others. However, they felt they were not well prepared to act as TAs during the group exercises and need to practice more beforehand. Language barrier was a challenge as most people spoke in Bahasa during the discussions. Participants may also be reluctant to participate or have a leading role. Some participants also left and did not attend the rest of the workshop. Some people cannot remember or understand the lecture. Some ways to improve include:

- Ask the participants to send their CVs beforehand.

- Prepare by meeting with the team two or three times before the workshop or meeting. Arrange TCs with the local focal points to try and prepare for administration and logistics of the meeting.
- Place an HIU staff on the ground to facilitate the admin work beforehand.
- Lectures may be improved to be easier to understand and have group work that all participants can participate in (e.g. the investment and disinvestment). However, HITAP may need to limit the number of participants. Another option is to have the organizer limit the participants to a certain number only (e.g. 20 for technical work).
- If the participants don't have technical backgrounds, then the group work should also be less complicated (e.g. remove exercise 2).
- Translators may be hired to account for the language barrier.
- Evaluation forms sent to the organizer were not printed and have to be sent retrospectively via email.

- The HITAP team have a collective responsibility to assist the group and any work needed. During group work, the team should be assisting and forego working on other HITAP-related work.

HTA Development: Meeting with the InaHTAC

HITAP had a meeting with the Indonesia HTA Committee (InaHTAC or Komite Penilaian Teknologi Kesehatan/KPTK) and the Centre for Healthcare Financing (PPJK), Indonesia Ministry of Health. The objective of this meeting was to discuss the progress so far and the collaboration going forward between the InaHTAC and HITAP.

The PPJK presented on the progress of HTA in the country. Now, 169 million people are now covered under the JKN (Jaminan Kesehatan Nasional or the universal coverage scheme) as such, the government needs more and more the benefits provided by an evidence-informed system. The PPJK is now trying to finish the HTA guidelines, which specifies the requirements for conducting HTA. The teams are also meeting routinely to discuss these issues. Under the MOH team, there are 5 main themes - the first one is the tariff, HTA, clinical advisory team, monitoring and evaluation team, and the last one is the national formulary team which is under the pharmaceutical department. The first four teams are under the PPJK.

For the HTA team, they are working in reference to the presidential decree (no. 71, 2013), which has two articles outlining that the development of the use of technology should be informed by HTA and that programs have to be informed by HTA. There is an article mandating HTA under the government. HTA is one of the ways that the JKN program can be sustained. There are many medicines and drugs that have been used for the JKN, especially high-cost drugs (e.g. for chemotherapy and monoclonal antibodies). In the future, these medicines must be explored in more depth. There is also a ministerial decree mandating HTA. For this decree, HTAC will provide policy recommendations to the Minister on the feasibility of the health service/technology being considered. HTA is the bridge between science and decision making so it is important for the JKN benefit

Members of the HTAC come from stakeholders (based on an accountability principle). The core team consists of 9 reputable persons, with assistance from ad hoc panels comprising 15 additional persons, and there are new members this year. From the HTA team, all kinds of studies

including economic evaluation have been conducted. In this case, it should help to ensure that the results are valid and accurate. The Minister will make decisions based on this. PPJK (center for health financing and health insurance) due to its role within the JKN has the responsibility to facilitate HTA with the support of HTAC. Specific organizations, hospitals, and units are allowed to conduct HTA and must adhere to the guidelines.

As for the research conducted, in 2016, KPTK worked on 2 topics (prostaglandin E1/alprostadil and digital subtraction angiography). However, the first study was halted due to issues on the provider tariff and the INA CBG coding. They have had the following challenges: strengthening HTA institutionalization, guideline development, human resources (quantity and quality, e.g. frequent rotation of staff, which is an issue in terms of increasing capacity), facilities and infrastructure, funding (support from development partners, also other institutional activities such as PD first policy), technical assistance, dissemination of HTA products, and thresholds to be used in the studies (as well as conducting a threshold study). They aim to produce HTA starting with preparation in 2014, then have 2 outputs in 2015, 1 output in 2016, and more in the coming years.

HITAP then provided a presentation on what HITAP has done in Indonesia. BMGF has hired evaluators to assess iDSI work (through HITAP) so this was shared with partners as well. HITAP is keen to work in Indonesia and would like to know how best to do so, particularly since the evaluation found that there were issues in communications with multiple partners in the same country. However, the partners mentioned that this may have arisen because of the beginning of establishment of HTA. Now that the InaHTAC will focus on appraisal, then the technical work can be allocated to PICs. HITAP also was encouraged to continue with the same level of support and type of support (e.g. visits to the country for intensive technical support and coupled with remote assistance). HITAP will also incorporate implementation and policy making based on the previous 3 studies done.

For the study on sildenafil which is an example of off-label medicine use, HITAP is supporting this through two studies to understand the laws, regulations, and use of off-label medicines in Indonesia and internationally. This will assist the country understand the choices in terms of off-label medicines. The Indonesian partners shared that there may be a Special Access Scheme to allow the use and reimbursement of sildenafil through their universal healthcare scheme. In the future the minister will need to work together with Badan POM, MOH, and BPJS, especially for drug registration. Currently, there is a 10-year registration process. The target is to have sildenafil registered and reduce the burden of the process.

For capacity building and continued support for Indonesia, HITAP proposed supporting one Indonesian to a Masters or PhD program at the Mahidol University HTA program. The partners also agreed that capacity building should be focused and well-planned to ensure that the training doesn't go to waste or is lost (e.g. the trained person leaves the unit). The InaHTAC also proposed collaborating with Mahidol University on research projects. HITAP emphasized the need to have an Indonesia-based HTA system, as well as having a proper process that includes topic nomination. In general, Indonesian partners expressed that they still need HITAP support, especially in conducting the studies for economic evaluation. For institutionalization, there is still a need for capacity building. The local partners may prefer to have workshops similar to the April workshop (e.g. inviting university to conduct the workshop together and refresh the material). The partners also agreed that the work would come under the WHO Indonesia HTA program, which should be partnered or work in conjunction with a coordinating body within the Ministry

of Health. International partners are waiting for a concrete action plan for the next year and can also provide input to the plan. The international assistance should complement the local partners' plans.

Other activities proposed were: public lecture in University of Indonesia on HTA, short courses or programs on HTA, model course for HTA in Indonesia, threshold study, and costing study. For short courses, HITAP recommends that they conduct HTA relevant to policy. One day, there should be a critical mass of researchers to train others; it can begin with the requested training. Other materials, such as the policy brief on the study on pulmonary arterial hypertension, will be shared with international partners. Finally, there are many efforts to institutionalize HTA: the roadmap will be completed soon and shared with international partners; and, there is a new senior adviser on health technology and globalization (dr Slamet) and for the next meeting, he will be invited. He also mentioned about the WHO resolution during his lecture.

Access and Delivery Partnership (ADP) Forum

On October 19, 2016, some HITAP staff also attended the PATH Access and Delivery Partnership public forum. The public forum aims to discuss a multi-sectoral approach towards access and delivery of new health technologies in Indonesia with the ADP project partners, including United Nations Development Programme (UNDP), Tropical Diseases at the World Health Organization (TDR) and PATH as well as key country partners and government agencies from Indonesia. The main objective of the ADP project partners is to set up a system in Indonesia and build capacity to ensure that the system will run effectively.

The ADP, which also supports some of HITAP's projects, supports 6 key aspects namely:

1. Enabling policy and legal framework
2. Strategic information and evidence
3. Evidence-based resource allocation
4. Safety monitoring and pharmacovigilance
5. Implementation research
6. Procurement and supply chain

The presentations and discussion cover collaborative projects under ADP project partners as follows.

1. A pharmacovigilance study of national Tuberculosis (TB) program to prepare for an introduction of new multi-drug-resistant tuberculosis (MDR-TB): the key country partner is Ministry of Health, Indonesia. Activities supported by ADP include:

    - Technical guideline for Cohort Event Monitoring (CEM)
    - A pharmacovigilance workshop: introduction to CEM in April 2015
    - Pilot project of CEM in three sentinel sites
    - Advocates stakeholder partnerships
    - Report of adverse drug reaction and adverse drug event
    - Guideline for drug used in primary health care

2. Implementation and operational research to assess the needs and identify barriers to the effective introduction and scale up of health technologies: the key country partner is National Institute of Health Research and Development (NIHRD), Ministry of Health, Indonesia.

