2017

iDSI Indonesia – Mission Report

FOLLOW – UP VISIT (21 TO 23 NOVEMBER 2017)

MANUSHI SHARMA

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List of Acronyms

BIA	Budget Impact Analysis
BPJS	Badan Penyelenggara Jamina Sosial (Social Insurance Administration Agency)
CEA	Cost-effectiveness Analysis
CML	Chronic Myeloid Leukemia
CRC	Colorectal Cancer
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	Health Technology Assessment Committee, Indonesia
IDR	Indonesian Rupiah
iDSI	International Decision Support Initiative
JKN	Jaminan Kesehatan Nasional, the universal healthcare program
mCRC	Metastatic Colorectal Cancer
MoH	Ministry of Health, Indonesia
MoPH	Ministry of Public Health, Thailand
MoU	Memorandum of Understanding
PAH	Pulmonary Arterial Hypertension
PEN	Package of Non-Communicable Disease Interventions
PICs	Persons in Charge
QALY	Quality Adjusted Life Years
QoL	Quality of Life
TKI	Tyrosine Kinase Inhibitors

UHC	Universal Health Coverage
UI	University of Indonesia
UGM	University of Gadja Mada

I. Introduction

The Health Intervention and Technology Assessment Program (HITAP), Ministry of Public Health, Thailand, has been working closely with the Health Technology Assessment Committee (HTAC), Ministry of Health, Indonesia, since 2014 under the auspices of the International Decision Support Initiative (iDSI).

The year 2017 commenced with the HTAC conducting a topic selection workshop independently, funded by the Healthcare and Social Security Agency in Indonesia, BPJS Kesehatan (Badan Penyelenggara Jaminan Sosial); This report is designed to summarize the main activities which took place in the November visit to Indonesia. This follow-up country visit intended to provide technical support to the four teams conducting Health Technology Assessments (HTA).

The studies are described in brief below:

a. Factors associated with the use of nilotinib and imatinib amongst patients with chronic myeloid leukaemia (CML) under the universal health coverage (UHC) in Indonesia.
   This study intends to assess the use and the prescription pattern of Tyrosine Kinase Inhibitors (TKI) used in the treatment of CML in patients covered under the Universal Health Coverage. Given that both kinds of TKIs i.e. cetuximab and nilotinib have a high cost to the BPJS and nominal benefits to the quality of life outcome for patients, this study will provide a clear picture of the countrywide prescription patterns for the two TKIs, ascertain if the prescription pattern is in line with the national clinical practice guidelines and lastly identify the gap in current prescription practices vis-à-vis clinical practice guidelines.
b. A systematic review of the effectiveness of insulin analogues compared to human insulin for treatment of type 2 diabetes
   Indonesia currently uses Insulin analogue to treat 99.5% of diabetic patients requiring insulin, in contrast to global norms of using human insulin as the first line treatment (American Diabetes Association). Long-acting insulin analogue has benefits in reducing some forms of hypoglycemia and increasing the number of patients achieving the haemoglobin A1c (HbA1c) target, but not in reducing the mean difference of HbA1c. Although, human insulin is slightly cheaper than insulin analogue in Indonesia when compared to neighbouring countries such as Thailand, the price of human insulin is significantly high. This study aims to examine the costs and clinical benefits of analogue and human insulin.
c. Clinical effectiveness of EE of cetuximab on metastatic colorectal cancer
   There are currently 8,000 patients with colorectal cancer in Indonesia, of which 12% are in the metastatic stage. If left untreated, only 25% of patients (in the advanced colorectal cancer stage) survive in the two-year time. The main treatment of mCRC is the use of standard chemotherapy, i.e. 5-Fluorouracil, leucovorin, combined with irinotecan (FOLFIRI) or oxaliplatin (FOLFOX). The National Drug Formulary indicates that Cetuximab should be used in combination with standard chemotherapy for mCRC patients with positive KRAS wild-type; also, for patients with head and neck cancer. However, in practice, Cetuximab is used not only for indications as stated in the National Drug Formulary. Total claim data has shown an enormous economic burden up to 140 billion IDR or over 1 million US$ from 2014 until mid of 2017.

The Indonesian HTA Committee commissioned Universitas Indonesia to assess the clinical effectiveness and economic evaluation of adding Cetuximab to the standard chemotherapy for mCRC patients with KRAS wild-type.

d. Economic evaluation of bevacizumab in addition to chemotherapy for metastatic colorectal cancer (mCRC) in Indonesia.
For the year 2015, BPJS drug reimbursement data shows that Bevacizumab ranked ninth in terms of cost to BPJS. Even though Bevacizumab is an effective drug, the costs associated with this drug are significantly high compared to chemotherapy alone. Eliminating Bevacizumab would imply a marginal loss to patients but would save significant budget to BPJS which can be redirected to other interventions, such as screening and early detection of colorectal cancer. This economic evaluation study is conducted to assess the value for money and the budget impact of using bevacizumab compared to chemotherapy.

