INDONESIA MISSION REPORT

Follow Up HTA Workshop on PAH and RRT HTA Studies
28-29 April 2015

This document reports on the two-day follow up workshop of the PAH and RRT HTA Studies in Jakarta, Indonesia. The workshop was held on 28-29 April 2015.

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Background

This two-day Health Technology Assessment (HTA) workshop from 28-29 April 2015 is a part of a series of workshops to provide HTA technical assistance to the Persons in Charge (PICs) responsible for conducting two HTA studies (see Report on Study Visit to HITAP on HTA for Indonesian Delegates, February 2015). It is a part of the work being conducted under the international Decision Support Initiative (iDSI) to provide coordinated support in priority-setting as a means to UHC, with a pilot demonstration project focusing on building HTA capacity in Indonesia as well as under PATH's Access and Delivery Partnership (ADP) project. The iDSI is jointly funded by the Bill & Melinda Gates Foundation (BMGF) and the Department for International Development (DFID), UK while ADP is funded by the government of Japan.

Prior to this two-day workshop, a two-week workshop was held in Bangkok, Thailand for eight PICs to gain hands-on experience on conducting two HTA studies on:

1. Economic evaluation of sildenafil for the treatment of pulmonary arterial hypertension (PAH) (proposed by patient association)
2. Economic evaluation of continuous ambulatory peritoneal dialysis (CAPD) versus hemodialysis (HD) for terminal stage renal disease (proposed by professional organization)

This two-day workshop was conducted in order to determine the additional support needed to begin primary data collection and provide further technical support to the PICs for the economic modeling portion of the HTAs (see Appendix 1 for the workshop agenda). This workshop was attended by the HTA Committee (HTAC), PICs, and professional experts on each topic (see Appendix 2 for a list of participants) and made possible by collaboration between and support from the HTAC, PICs, iDSI, and PATH.

Objectives of the Visit

1. To provide follow-up technical support for the PAH and RRT HTA studies
2. To impart knowledge on economic modeling and introduce the Markov model
3. To discuss data collection methods and clarify any concerns in order to begin primary data collection

Summary of Activities

Day 1 – Workshop

The workshop began with a welcoming and introduction by Professor Sudigdo Sastroasmoro, the Chair of the HTAC. He proceeded to make a presentation on HTA in Indonesia, indicating a very ambitious UHC scheme and the need for international support to implement HTA in Indonesia. During the initial stages of beginning work with the HTAC, one of the primary concerns was the lack of full-time staff to conduct the HTA studies; however, the participants were informed that two full-time staff members have been recruited with support from the Australia-Indonesia Partnership for Health Systems Strengthening (AIPHSS). He also briefly touched upon the two HTA studies and remarked that collecting primary data samples for the PAH and RRT projects is difficult (see more details below). Nevertheless, the HTAC aims for the original timeline of completing the two studies by July 2015, followed by the conduct of an additional four topics between August and December 2015.

This was followed by a discussion session led by Dr. Yot Teerawattananon, who began the session by playing an animation on HTA in Thailand to communicate the power of HTA. Afterward, he opened discussion with the participants to explain how to conduct useful HTA work to support the Ministry of Health (MoH). Some experts raised questions and concerns during this session as follows:

- The term 'palliative' is not well accepted in the nephrology community and it is unethical not to treat end-stage renal disease (ESRD) with RRT
- Rather than comparing a new intervention to a current one used in policy, the experts argued that the study should compare CAPD with HD to inform the government that CAPD is a better choice
- Professor Sudigdo remarked that there has been criticism about conducting studies on Sildenafil and RRT because both have been evaluated in Thailand already

All the concerns were addressed and the session was concluded by reiterating that the HTA studies were selected by local stakeholders with the objective of supporting local authorities; also, although similar HTA studies may have been conducted in other countries, the context and data differ in each setting and may lead to different results so HTA should be adjusted to be relevant to current practice, i.e. the studies will be context specific. The session was followed by specific presentations on each project to provide updates and concerns (see Appendix 3 for presentation slides). The section below provides details on the discussion that ensued.