   Activity supported by ADP is to develop a national strategy for Implementation and operational research focusing on the prevention and control of TB, malaria, and neglected tropical diseases (NTD) in Indonesia. There is a request for financial support to implement the national strategy.

3. Health technology assessment to strengthening evidence-based priority setting: the key country partner is Centre of Health Financing and Insurance, Ministry of Health, Indonesia. Activities supported by ADP in a collaboration with iDSI (through HITAP) and WHO Indonesia include:

   - Training to Persons-in-Charge (PICs) for the HTAs at HITAP in Thailand in HTA methodology and process.
   - Training to members of Health Technology Assessment Committee (HTAC) on incorporating economic evaluation into HTA.
   - Support HTAC to conduct two HTAs in 2015 on treatments for end-stage renal dialysis and pulmonary arterial hypertension.
   - On-going support on disseminating the results of these HTAs to stakeholders and Health Minister, including publishing a Policy brief on the findings of those two HTAs.

   Also, Prof. Dr. dr. Sudigdo Sastroasmoro, Chairman of HTAC mentioned about the appointments to the new HTA shall be from 2016 to 2019. As a result of capacity building in HTA, HTA process is currently incorporated in decision making in Indonesia. If HTAC requires evidence on cost-effectiveness of medicines, the process will be involving universities and research institutes to conduct economic evaluation, and results of those studies will be appraised by HTAC.

4. Procurement and supply chain of medical device, medical equipment, and new medical technology in a cost-effective manner: the key country partner is Ministry of Health, Indonesia.

   Activity supported by ADP is to develop the procurement training module with the aim of providing training to official commitment makers and the procurement service unit members. ADP provide support to Ministry of Health, Indonesia on both financial support and assistance in the development of training module.

HTA Topic Selection Workshop

The HITAP team led by Dr. Yot Teerawattananon presented on the importance of topic selection in HTA. It should be clear, transparent, and understandable for decision makers. All process and criteria of topic selection in HTA should be appropriate in the context in which it is conducted. An HTA question can be two types: investment and disinvestment. The former evaluates new, expensive, and innovative drugs and devices, whereas the latter evaluates interventions that are

already included in the benefits package but which may have unclear or harmful effects, be cost-ineffective, or have better alternatives. A Thai case study was given as an example of the investment type and the disinvestment example was given from a case in Vietnam.

In Thailand, there has been an obvious process of development of the Universal Health Coverage Benefit Packet (UHCBP) since 2009. The process includes three features i.e. topic selection, assessment, and results dissemination. Relevant stakeholders were identified for each step and assigned their roles. The criteria for topic selection in Thailand contains 6 aspects, they were discussed in detail by the participants in order to apply with Indonesia context as follows:

- How to deal with the variation in practice? HITAP suggested that if there are more than two sources used for evidence on national-level decision making (e.g. clinical practice guidelines and primary study) with the same results or information, this criterion should be scaled to highest score or 5.
- The equity/ethical and social implication was suggested to be considered in terms of geographical variation because there are large and varying equities in the Indonesia context.
- What is the source of the numbers of economic impact on household expenditure in Thailand? Dr.Yot explained that those were derived from a household study which inform catastrophic health expenditure in Thailand. They excluded the treatment costs under the public health insurance schemes; only the costs shouldered by the patients and their household members, such as informal care, out-of-pocket expenditure, travel and accommodation costs for seeking care.
- The severity of disease or heath problem: there was a doubt about the scale of this criteria and the expert described that it depends on nature of the disease, type of disease, as well as stages of disease. In Thailand, severity is considered in terms of levels, such as disability.
- Will the final score be changed later? Dr.Yot explained that HITAP has a rapid review and have scores following the evidence. The score could be changed by the topic selection working group consisted of independent key stakeholders in the prioritization process. HITAP's initial score works as a starting point for the working group discussion.
- How was the working group established in Thailand? And what are their roles? Waranya answered that the working group was identified from all stakeholders, with 3 representatives per group. Each relevant group will be provided financial support for meeting among members before the meeting with the wider group of stakeholders. The function of the working group is to prioritize topics following the rapid review results. The working group will be changed every 3 years. However, industry and policy makers are not allowed to involve in the working group because they have a conflict of interest. For example, industry company that sells a medical device may pursue promotion of its own product and rank it highly.
- Regarding the case study 1 showing the budget impact of an intervention on NHSO funding, how would this be applied in Indonesia where the budget data of BPJS is not published? In this case, it was suggested to use other approaches to present the burden of the intervention.

- Should there be a study before submitting the topic into the selection process? Dr. Yot answered that it would be great to have a study for supporting the information before if there is no clear process and criteria of topic selection.

Exercise: identifying the involved stakeholders in HTA topic selection

Stakeholders were identified suitably with each step:

Step 1: Topic selection
- Academic groups
- Health professionals
- Patient groups
- Healthcare Industries (Pharmaceutical Companies/Manufacturers)
- Policy makers
- BPJS Kesehatan
- Non-Government Organizations (NGOs)
- Civil Society/ Community leaders
- Provider Organizations (Private hospitals)

According to the specific country setting, there may be a separation between manufacturers and private hospitals. They have different ideas and objectives in the healthcare system. Moreover, local governments in each province was not considered in the group because it does not take a role in healthcare designing.

Step 2: Rapid review
- HTA Committee (Technical team)

HTA Committee are set to work on HTA, including health researchers and professors from university.

Step 3: Topic prioritization
- HTA Committee
- Health professionals
- Academic groups
- BPJS Kesehatan
- National Formulary Committee

NGOs were not included in this process because it is too hard to identify a representative of all NGOs in the Indonesia context.

Additional notes during the discussion section are found in *Topic Nomination Workshop Notes*. During this day, as well, some HITAP staff assisted in the completion of the manuscript for the HTA on renal replacement therapy options in Indonesia.

Off-label Medicines Proposal Development

Dr. Prastuti Soewondo, from the Faculty of Medicine and the lead researcher for the Indonesia study, introduced the meeting, the objectives, and the participants. This is a meeting with two

groups that are doing off-label medicines studies. These studies were conducted to support HTA for PAH that found off-label medicines can be positive at the same time disadvantageous, particularly in response to the study that found sildenafil as treatment for pulmonary arterial hypertension (PAH) as a cost-effective option to the current intervention. However, it is not allowed for reimbursement under the law. The first study is for Indonesia and the second is for international settings. This is the first meeting for to finalize the proposals of work, ensuring both teams are in line. The work is still at the beginning phase so the discussion will not be around results but to fine-tune proposals and study.

The Indonesia team gave a presentation of their proposal, which will examine the laws, regulations, and use of off-label medicines in the Indonesia. They've already looked at hospitals that have off-label medicine use. Off-label medicines is one of the areas that they will explore in their faculty of medicine. Their literature review showed that off-label use is associated to label or formulation. Study location will be mostly in Jakarta, and they will look at both a public and private hospitals. On their first proposal, the reviewers' comments were very concerned about whether the selected hospitals are representative or not. However, they mention that they just want to explore the current practice in public and private hospitals. With the current budget and time, it is not possible to be more comprehensive. Some guidelines for in-depth interview/focus group discussion will be explored. Policy of the Badan POM distribution is for license basis (not including CE), and they will identify policy and regulations. For existing practice part, it will be difficult for practitioners to admit their use of off-label drugs in their prescriptions. For example, there is no medical prescription for certain things but they will prescribe to generate insurance payments for the patients.

The international study team discussed their proposal, which will pick a handful of countries and examine the laws, regulations, and use of off-label medicines in these settings. They discussed the drug approval process and the processes in different countries. In Canada, off-label drugs use prescribed by primary care. In the US, the researchers measured the use of off-label in USA. Australia has a comprehensive process for the evaluation of inclusion of off-label medicines. The study will primarily be a literature review but they will also have a questionnaire. They will ask interviewees to provide 3 examples of off-label medicine use, among other process-related questions.