Since the last visit to Indonesia (in August), HITAP team has been actively providing input and technical support to the local team remotely. We learnt that due to budget cuts, the first two teams i.e Project a: Factors associated with the use of nilotinib and imatinib among chronic myeloid leukemia (CML) patients under universal health coverage (UHC) in Indonesia and Project b: Systematic review of the effectiveness of insulin analogues compared to human insulin for treatment of type 2 diabetes, will no longer carry out the qualitative studies. The first team will focus on a literature review and perform a desk search of all the document and peruse the grey literature; the second team will perform a systematic review and meta-analysis.

The primary objective of this visit was to provide technical input to the four teams, review their progress and support the data analysis. The summary of the discussions and recommendations are provided below.

II. Summary of the visit

a. Project a: Examining factors associated with the use of nilotinib and imatinib among chronic myeloid leukaemia (CML) patients under universal health coverage (UHC) in Indonesia

The main objective of this visit was to plan for the report comparing reimbursement practices and clinical guidelines for Chronic Myeloid Leukemia from Indonesia and other countries.

Discussions and recommendations

The survey questions have been developed and will need to be verified as well as articulated in English for approval from the HTA Committee. There was a concern that the survey questions were similar to a medical audit, however, given that the questions were qualitative rather than quantitative in nature, it was agreed that this would not duplicate medical audits that are already conducted.

It was discussed whether patients and pharmaceutical groups were useful groups to survey or interview. Some argued that these groups were not relevant because we were interested in the government perspective. On the other hand, these groups could still provide useful information and should be included in the study. It was agreed that patients will be surveyed because this can be done at little cost through the patient association. Pharmaceutical representatives will be interviewed but if there are budget cuts in February, a questionnaire will be circulated among key informants. Dr Yot Teerawattananon further

suggested that the patients should be asked broader questions such as their feelings toward UHC and medication being prescribed irrationally.

Going forward, the team would need an ethical approval for surveys and interviews. The approvals incur a fee, thus the original sample of surveying 20-30 hospitals would not be possible. As a result, the hospitals targeted was reduced to 5 and more information will be drawn from the Hematologist and Patient associations which do not need approval/ charge a fee. A new patient survey will be included.

The last step would be to classify data from hospitals by a range of criteria to draw out expenditure and prescription trends in the data. HITAP team supported the local team and some of the findings are as follows, the details are in the document attached in Annexure d.

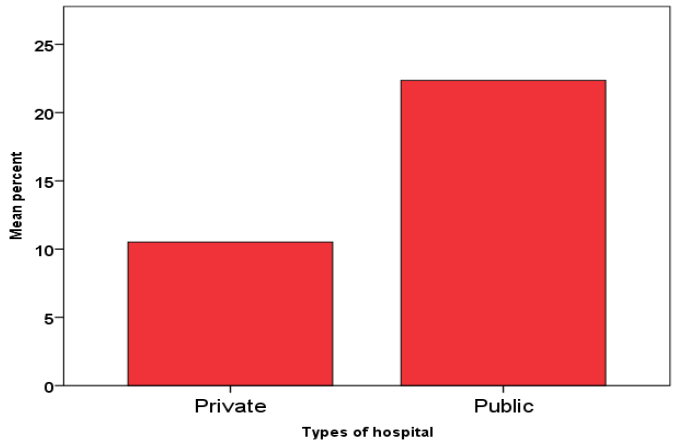

Figure 1: Percentage of Nilotinib prescription amongst Private and Public hospitals

As Figure 1 indicates the percentage of hospitals prescribing Nilotinib are majorly public owned hospitals.

Figure 2 depicts that the mean percentage of nilotinib prescription varies across provinces.

A study detailing the cost-effectiveness and the budget-impact of Nilotinib used as first-line drug in CML would be helpful and was recommended as a potential topic for the next round of studies.