Cost Utility Analysis of CAPD Compared to HD for ESRD Patients

The proposal for the RRT study was presented to the workshop participants, followed by a question and answer session. Questions regarding data analysis and collection were raised by experts, such as nephrologists, and were addressed satisfactorily. For example, one of the main issues raised by nephrologists and other experts was the calculation of sample size for the study. Although sample size is important in clinical studies, it was explained that a scientific reference for calculating sample size does not exist for economic evaluation/costing. As such, it was suggested that a sample size of between 20-30 would be sufficient for completing the study with the option to estimate the value of having a bigger sample to see whether more subjects should be included after completing the study. Conclusively, it was agreed that primary data collection would be conducted for indirect and direct costs as well as data for sensitivity analysis while base case analysis would use data from health professionals and the Malaysian tariff would be borrowed for the EQ5D.

Cost Utility Analysis of Sildenafil for the Treatment of PAH in Indonesia

The proposal for the PAH study was presented, followed by a discussion session. The issue on the use of sildenafil for treating PAH, which was now off-labeled in Indonesia, was raised with the concern that the government should not promote the off-labeled use of drugs. Meanwhile, it could also be argued that the government should actively seek for a better treatment option for their patients if there were strong evidences supporting the use of that treatment option even if it was off-labeled. It was also noted that Pfizer was now preparing to register sildenafil under the indication for treatment of PAH in Indonesia. In terms of the scope of the study, it was suggested by a clinical expert that if the frequency of dosing per day was different between the two alternatives, compliance should be taken into account in the model. Also, some PAH patient in Indonesia could completely recover from PAH if they were eligible for undergoing surgery. This group of patient benefited more from using sildenafil, so not including surgery in the model might underestimate the benefit of sildenafil. However, the majority of patients could not undergo surgery. Therefore, the points will be taken into account and a subgroup analysis for this group of patient would be done if it turned out that sildenafil was not cost-effective for the whole study population.

Day 2 – Group Work

RRT

The session began with HITAP giving a review of the Markov model (as the PICs had received a lecture on economic evaluation during the two-week workshop at HITAP), which will be used for the economic evaluation of RRT. The participants requested for an explanation of the basic principles of the Markov model as well as the components of the model. As such, Francis Ruiz from NICE International presented a few slides on the fundamentals of economic evaluation, including a basic introduction to the Markov model. There were a few questions from the participants regarding the components of the model, such as why a certain time horizon is chosen or where the comparator is shown in the model. It is also noted that Professor Sudigdo would be responsible for writing the methodological guidelines for HTA.

After teaching the participants how to use the model specific to evaluating RRT, a discussion on the background of dialysis in the context of Indonesia and timeline for the next steps ensued. Some concerns about the model, parameter used, and the difference in practices in Thailand and Indonesia were raised as follows:

- In Indonesia, for patients who should start with PD, doctors initially give HD beforehand to stabilize the patients. However, the model seems to clearly distinguish the modality of the treatment choices. So, they had a discussion about policy questions and agreed to retain the model.
- There were some discussions around parameter issues and the group agreed on the following:
    - For survival data of dialysis options, there is an Indonesian study that indicates survival time of patients receiving HD. So, for the first analysis, the group agreed to use HD data to reflect survival of both HD and PD options. Afterward, the Indonesian team will update the study when the researcher of the survival study has completed the analysis of patients receiving PD. (There was also a concern with regard to patients' characteristics between the PD and HD groups as it is likely that patients who receive PD are younger than those who receive HD.)
    - For the sources of data:

Survival data of conservative treatment	Review international data, or consult the experts. Another choice is to adopt survival data from Thailand.
Direct medical cost	Unit cost study in database
Direct non-medical, indirect cost, utility data	Questionnaires are already designed and the team will collect data from 2 hospitals (one in Jakarta and one in another region)

Timeline

- Sensitivity analysis lectures will be provided to the team during the next visit
- After ethical approval, the team will start data collection in late May
- The team requested for HITAP's support at the beginning of June for data analysis and sensitivity analysis
- The team plans to hold a stakeholder meeting for preliminary results during the first week of July and have requested for HITAP's participation

*Note: fasting month begins on 18 June 2015

PAH

HITAP team introduced the economic model used for PAH in the Thai study to the PICs. Firstly, HITAP team went through the list of parameters needed as the input for the model. After that, the team demonstrated how to construct the Markov chain in the model.