HITAP and PATH provided suggestions to both studies' proposals. For the Indonesia study, they suggested that Pfizer, the company that produces sildenafil, should be interviewed. Another suggestion is to have different kinds of companies represented. HITAP suggested that the pharmaceutical therapeutic committees, responsible for medicine inclusion in hospitals, should be interviewed. The study should also be pushed in the local government, so the researchers should try to speak to PPJK and BPJS on the matter. For the international study, they suggested that international companies should also be interviewed. The issue can be an ethical problem, given the different approaches of companies to the same medicine in different countries (e.g. sildenafil is registered for PAH in the US, but not in Indonesia).

They discussed that there are three types of off-label drugs: off label without evidence, and off-label with evidence but not registered in countries, and finally off-label with evidence and registered in some countries but not others. If off-label drugs are graded into three categories, then it would be easier to understand. Some issues are also more ethical, e.g. for life threatening illnesses wherein doctors will prescribe treatments that don't have evidence.

The partners also agreed to present the preliminary results during the Prince Mahidol Awards Conference (PMAC) in a small side-event to be jointly sponsored by HITAP and PATH. The contracts were signed and the group agreed there will be teleconferences every month to discuss the progress of the studies.

Additional notes are in *Off-label Medicines Proposal Development Notes*.

PATH-HITAP Meeting

HITAP and PATH partners met to discuss the developments in their work and the next steps. HITAP updated PATH on their activities over the past week, including the introductory workshop for HTA with the NIHRD, which seems to be interested in working as a lead on HTA in Indonesia. Given that the InaHTAC under the PPJK's direction has been working on HTA for a few years now, however, it is likely it will continue to be the lead. In addition, one of the new members, Dr. Slamet, has proposed that HTA be implemented in all departments of the ministry, though there are some members also believe that it should be better established before this is pushed.

PATH then mentioned that they have worked on areas such as malaria and other vertical programs; HTA is not seen as separate to this. In addition, PATH and other international partners such as the World Bank are interested in seamlessly merging these vertical programs to the Jaminan Kesehatan Nasional (JKN). Finally, many departments they work with have claimed that they are doing HTA, but it is unclear if this is truly the case and may be happening in isolation.

The partners then discussed the role and institutionalization of HTA. They mentioned that the HTAC can have a more facilitative/secretariat/authority role. The methods guidelines should be published to support this function and ensure standardized HTA process is conducted throughout the country; however, international partners are still waiting for this to be translated. The roadmap written by Prof. Hasbullah Thabrany still needs to be revised and supported by other departments in the MOH.

PPJK has requested HITAP's support for a training; however, given that HITAP has already provided this in the past, the following were requested from the partners before pushing through. The guidelines should be published and supported by national authorities. The training should be conducted by local partners (e.g. those trained in the past, the PICs Levina Khoe, Septiara Putri, and Nur Atika, and be considered a Training of Trainers or ToT). This can be a collaborative work with PATH, with 1-3 sharing sessions from both PATH and HITAP. The training should be open to all interested (including the private sector), and can be paid or unpaid. However, the participants will not be compensated for attending. The training can be technical or mid-level. This work needs consensus building (consistency and normative work) about HTA. PATH agreed to push this as well as the work plan and the guidelines in their own meeting with PPJK. They can discuss the workshop dates for next year (e.g. April 2017) given that the HTAC mentioned the guidelines will be endorsed next month.

For the PD implementation and assistance in finalizing their pilot program, Maya Amiarny (Director of Health Services in the BPJS), Komaryani Kalsum, and Ari Syam can be tapped to help. Dr. Donald Pardede is still a key person as well.

In terms of the international grants in Indonesia, HITAP's grant with the BMGF is ending in 2018, though there is a possibility of continuing or having no cost extension to 2019. There is confusion with the relationships between the ADP, PATH, HITAP, iDSI, and the WHO. WHO, through Dr. Salma Burton, can act as a coordinator for international partners. PATH is also looking for a new in-country representative. HITAP will email Dr. Burton on the work to be done and can request her to facilitate the work with PPJK. Local partners should have a concrete plan (more practical, short-term, more stakeholder involvement). The partners can then align with them and through their action plan. Local partners should play the advocacy role in-country. The two studies completed (RRT and PAH) should be pushed locally but the local partners must lead this. HITAP also suggested that they translate the Bahasa guidelines.

Regarding the off-label medicines studies, HITAP has supplemented the funding from PATH with the Thailand Research Fund. HITAP then suggested having an event during the Prince Mahidol Awards Conference (PMAC). The partners agreed to split the cost, with PATH shouldering the costs for the Indonesian participants to travel and attend and HITAP can arrange the venue and in-country costs. HITAP can prepare a concept note for the side meeting, which would include the objectives, outcomes, and introduction to both iDSI and ADP. ADP will also be having an event during the PMAC. HITAP will also request support from the WHO for the March policy forum.

PATH aims to produce concrete outputs such as policy briefs, blogs, etc. They will prepare something of a fact sheet and disseminate to participants in March. HITAP also recommended that PATH consider supporting Indonesian partners to the HePTA/HTA Mahidol University program. The WHO is also providing support. Ghanaians and Tanzanians may also be supported, though they may consider having conditions like the HITAP support: they must be endorsed by their employers and return to work in their countries for twice the time that they had their scholarship program (e.g. the duration of the masters or PhD). This is a good south-south collaboration opportunity, and others could be short-term training. They expect that there can be a certain number of graduates after a certain year for Indonesia. HITAP also mentioned that they have an internship program in 2017, to which PATH can send potential candidates.

Appendices

Appendix 1: Agendas

The International Symposium on Health Research and Development

Organizer: National Institute of Health Research and Development

Date: Tuesday, October 18, 2016

Location: Siwabessy Room in The Achmad Sujudi Ministry of Health Building, WHO Adhyatma Building Blok A 6th floor #602, Jl. H. R. Rasuna Said, DKI Jakarta, Daerah Khusus Ibukota Jakarta 12950, Indonesia (TBD)

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Waranya Rattanavipapong, Researcher
3. Dr. Pattara Leelahavarong, Researcher
4. Chutima Kumdee, Researcher
5. Nittichen Kittiratchakool, Research Assistant
6. Alia Luz, HIU
7. Sneha Rajbhandari, HIU

Time	Activity and Presenter	Notes
9:00 – 9:15	Introductions and Welcome - HITAP and partners	
9:15 – 9:45	Introduction to HTA – process and methods - Dr. Yot Teerawattananon, Program leader	
9:45 – 10:00	Break	
10:00 – 11:00	Overview of economic evaluation - Waranya Rattanavipapong, Researcher	
11:00 – 12:00	Model-based economic evaluation - Pattara Leelahavarong, Researcher	
12:00 – 13:00	Lunch	
13:00 – 14:00	Exercise 1 (group discussion): Model planning and conceptualisation	TAs are Chutima Kumdee and Nitichen Kittiratchakool
14:00 – 15:15	Exercise 2 (hands-on): Decision tree model	TAs are Chutima Kumdee and

		Nitichen Kittiratchakool
15:15 – 15:30	Break	
15:30 – 16:00	Group presentation on exercise 1	
16:00 – 16:30	Policy Implication and Implementation of HTA - Dr. Yot Teerawattananon, Program leader	
16:30 – 17:00	Q&A	

Name of Activity: The International Symposium on Health Research and Development

Date: Wednesday, October 19, 2016

Location: Siwabessy Room in The Achmad Sujudi Ministry of Health Building, WHO Adhyatma Building Blok A 6th floor #602, Jl. H. R. Rasuna Said, DKI Jakarta, Daerah Khusus Ibukota Jakarta 12950, Indonesia (TBD)

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Waranya Rattanavipapong, Researcher
3. Dr. Pattara Leelahavarong, Researcher
4. Chutima Kumdee, Researcher
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6. Alia Luz, HIU
7. Sneha Rajbhandari, HIU

Wednesday, October 19, 2016 *9:00 – 15:00* *Jakarta, Indonesia*		
Time	**Activity and Presenter**	**Notes**
9:00 – 13:30	The International Symposium on Health Research and Development - HITAP	
13:30 – 15:00	Developing health care quality indicators for UHC - Dr. Yot Teerawattananon, Program leader	

Meeting on HTA Development in Indonesia
Date: Wednesday, October 19, 2016

Location: Pusat Pembiayaan dan Jaminan Kesehatan Kementerian Kesehatan R.I Office, Jln H.R Rasuna Said Blok X5, Kav 4-9 Lantai VII, Ruang 713, Jakarta -12950

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Waranya Rattanavipapong, Researcher
3. Alia Luz, HIU
4. Sneha Rajbhandari, HIU

Objective

1. To discuss HTA and its role in decision making.
2. To outline the progress on its development and the collaborations and projects that have advanced HTA use
3. To initiate future collaboration on HTA development.