Along the demonstration and discussions, issues on the study design were also brought up to discuss. Outstanding points are as follow.

Study population

Majority of PAH patients in Indonesia is different from Thailand. In Thailand, the most comment types of PAH are PAH due to connective tissue disorder (PAH-CTD), PAH due to congenital heart disease (PAH-CHD), and idiopathic PAH (IPAH). Meanwhile, in Indonesia, majority of PAH patients are those with PAH-CHD. Therefore, the study population will focus on only PAH-CHD.

About one-third of PAH-CHD patients in Indonesia are adolescents, which tends to benefit more from sildenafil. As a result, it may be necessary to sub-group analyze the adolescent group if the result for the whole study sample turns out that sildenafil is not cost-effective.

Transition probability

There is a local clinical trial comparing effectiveness between sildenafil and beraprost, which is the comparator for this economic evaluation. Thus, transition probability can be derived from this clinical trial. However, the follow-up period as of the date this report is written is only 3 months. The researcher for the clinical trial will continue following-up with patients. However, the length of follow-up might be too short to be projected onto whole-life period. Therefore, data from literature review will also be used concurrently.

Cost and utility data collection

To identify patients who are admitted with PAH, in the Thai study, ICD-10 for PAH and ICD-9 for right heart catheterization and echocardiogram were used. This could also be applied to this study.

According to rule of thumb, the number of sample for costs and utility data for each health state should be at least 20. However, due to the lack of data the classify patients and limited timeline, the PICs plan to collect data from smaller sample in 2 hospitals, 30 patients each. In total, the sample size will be 60 altogether.

Cost data

Costs of other comorbidity due to CHD (other than PAH) will be excluded since the focus of the study is on PAH only.

For the number of hospital visit, data from patient survey will be used instead of data from medical record. This is because the hospital in which the PICs plan to collect the data is a referral center, and therefore some data for hospital visit tends to be missing since patients may go to other hospitals that are close to their accommodation.

At the end of the day, the PICs have the opportunity to try constructing the Markov model. However, there exist points that the PICs feel unclear. HITAP team will further work together with the PICs on this through emails or potentially Skype calls.

In the end, HITAP team discussed with the PICs on the timeline for the next steps. An issue preventing the PICs from proceeding on the data collection process as soon as they wish is

the time needed for ethical clearance, which normally takes a month. The PICs aims to start collecting data at the end of May. For the summary of the activities and timeline, please see the following table:

Activities	Timeline (finished by)
Ethical clearance	April-May
Literature review for probabilities	May-June
Cost and utility data collection	End of May-Middle of June
Update HITAP about the progression	May
HITAP visit/visit HITAP	June
Analysis of the results	June
Send the results for HITAP to review	End of June
Expert consultation meeting	July

Outstanding Points

The following are outstanding points that may need to be addressed in the future:

- How were the experts for the panel chosen? This is to address the issues of transparency and participation.
- Given that the ethical approval and data collection phases of the RRT and PAH studies are still in progress (as of May 8, 2015), there could potentially be delays to the original goal of completion by July 2015.
- In the same vein, the HTAC aims for 4 more projects between August and December 2015, which may be an unrealistic expectation.

Next Steps and Conclusion

The PICs will begin data collection in May 2015 and the HTAC expect to have the studies completed by July 2015. Experts have been requested to assist with the data analysis and attend the stakeholder consultation workshop. In terms of the objectives, all three were completed satisfactorily during this visit.