List of attendees (15 - 20 participants)
Attendees expected are representatives from:

- PPJK
- BPJS
- HTAC
- PATH
- WHO Indonesia Country Office
- Others (as recommended)

Time	Activity and Presenter	Notes
15:30 – 15:4	Opening Remarks - Dr. Komaryani Kalsum, Head of PPJK	
15:45 – 15:50	Introductions and Welcome - HITAP and partners	This will also include an introduction from the partners involved in HTA development in Indonesia
15:50 – 16:10	HTA developments in Indonesia - PPJK representative	This will include the guideline and roadmap
16:10-16:55	Progress in HTA, Collaboration, and Future Goals - Presentations and discussion	This will include a discussion on the International Decision Support Initiative (iDSI) Mid-Term Learning Review (MTR)
16:55 – 18:00	Future Collaboration - Discussion amongst partners	
18:00 – 18:15	Closing Remarks - Dr. Komaryani Kalsum, Head of PPJK	

HITAP International Unit

From the People of Japan

THE ACCESS AND DELIVERY PARTNERSHIP

New Health Technologies for TB, Malaria and NTDs

TDR For research on diseases of poverty
UNICEF · UNDP · World Bank · WHO

PATH

Empowered lives. Resilient nations.

Public Forum:
The Access and Delivery Partnership in Indonesia

1430 hrs – 1730 hrs, 19 October 2016
Hotel Borobudur (Sumba C, Third Floor), Jakarta

The Access and Delivery Partnership (ADP) is a project, led and coordinated by the United Nations Development Programme (UNDP), in partnership with TDR (the Special Programme for Research and Training in Tropical Diseases at the World Health Organization) and PATH. This collaborative project aims to assist low- and middle-income countries strengthen their capacities to enable equitable access to, and sustainable delivery of, new health technologies for TB, malaria and neglected tropical diseases (NTDs). The ADP is supported by the Government of Japan.

The ADP is holding a Public Forum, which will be a panel discussion to share and exchange information about the ADP's work in Indonesia with a broader audience, including national stakeholders, civil society and development partners. The objective is to facilitate a discussion with relevant stakeholders on the promotion of a multi-sectoral approach towards access and delivery of new health technologies in Indonesia. The Public Forum will comprise a panel of speakers drawn from the ADP project partners – UNDP, TDR and PATH – as well as key country partners and government agencies from Indonesia. The Public Forum will be an opportunity for ADP project and country partners to share and exchange information with donor and development partners, so that they can be updated on ADP activities, as well as to engage with ADP project and country partners to identify synergies with other projects and initiatives.

Background

Working together, the ADP project partners leverage their respective expertise on a range of technical skills to strengthen national capacities for access and delivery of new health technologies. The ADP's strategic approach focuses on strengthening decision-making processes across multiple sectors and actors, to enable efficient functioning of the systems and mechanisms critical for the introduction of new health technologies. The

ADP has identified six 'pathways', within which interventions are designed to promote the multi-sectoral approach towards access and delivery. These pathways aim at activities to develop capacities for: (1) an enabling national policy and legal framework; (2) country-specific implementation research agenda for health; (3) safety monitoring and pharmacovigilance system; (4) evidence-based national resource allocation; (5) effective delivery and supply chain systems; and (6) use of strategic information and evidential base for decision-making. Since its inception in Indonesia in 2014, the ADP has initiated a range of project activities in Indonesia, guided by a country workplan jointly developed with national stakeholders.

Draft Agenda

1430-1450 **Welcome remarks**

- Representative of Embassy of Japan (TBC)
- Christophe Bahuet, Country Director, UNDP Indonesia

1450-1530 **Keynote Speeches**

- Edy Putra Irawady, Deputy Minister of Coordinating Economics on Industry and Trade Coordination
- Untung Suseno Sutarjo, Secretary General, Ministry of Health
- Dr. Syarkawi Rauf, Head Commission for Supervision of Business Competition (KPPU)

1530-1545 Coffee/Tea

1545-1645 **The ADP in Indonesia: Pathways to integrated access and delivery**

This session will have brief presentations from ADP project partners and country partners on the work of ADP in Indonesia. The presentations will illustrate the multi-sectoral approach towards addressing capacity issues on key components of the access and delivery value chain, including the policy and legal framework, implementation research, drug safety monitoring, health technology assessments and supply chain management. Q&A session to follow.

Speakers:

- Cecilia Oh, UNDP
- Prof. Sudigdo Sastroasmoro, Head of the HTA Committee, Ministry of Health
- Dr. Siswanto, Head of NIHRD, Ministry of Health (TBC)
- Tatang Rustandar Wiraatmaja, Director for Competency Training, LKPP Indonesia

- Siti Asfijah Abdoellah, Head, Sub-Directorate of Surveillance and Risk Analysis of Therapeutic Products, Directorate of Distribution, NADFC/BPOM

1645-1730 **Panel Discussion**: Building synergies for South-South learning

This session will discuss ADP approaches to building synergies, including examples of South-South learning and exchange between ADP focus countries in Ghana, Indonesia, Tanzania and Thailand. Q&A session to follow.

Speakers:

- Olumide Ogundahunsi, WHO/TDR
- Aziza Mwisongo/Mutsumi Metzler, PATH

1730 **Close**

1730-1900 **Cocktail reception** [venue detail to be provided]

Topic Nomination Workshop for Indonesia
Date: Thursday, October 20, 2016

Location: Harris Hotel Tebet-Jakarta, JI. Dr. Saharjo No. 191, Tebet, Daerah Khusus Ibukota

Jakarta 12960, Indonesia

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Waranya Rattanavipapong, Researcher
3. Chutima Kumdee, Researcher
4. Nittichen Kittiratchakool, Research Assistant
5. Alia Luz, HIU
6. Sneha Rajbhandari, HIU

Attending partners: PPJK, BPJS, HTAC, University of Indonesia, PATH, WHO

Thursday, October 20, 2016 *9:00 – 13:30* *Jakarta, Indonesia*		
Time	**Activity**	**Notes**
9:00 – 9:15	Opening remarks - Dr. Komaryani Kalsum, Head of PPJK	
9:15 – 9:30	Opening remarks - Dr. Sudigdo Sastroasmoro, Head of Indonesian HTA Committee	
9:30 - 9:45	Importance of topic selection in HTA - Dr. Yot Teerawattananon	
9:45-10:15	Topic Selection in Thailand and Vietnam - Waranya Rattanavipapong, Researcher	
10:15 – 10:30	Topic Selection Process in Indonesia - dr. Eva Herlinawaty, PPJK	
10:30-11:30	Brainstorming session for Topic Selection Process in Indonesia - HITAP with Dr. Yot Teerawattananon	Objective of session is to develop a proposal for topic selection in Indonesia Participants will be divided into two groups (1 hour): Group I = identifying stakeholders Group II = determining topic selection process and criteria
11:30-12:30	Discussion and Next Steps - All	
12:30 - 12:45	Closing Remarks - Dr. Komaryani Kalsum, Head of PPJK	

Renal Replacement Activity Manuscript Revision

Date: Thursday, October 20, 2016 (TBC)

Location: TBD

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Sneha Rajbhandari, HIU

Attending partners: PPJK and University of Indonesia (dr. Levina Chandra Khoe)

Wednesday, October 19, 2016 *15:30 – 17:30* *Jakarta, Indonesia*		
Time	**Activity**	**Notes**
13:30 – 17:30	Manuscript Revision - HITAP and partners	

Off-Label Studies Stakeholder Consultation

Date: Friday, October 21, 2016

Location: Tim Nasional Percepatan Penanggulangan Kemiskinan (TNP2K) Office, Grand Kebon Sirih Lt.4, Jl. Kebon Sirih Raya No.35, Kota Jakarta Pusat, Daerah Khusus Ibukota Jakarta 10110, Indonesia

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Waranya Rattanavipapong, Researcher
3. Chutima Kumdee, Researcher
4. Nittichen Kittiratchakool, Research Assistant
5. Alia Luz, HIU
6. Sneha Rajbhandari, HIU

Participants:

1. Dr. Prastuti Soewondo and team, TPN2K
2. Dr. Nattiya Kapol, Silapakorn University
3. Mutsumi Metzler, PATH
4. Aziza Mwisongo, PATH

Friday, October 21, 2016 *9:00 – 13:30* *Jakarta, Indonesia*		
Time	**Activity**	**Notes**
9:00 - 9:40	Present each proposal - Dr. Prastuti Soewondo - Dr. Nattiya Kapol	

9:40-12:30	Discussion on each proposal - HITAP and partners	
12:30 - 13:30	Lunch Break	

HITAP-PATH Updates Meeting
Date: Friday, October 21, 2016
Location: Pullman hotel, Thamrin, Jakarta

HITAP staff:

1. Dr. Yot Teerawattananon, Program leader
2. Waranya Rattanavipapong, Researcher
3. Alia Luz, HIU
4. Sneha Rajbhandari, HIU

Participants:

1. Mutsumi Metzler, PATH
2. Aziza Mwisongo, PATH

Friday, October 21, 2016
Jakarta, Indonesia
14:30 – 15:30

Time	Activity	Notes
14:30 - 15:30	Discussion	

Appendix 2: Miscellaneous Notes

Introductory HTA Workshop Notes

- Introductory speeches by department heads of Litbangkes: Dr. Nana Mulyani (Director of Health Resources and Health Services) and Dr. Slamet (Senior Advisor for the Minister for Health Technology and Globalization)
- Introduction to HTA by Dr. Yot
    - Definition of technology according to the WHO: *"the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives"*
    - Technological change is a key driver in healthcare spending
    - It's not always the case that more money brings more health (e.g. US health spending vs. Japan)
    - 20-40% of healthcare spending is wasted on inefficient use of resources
    - Concerns in using HTA: safety, efficacy, cost-effectiveness,
    - Economic evaluation: comparative analysis of costs and outcomes
    - Types of economic evaluation: Cost minimization, CUA, CEA, CBA; CBA is not used as much because of ethical reasons (i.e. giving a monetary value to a life)
    - QALY: how much are the gains in terms of health if the intervention is invested in by quality of life and life years. For quality of life, 0 is assumed as death or the poorest quality and 1 is perfect health. Somewhere in between is with disability or illness.
    - In Thailand, the government invests in cost-saving and cost-effective interventions; however, they also take into account the ethical and social implications of their interventions, so even an intervention that is high cost but targets a minority group, for example, may be selected for investment (e.g. imiglucerase)
    - HTA can be used to negotiate prices; for example, given that the results indicate a medicine is not cost-effective in the Thai context, then this can be used to negotiate with pharmaceutical companies to lower the prices and allow the government to purchase them
    - These kinds of technical knowledge should be able to support decision making, but it also relies on an appropriate process and ensuring that the results are robust, transparent, etc.
    - For example in Thailand, there is a specific process for including interventions in the benefits package, and ensures that it does not allow for much conflict of interest

- Discussion:
    - Representative from Faculty of Medicine in a university in East Java: the QALY score increased from treatment, is there a qualitative measure for QALY that would allow them to classify them as effective or good interventions?
        - Response: as an economist, this may be only one side of the coin. If the quality of life (benefit or life expectancy) is good, but if the money needed to spend is a lot then it may not be good for society. It is important to ensure the maximum benefit. There is no rule of thumb in terms of gains of quality of life then privilege is given

to that patient. However, as a doctor, there is emphasis on providing the intervention that provides the most benefit.

- Overview of Economic Evaluation
  - Role of economic evaluation in healthcare decision making includes: comparative analysis of different healthcare interventions, explicit analytical framework, best use of available data, quantification of uncertainty
  - Steps to conducting an economic evaluation:
    - Clarification of study question
    - Identifying all possible interventions
    - Identification and quantification of all health outcomes and resources
    - Valuation of above
    - Analysis
    - Interpretation of results
  - Example of type of economic evaluation from the audience: two types that depend on the type of outcome needed
  - Choice of comparison will include the most likely replacement of the current treatment choice
    - Current practice: can be the most effective OR the one most often used (though this may not reflect the best choice in terms of evidence based medicine)
    - Minimum clinical practice: the lowest cost or equivalent to having a placebo. This can also be the option of "do nothing"
  - Identification, qualification, and valuation of all resource and health outcomes (expert panel is helpful here)
  - Components of economic cost
    - Divided into:
      - Direct
        - Direct medical costs: medicine, procedures, in-patient costs, lab tests, etc.
        - Direct non-medical costs: transportation, additional food costs, accommodation costs, informal care costs, home modification, etc.
      - Indirect: productivity cost of illness (also informal care). Time loss will be a result of premature mortality and/or disability. Working time loss from illness is from receiving treatment and recovery period
  - The components included will be a result of the choice of perspective (e.g. societal vs. provider, the latter will not include non-medical costs)
  - There are different types of outcomes: clinical (e.g. mortality, number of cases, decrease in blood pressure, etc.), economic (cost), humanistic (quality of life survey)
  - How to collect data: primary data collection (retrospective, prospective), literature review, expert opinion
  - There is a process for systematic review and meta-analysis. There is an hierarchy of evidence, with literature review as one of the best, and expert opinion as the lowest
  - Costs must be adjusted to the present (discounting and consumer price index) to account for inflation in the future

- Presenting results (e.g. imagine that the economic evaluation is completed)
  - Incremental cost-effectiveness ratio: comparing cost of new treatment with the standard treatment
- Use of a threshold that will allow a drug or intervention to be included or not in their benefits package (e.g. in the UK less than 20,000 pounds per QALY gained)
- The cost-effectiveness plane: in the middle, the cost and outcome of the current practice is compared with the others around the area, wherein each plane corresponds to specific cost and health quantification as opposed to the current treatment

- Discussion
  - On choice of comparator, it is a bit confusing. If you want to compare the method of practice used, what do you use? Is it the most effective? Or is it mentioned in a standard or guideline?
    - Response: it has to match with the same indication of the patient. For example, treating a patient who has the same illness. E.g. cancer patient for stage one, then they can include several available options. Then you can compare them. Alternatively, then you can compare with supportive care if there is no other option. Many clinical studies (more than half) are funded by industries, which goes through phases 1-3 (safety, safety and surrogate indication, and effectiveness). This is to ensure that they can register their products. They will also not identify the best or base treatment available in the market because it is risky for them. Sometimes, some treatments, there is more than one treatment available in the market. Economic evaluation can compare these different treatments and interventions. Vaccination, for example, can include these different types also the "no vaccine" option.
  - For the threshold, are there thresholds for each of the health technology devices or procedures globally? Who sets up the threshold and how do you compare between countries?
    - Response: in Thailand and perhaps other countries, they use a single threshold for every type of intervention. In the UK, however, they give more privilege to end-of-life patients for ethical reasons.
  - Which particular phase is difficult? What difficult place? Or the scale of the work needed?
    - Response: Perhaps different for each researcher, but one of the most difficult may be in presenting to decision makers.
    - When HITAP does this kind of research, the aim is to have a national policy. Some policies may focus on primary care. Different islands in Indonesia may have different quality and sizes. In Thailand, there are some hospital promotion programs with different sizes so this needs to be taken into account as well.
    - Response: At HITAP, the research may be different from Litbang. HITAP conducts around 40-50 research per year. HITAP does not initiate its own research (neither does its researchers). The topic comes from topic selection and there are so many topics nominated so priorities are set. HITAP receives topics from stakeholders and use a criteria to select them. One of the criteria is magnitude of problem (e.g. burden of disease). The second is severity of disease. The third is financial expenditure by

households. The fourth is variation in practice to ensure uniform practice. The fifth is if it happens to a rare disease group or minority or the poor.