Appendices

Appendix 1: List of Participants

Local stakeholders

Name	Affiliation
Rachmai Hamonangan	PAPDI
Anggita B.A.	Litbangkes
Cicih Opitasari	Litbangkes
Septiara P.	CHEPs UI
Hariadi Hariawan	Jantung
Fara Rosalina	Dit BUKR
Appolina S	PATH
Oktavia Lilyasari	PERKI
Mardiati Nadjib	
Nur Atika	HTA
Windi	
Saryo Pramono	PPJK
Nacita Putn	HTA-AIPHSS
Hagigdh	PPJK
Irma Novala	PPJK
F Ginanjar	PPJK
Levis K	PPJK
Baguas	PPJK
Eman Silaeman	PPJK
Bambaing	HTA-RSJHK
Erna Kristin	FKUGM
Afiatin	FKP-RSKS
Jojor Simarjuta	Prodis Atkes
Santoso Soerno	HTA
Sudigdo Sastroasmoro	HTA
I.B. Anom	BUKK
Lusiana S	PPJK
Levina Chandra	HTA
Eva Herlinawati	PPJK
Erie Gusrellyant	Binfar
Gema Asiani	KMPYP
Febrasyan	KMPYP
Agustini B.S.	HTA
Suhardjaro	
Ully A.M.	Balitbangkes

International experts

Name	Affiliation
Francis Ruiz	NICE International
Yot Teerawattananon	HITAP
Varit Chantarastapornchit	HITAP
Pitsaphun Werayingyong	HITAP
Benjarin Santatiwongchai	HITAP
Thanaporn Bussabawalai	HITAP
Nattha Tritasavit	HITAP

Appendix 2: Agenda for two-day workshop, 28-29 April 2015

DAY 1	28 April 2015	Venue: Royal Kuningan Hotel
13.30 – 14.00	Registration	
	Session I: Welcome and meeting objectives	
14.00 – 14.30	Opening remarks and introductions: • Greeting, sharing about Ministry of Health view to the Health Technology Assessment process and the expected output from this meeting *10 minutes* • Reflections about HTA Committee and update about the assessment process for both renal dialysis assessment and sildenafil for pulmonary arterial hypertension assessment *10 minutes* • Introduction from each and every participants Photo session	*Dr Donald Paerdede, MPPM, Head for Health Financing and Health Security Ministry of Health* *Prof.Dr. dr. SudigdoSastroasmoro, Sp.A(K), Head of HTA Committee of Indonesia* Moderator :drg. Armansyah MPPM
	Session II: Sharing Sesssions	
14.30 – 15.00	• Development of Health Technology Assessment in Thailand *10 minutes* • Discussion *20 minutes*	YotTeerawattananon, MD, Ph.D,HITAP
15.00 – 15.15	• Break	

15.15 – 15.55	• Proposal presentation : Cost Utility Analysis for Continous Ambulatory Peritoneal Dialysis (CAPD) and Hemodialysis (HD) FOR End-Stage Renal Disease Patient (20 minutes) *10 minutes* • Discussion • *30 minutes*	Presenters: PIC
15.55 – 16.35	• Proposal presentation : Cost Utility Analysis for Sildenafil as Pulmonary Arterial Hypertension(20 minutes) *10 minutes* • Discussion • *30 minutes*	Presenters: PIC
DAY 2	**29 April 2015**	**Venue: PPJK Office – MoH, Kuningan – Jaksel**
09.00 – 09.30	Opening of the day • Overview of the day	Drg. Armansyah, MPPM Dr.drg. MardiatiNadjib, MSc
09.30 – 11.00	Economic Evaluation Modelling Theory and exercise. There will be two groups, working separately for each topics	HITAP team
11.00 – 12.00	Data Collection and Analysis	HITAP team
12.00 – 13.00	Break	
13.00 – 14.00	Continued: Data Collection and Analysis	HITAP team
14.00 – 15.00	Report writing	
15.00 – 15.15	Break	
15.15 – 15.45	Summary and action plan	
15.45	Closing session	