- Most of the presentation related to the clinical device, etc. Can you give an example of other types of interventions, e.g. non-clinical, but public health intervention?
  - Response: One example is adult diaper, which is registered as a medical device. It costs about a $1000 per month. This topic was received from stakeholders and HITAP conducted an economic evaluation for Thailand. There are some issues (e.g. some difficulties in distributing to poor). Another example is the hearing aids provision. But on average, Thai people don't use them after on average 2 months. The problem is battery, which is expensive due to it being safe for use for humans.
- Did you do some campaign for the community not to use diaper for children?
  - Response: HITAP did not assess the diaper for children. For adult diapers, HITAP found it is good and recommended them but that the local authority may not fund it.
- Do you recommend from that interventions should all have cost effectiveness analysis?
  - Response: Health technology assessment does not need to only be done only before, though this is good, but this can be done after as well. Ex ante (the former) vs. ex post. If there is a national policy, there should not only be Java as the representative of Indonesia. As such, there should also be HTA in other areas.

- Model-based Economic Evaluation
  - Conceptualizing a model - different modelers will think differently and have their own styles. They think about:
    - How to model effects
      - What is the effect, how long is the duration, impact on mortality or quality of life, and the treatment
    - Structure should be determined by understanding of health problems and health effects of interventions
    - Limitations of availability and quality of data
    - Simplified model may be used in response to limitations
    - Adding complexity can increase evidence burden
  - Defining the decision problem
    - Think about the study population (e.g. general population, and sub-group populations by geographical areas);
      - Define the population in need of interest
      - Product's licensed for population
      - Other considerations (e.g. trail inclusion criteria e.g. routine practice? Generalizable across settings? Consistent with any product licenses?)
      - Subgroup analysis: outcomes and costs may be different depending on the sub-group and geographical areas, after which a subgroup analysis may be performed
    - And then consider the current practice, the new intervention (s)
      - All actual and feasible options should be included (start by defining the reimbursement process or usual care)

        - Intervention of interest should be selected based on the decision problem e.g. substitute current practice or add-on therapy
    - General methods issues
        - Perspective of costs and effects -> what is CEA for? It has to link to the decision making process. This should mean societal or payer perspective given the responsibility of the government to provide these services
        - Measure of health effects -> use a generic tool that can be compared (e.g. QALYs), disease-specific or intermediate outcomes
        - Time horizon -> fixed to evidence or period of potential differences (e.g. lifetime)
        - Boundaries of a model
            - Scope the effects to include, they must be plausible and expected to impact results significantly
            - Model structure should capture the major characteristics of disease and intervention, providing guidance on the adoption and research decision and able to reflect the uncertainty of the decisions
    - Model Selection
        - Cohort models: decision tree
            - Diagrams the risk of events and states of nature over a fixed time horizon
            - It is suited for interventions with the relevant time horizon (short and fixed)
            - There are decision nodes which reflect possible decisions. The decision maker controls which one will be chosen. After the decision node, the stems reflect the choices.
            - The chance node reflects the probability of a state happening (e.g. disease absent or present)
            - Terminal node is the final state associated, e.g. death or cured.
            - Specify the consequences and probabilities (likelihood of an event happening). As such there may be more than one event after a specific treatment.
            - Validate these values through consultation.
            - Determine the value of each outcome, which will multiply the probability of the state with the cost and sum up all the relevant costs.
        - Cohort models: Markov model

- Discussion
    - How are these probability values taken? This may not be available in Indonesia.
        - Response: Systematic review can be conducted to get these information, but it has to be justified. This may be combined with meta-analysis to arrive at the best number to be used for the analysis.
    - When are the model values validated and how is this done?
        - Response: The life expectancy of patients in different subgroups will be run, and then they can be compared. These will be consulted with experts and other relevant stakeholders

NIHRD Seminar Notes

19 Oct 2016
Emerging infectious diseases and global health security
Dr. Heather Menzies

- *Country Director*
- Center for Disease Control and Prevention, Jakarta-Indonesia
- (Presented in English)
- The speaker showed the threats of infectious diseases, such as HIV/AIRDS, SARS, Ebola, and Zika, from the past to the present.
- The Global Health Security Agenda (GHSA) was launched in February 2014 and is a growing partnership of over 50 nations, international organizations, and non-governmental stakeholders to help build countries' capacity to help create a world safe and secure from infectious disease threats and elevate global health security as a national and global priority.
- GHS aims to prevent the problems of proliferation of disease, unpreparedness in the face of infectious disease challenges, and dealing with the economic impact.
- The GHS nowadays have several features to help address these problems: laboratory facilities, survillence, emergency operations, and workforce development.
- The Joint External Evaluation (JEE) is used for preventing, detecting, and responding to infectious diseases.

Zika virus: Invasion of the Western Hemisphere
Dr. Ronald Rosenberg

- *Division on Vector Borne Diseases*
- Centers for Disease Control and Prevention (CDC),
- Fort Collins-USA
- (Presented in English)
- The speaker presented about the history of Zika virus which was first discovered in Brazil in 2007. It is important that physicians are concerned about zika virus infection.
- There are some problems about diagnosis and differential diagnosis of Zika virus infection given that its symptoms are similar to dengue and chikungunya, such as fever, rash, arthralgia, myalgia, etc. It seems that the only difference between these diseases and Zika is that there is only conjunctivitis that manifests for Zika virus patients.
- A severe outcome of Zika infection is Microcephaly, which occurs in newborns who are born from infected mothers.
- Challenges of laboratory testing for Zika virus are that there are many asymptomatics and the date of onset is unknown. Moreover, it cannot be used PCR (polymerase chain reaction) because Zika virus viremia is low (false negative), and cannot use serology because previous flavivirus exposure cross-reacts (false positive). In additional, testing guideline is very

complicated. For example, in Brazil, there is misdiagnosis of Zika virus with dengue and chikungunya.
- The knowledge that we need to improve about the Zika is epidemiology, birth defects, transmission, and ecology.
- Tools that that we need about the Zika is diagnostic, vector control, and vaccine.

Lessons Learned from Malaysia: how to establish Clinical Research Centre as National Focal Point for Clinical Resear ch
Dr. Goh Pik Pin
- *Director of Clinical Research Centre*
- CRC, Kuala Lumpur-Malaysia
- (Presented in Bahasa)
- There are 2 targets for clinical research that are better health of people and to generate wealth for the nation.
- Clinical reseach needs multidiscliplinary team because to design and conduct modern clinical research is a complex undertaking requires many professionals from diverse disciplines to perform the variety of work process but the process is also most regulated.
- A good study should not come from only a setting, but it should be combined from many settings in order to be a representative data of the whole country.
- Thre is some question from audience that how to do if pharmacist initiated research that conflict with policy recommentation. The speaker explain that when investigator finished their research, they have to published so that the sub-committee can review the paper and compare with other papers that the conclusions are in line or not.

Developing health care quality indicators for UHC
Yot Teerawattananon, PhD
- *Senior Researcher*
- The Health Intervention and Technology
- Assessment Program, Bangkok-Thailand
- (Presented in English)
- Concise set of measurable indicators aimed at driving quality improvement in a specific area of care.
- UHC needs not only health service coverage but also quality; it needs to be effective coverage.
- Paying providers based on ‘capitation’ or ‘case mix’ cannot guarantee effective coverage.
- UHC needs to link evidence to policy and practice to ensure impact.
- The development of quality outcome framework (QOF) in Thailand was presented step by step.
- The recommendations are to create infrastructure and measure baseline performance, to make payments large enough to be meaningful and small enough not to distort priorities, to

re-calibrate incentives so that they remain challenging but attainable and to monitor patient outcomes & unintended consequences.

- Discussion:
  - Question:
  - Can we choose some indicators to represent all?
  - How much is it spend to generate one indicator?
  - Was the road map used to set up indicators?
  - How to include priority indicators for health services?
  - Answer:
  - They find that not all indicators are useful so they need to be tested.
  - Indicators need to be important and limited, so it is not a burden to the providers.
  - Some indicators are very expensive, so it is important to do EE. You can provide incentives to meet indicators but you have to ensure you are not spending most of the budget of healthcare activities.
  - There is prioritization in Thailand to see where there has been inappropiate medication use, such as overprescibe of antibiotics for diarrhea and upper respiratory infection (URI).

Health Service Financing and The Sustainability of Health System
Dr. Vikram Rajan

- *Senior Health Specialist*
- World Bank, New Delhi-India
- (Presented in English)
- Many countries have a commitment to UHC.
- How much should be spent on UHC? The practical answer is based on the willingness- and ability-to-pay.
- Global benchmarking clearly indicates that Indonesia needs to spend more, spend right, and spend better to make progress towards UHC objectives.
- The way a health system is financed is intrinsic to UHC: important to reduce OOP (out-of-pocket spending) share and increase public financing share of total health spending.
- UHC objectives should be commensurate with a country's capacity to raise revenues and deliver health services; otherwise, there will be "implicit rationing" and risks related to financial sustainability.

Synergies in Child Nutrition: International Evidence from Interactions of Food Security, Health and Environment, and Child Care
Dr Emmanuel Skoufias

- *Lead Economist at the Poverty and Equity Global*
- *Practice*
- World Bank, Washington DC-USA

- (Presented in English)
- Increased GDP and/or income is inadequate for reducing malnutrition in children.
- There are major gaps in data collected by the DHS (Department of Homeland and Security) and other nutrition-related surveys (e.g. they found that there are fewer data gaps for health and environment compared to food and care).
- In most countries, the ranking of percentage of child population with adequate basic needs in the area outlined (e.g. adequate care) is Care, Food Security, and Health & Environment.
- The low ranking of Health & Environment is not due to poor data or bad measurements. Community level of sanitation in all countries is the component that lags the most of the components of Health and Environment.

- Implication of health research on health systems strengthening
- Dr. Rosalia Sciortino Sumaryono MA, PhD
- *Associate Professor*
- Institute for Population and Social Research,
- Mahidol University, Bangkok-Thailand
- (Presented in Bahasa)
- Difference between public health sector and private sector are in places, staffs and facilities, for example, almost private hospitals are have more financial resoources while public hospitals are in rural areas.
- The next step is to link economic and social aspects of health, to initiate discussion on pro-public health and pro-equity policy or interventions, to appoach holistically beyond technical (UHC important, but not panacea), to generate regional goverance mechanisms for the health sector, and to engage civil society and consumer groups.

Topic Nomination Workshop Notes

Discussion on Thai topic nomination:

- Question: Is variation in practice includes also traditional medicine? And for equity and ethical consideration, do you also consider the geographical variation?
- Response: Yes, that is included. For the second question, in Thailand, this is also considered but there is not so much geographical variation. In the national health development plan, it is included. In Thailand, rare diseases or minority groups may also be given priority. Geographical variation may be included as a criteria for Indonesia given this constraint in the country.
- Question: There may be a causal relationship between different groups. Can you divide between these interventions?
- Response: In Thailand, there is a cut-off for each medicine for each patient. For example, a medicine can be used for only adjuvant breast cancer and not other indications.
- Question: Who makes the decisions on these criteria?

- Response: The scoring sheet is presented to the working group and they will enter a deliberation process. HTA in this case is used to finalize debate with health professionals.
- Question: For the economic impact criteria for households, is this on average? Is this updated yearly?
- Response: Yes, on average, Thai people will be hit with catastrophic spending if they over the threshold outlined. This is updated but not often.
- Question: Is this economic impact 30% of household income, which is the catastrophic spending according to international literature and WHO?
- Response: Yes, it comes from that. One of the selling points of NHSO in Thailand is that after introduction of UHC, less of the population has catastrophic expenditure (less poor) due to health spending. No more catastrophic expenditure due to the health benefits package.
- Question: For severity of disease or health problem, do you put advanced cancer cases also?
- Response: It depends on the kind of cancer, the stage, and condition. Sometimes it can be subjective. For example, all scores are presented to the working group and HITAP/researchers cannot make the decision.
- Question: Is there a quality control process?
- Response: Yes, the PI will oversee the research but there will be an adviser/supervisor to assure the quality, in addition to the appraisal process, etc.
- Question: I would like to ask more information about the working groups. Why did you choose these groups? Do they work together all the time? What are their roles (do they look at all topics or only some)?
- Response: The idea is to have many stakeholder working groups and represent wider stakeholders. Each group will have 3 representatives. The working groups will have a meeting amongst themselves to prioritize topics as well. NHSO saw that patient groups may be supported by industries. So they support these patient groups with financial incentives to consult their groups. Among the 7 groups of stakeholders, 4 will do the prioritization itself. However, industry and policy makers are not included to minimize conflict of interest. Industry can nominate topics because they know new drugs and information in the market. Policy makers are not involved as well since they may choose topics that are easy and affordable without considering other criteria.
- Question: For the study on the disposable adult diapers, how did they decide to address the recommendations in case the budget is not known?
- Response: There is no threshold to decide, however, the budget comparison was made to show the importance of the topic.
- Question: There is a group for topic selection, assessment, and appraisal. Is it the same team for topic selection and appraisal?
- Response: the topic selection is done by working group but appraisal is done by a sub-committee of benefits package development, so it is part of the board. These are high ranking officials. In Indonesia, by law, the HTAC has that legal mandate. In Thailand, the NHSO by law has that mandate.
- Question: The topics should all go through topic selection first?
- Response: In the first year of operation, NHSO did not allow any other channel for topic selection. After a while, complaints arose that IHPP and HITAP are centralizing HTA. After, it is allowed to nominate and conduct the process but they have to follow a process and guidelines

manual. There are not many topics that come from the other channels, and most of them are from the formal channel.

Discussion for Vietnam topic nomination:

- Question: I am interested to learn more about the topic nomination in Vietnam. HITAP and partners found the problem, so how did they solve it?
- Response: They tried to send a letter to hospitals that there are indications with inappropriate use of medicines. They are also starting a project to provide incentives for appropriate use of medicines and technologies. They may not pay retrospectively anymore to prevent this.
- Question: In the first step, did you review value for money? Did you collect primary data? How long did this type of assessment take?
- Response: Yes, we collected from literature and in a systematic way. Vietnam can accept the limitation and they adjusted using PPP. But they also learned how to do individual studies. They took 3 months to do this.

Presentation part:

- Summarize the results of the group work.
- Question: For stakeholders, if they want to submit the topics, do they need to write the proposal or just the topics?
- Response: In Thailand, they have only one page and need to know some basic idea. Then the research teams will do a rapid assessment.
- Question: Based on the group discussion, it will be based on evidence. Does Indonesia need all the criteria?
- Response: Yes and may need context. But they don't rely on scoring only because there are some topics that are unique and can be discussed within the team
- Question: When HITAP supported Vietnam, part of the discussion was disinvestment. In Thailand is this the case also?
- Response: In this process, disinvestment is included also but doesn't often come from this process. In the end of the prioritization process, you will not get a research question but a policy question. This still needs to be identified. In this process, the research question may become either investment or disinvestment. This topic may come by accident or research and not by topic.

Off-label Medicines Proposal Development Notes

- Discussion:
  - Indonesia study:
    - It's important to have an introductory statement for the interviewees on what they expect to do and that it will not have adverse outcomes for them. It would be a benefit to them that they don't need to ask and register a drug.
    - In Thailand, if the providers prescribe off-label drugs, then they may be charged in court. But if it registered in the national formulary, then it is defensible for them to use, for example bevacizumab and ranibizumab. They've never compared the use of bevacizumab vs ranibizumab for macular treatment because the doctors have

already tested it. For treatment of eye disease, the latter was used for 80% of patients in Thailand and is less expensive. They requested the national authority to consider which medicine will be used under the UC scheme. Six months later, the use of ranibizumab for eye treatment is registered in the WHO essential medicines list.

- This study is also considering the negative effects of the use of off-label medicines.
- For the national formulary, only drugs included in the BPOM (which focuses on safety and efficacy, and does not include cost-effectiveness) can be included as a reimbursable medicine. They've also interviewed others to explore, and found that there are many instances of the off-label medicines practice. One of the benefits of this study is to present the evidence to the policy makers that this was done, which can be examples to show to the regulators.
- Dr. Prastuti raised a good policy question on whether the regulation authority and the reimbursement authority should be linked completely and comprehensively. Or should it be separate? In the practice before the JKN, one of the social insurance schemes is for the civil servants' scheme (Askes), which tolerated the off-label medicines and they were reimbursed. However, now the selection depends on the team, and the team refers to the formulary list. The point is good, however, on whether it is possible for the reimbursement authority to provide off-label medicines.
- Dr. Nattiya shared that many articles used databases to determine the use of off-label use so that the researcher can identify the magnitude. This is the practice in Thailand, however, this is still difficult. There are thousands of medicines and would need coding. This was done for UHC scheme, research purposes, and also for regulation.
- Ms. Aziza said that this was already included in the first proposal.
- There is no national hospital database in Indonesia. There is a tariff and claims data but it is not detailed. However, Indonesia is four times bigger than Thailand so the coding is difficult. During Askes, the medicines are detailed in lists but after JKN it was not practiced.
- Can the Askes data be used? They will try and it is a specific segment of the population. However, this may perhaps have the maximum magnitude of off-label medicines, which is also the case in Thailand. There is incentive for them to prescribe and please the company. After JKN, many civil servants complained that Askes was better due to the wide reach of interventions.
- A question on two facilities selected: why exactly were they chosen? These two hospitals are Type B hospitals (there are ABCD types). This is a tertiary type of hospital. If it is in Type A, usually the administration for accessing data is complicated, though they are similar in type. The difference is in number of beds. For type B, there is oncology, anesthesia, etc. and has complete specialists (more complicated diseases so use of off-label is more likely). They can choose many other kinds of Type B hospitals, but the CEOs are close to them so access to data is easier and willingness to participate is better. If they chose the Type C and D, there are not as many specialists. The Pelni hospital is unique because 90% of the patients are

JKN patients. They must do innovation in how to treat the patients in an efficient and short way (length of stay is short). They want to hear about the innovation. They also heard about how pediatricians use off-label medicines. It is important to remember that this is not for representation and just for exploration/scoping.

- They will use both in-depth interviews and FGDs. How do you divide these between the interviewees (there are 18)? In Indonesia, there has already been a lot of qualitative research. The audience must be understood, and sometimes they don't want to be included in a group. The specialists for example may be interviewed as a group.
- Some suggestions from Dr. Yot:
  - They plan to conduct interviews from representatives of 2 companies. It has not been mentioned yet who will be interviewed. It would be good to interview Pfizer (since sildenafil under Pfizer has been registered in the US for PAH) but they are not interested to register this in Indonesia. They question is why they don't put in effort. The assumption is that sildenafil is off-label, then there are many companies already producing this. Pfizer's registration may not benefit them (patent is already finished 2 years ago but they don't have the protection extended to them in the US) in this case. Indonesian officials already begged them to register but they did not respond.
  - Indonesia has state owned pharmaceutical companies (Indopharma, etc.) and private companies, how do you plan to interview from them? They will do the same analog with why they chose only 2 hospitals. They want to explore from the perspective of industries also. They want to approach Novartis because they know them well and that they have many cancer drugs. Cancer is the top claims in JKN. From the drugs study that they presented, they tried to analyze just the cancer drugs and they saw that this increased substantially. They can identify the names of companies.
  - Ms. Mutsumi said that it may be interesting to have 1 from multinational, 1 from private, 1 from state-owned industry. But the main goal is Pfizer.
  - Dr. Yot said that for hospital interviews, it would in interesting to interview the pharmaceutical therapeutic committee. They are the ones who are responsible to include medicines in the hospital. Are they supportive, are they reluctant, and do they know it is off-label?
  - The government now initiates the Special Access Scheme (SAS) to support the use of sildenafil after the study is completed. Government budget will be used to buy the drugs. It would be helpful to find out more about this. Can this be a long-term solution? Is it not possible, etc.?
  - Dr. Komaryani is interested about this study and expressed that she got the request from parliament to get information about off-label studies. It may be good to keep in mind how to link with her, e.g. sharing proposal or etc. In the end, PPJK can be the one to push the study into policy and practice.
  - Dr. Prastuti said she can speak to Dr. Komaryani. Many of their studies have been incorporated and presented to the Secretary General. Because of the good network and relationship, it is not a problem. However, off-label

medicines may not always be related to the MOH, and they will see how they can link it to other ministries in a more strategic way. Something that can be raised to the policy makers and ask them to do something. In addition to this, with Prof. Agus, they are exploring with UNDP why the price of drugs is expensive because these are one of the highest prices in the region. Ibu Becky just finished a study on the e-catalog and procurement, and they just called the related ministries and asked them to improve it. E.g. BPOM is not in the ministry and they report directly to the president. Health professionals can also be part of this discussion.

- International study:
    - The rationale is very important to understand what countries have done. They can address this question to the interviewees, particularly to regulatory agencies. These agencies can be asked to give their guidelines and proposal.
    - Other interviewees can be FDA, insurers such as BPJS, NHSO in Thailand, professional associations, HTA agencies. Some countries were proposed but the documents are not in English (e.g. Japan).
    - Another group that needs to be interviewed: multinational and national pharmaceutical companies. Is it ethical or not for companies not to register in particular countries where they see no profit?
    - Who has the power to register - is it the manufacturing companies or the country? Most countries have regulations and these rely on companies to label their medicines. There are not many countries that register drugs without application from companies. Most drugs registered are based on company policy. Even companies also have promotion of use of off-label companies. This is intentional for them to do. Both groups need to be clear - there are three types of off-label drugs: off label without evidence, and off-label with evidence but not registered in countries, and finally off-label with evidence and registered in some countries but not others. If off-label drugs are graded into three categories, then it would be easier to understand. Some issues are also more ethical, e.g. for life threatening illnesses wherein doctors will prescribe treatments that don't have evidence.
    - In looking at the questionnaire survey, what are the mechanisms for enabling off-label uses? It is important to explore, so this can be added to the questions and the process how this is included.
    - Should this be presented in PMAC? It can be done during a side-event. The disadvantage is that stakeholders in Indonesia cannot hear about it. So there will be another one sometime in March for the final presentation. There will be a side-event one or two days before 29 Jan.
    - This means that the draft results need to be available before end of January 2017.
    - For policy brief, how do the partners finalize this, but this will be needed end of February. They will have the results in January and finalize the policy brief by end of February.

- So for PMAC presentation - the results slides can be available one week before for presentation. The aim is more of academic.
- The partners need to present the case politically and correctly so they don't make enemies in pharmaceutical companies.
- For PMAC: this can be a 2-3 hour meeting, and PMAC meetings are very active. There can be no more than 3 presentations: 1 for PAH, then from Thailand and Beva, also case study about good and bad practices, then the 2 studies. There is a cost implication for this.
- Schedule now for March 16/17 can be booked for the policy forum. PPJK will organize and HITAP can facilitate with them.

Appendix 3: Photos

Photo 1 & 2: Introductory HTA workshop with the NIHRD Symposium

Photo 3: NIHRD Seminar on Health

Photo 4: HTA development meeting with InaHTAC

Photo 5 & 6: Topic nomination workshop