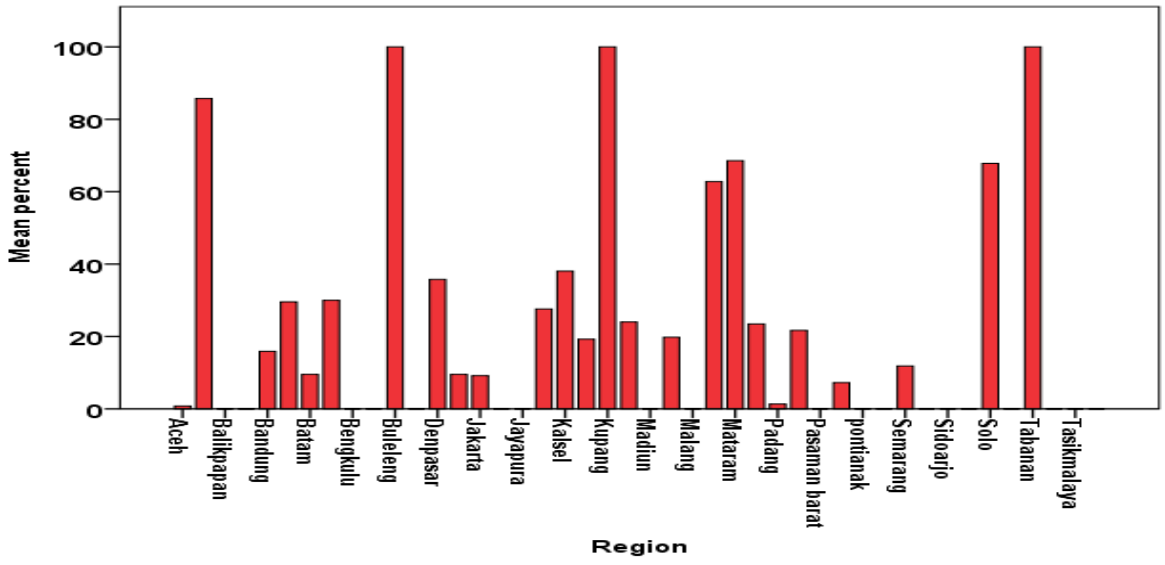

Figure 2: Percentage of Nilotinib prescription by province of Indonesia

Next, the literature review was discussed, the team faced difficulty finding the literature for the comparison of clinical guidelines of developed and developing countries. HITAP has agreed to locate the documents for the 6 countries and share with the team.

There is serious concern amongst the Committee members about the need for this study. The Committee believes that the finding will be that Nilotinib is prescribed irrationally, which is not in line with the national formulary guidelines and can be confirmed through a medical audit so there is no benefit to going ahead with the study. HITAP highlighted the importance of the study through a presentation to the Committee on the final day. The final decision was to conduct a desk review and perform tasks which do not require a substantial monetary input.

Next steps

HITAP team to share the documents for the international comparison of clinical guidelines and support the team with the literature review.

b. Project b: Economic evaluation of human insulin and insulin analogues for type 2 diabetes a Systematic Literature review

Discussions and recommendations

The aim of this study is to conduct a systematic review of the effectiveness of insulin analogue compared with human insulin in uncontrolled type 2 diabetes patients after oral antidiabetic drugs. A meta-analysis will be conducted to provide a summary of the treatment effect.

The research team with support from HITAP extracted the data for analysis and quality assessment from an additional seven RCTs. The research team finished the systematic review of updated single RCTs from 2012 to 2017 through MEDLINE and Cochrane Databases. Seven RCTs met the inclusion criteria; therefore, the final review includes nine RCTs in total. The research team should include RCTs from previous identified systematic review studies that are relevant to the research questions and selection criteria. A meta-analysis needs to be conducted to provide an overall summary of the treatment effect.

Meta-analysis combines data from multiple RCTs and is used to identify the common treatment effect. Meta-analysis of the following outcomes will be conducted:

- Glycemic control – change and difference in glycosylated haemoglobin (HbA1c)
- Hypoglycaemic episodes – numbers of overall, severe, nocturnal hypoglycaemia episodes

Next Steps

Due to inadequately skilled researchers, who are unable to carry out a meta-analysis, the HITAP team, in consultation with Assistant Professor Dr Thunyarat Anothaisintawee from Ramathibodi hospital, who is an expert in conducting systematic reviews and meta-analysis, will conduct the meta-analysis for the above-mentioned outcomes and share the results with the research team. A training on meta-analysis for research team has been planned for the next visit.

c. Project c & d: Clinical Effectiveness and Economic Evaluation of Cetuximab Therapy for Patient with Metastatic Colorectal Cancer (mCRC) and Economic evaluation of bevacizumab as an addition to chemotherapy for metastatic colorectal cancer (mCRC) in Indonesia

Discussions and recommendations

Transition probabilities will be retrieved from the systematic review (SR) and meta-analysis (MA) from published SR and MA and coupled with newly registered RCTs. Direct medical costs will be retrieved from a retrospective review of hospital bills. Most of the patients found in the hospital records do not get a full course of cetuximab because they were referred to other hospitals.
Two concerns related to this were:

- Firstly, there is no way to ensure that the patients continue to get treated;
- Secondly, as the data clearly shows that cetuximab is prescribed for indications other that mCRC,

This is not in line with the FORNAS's recommendation, and it is not clear whether this off-label prescription is reimbursed by BPJS. Thus, both the teams worked together and listed the parameters. The structure of the model of the two studies is comparable and the possibility of sharing utility score across the two studies was discussed. The cycle length was revisited and decided to be 1 month instead of 3 months and 6 months for the cetuximab group and bevacizumab group, respectively, because most patients do not survive long. The team will need to confirm with experts whether patients in progressive states can come back to stable states.

Next, second-line cancer treatment will also be included in the model and the regimen that is most common in the data the teams collected will be used to represent the overall second-line treatment. In the case of cetuximab, it is XELOX. However, the second line treatment is not yet clear for the bevacizumab and the research team will need some more time to review the data collected.

The discussion on the methodology and the results of the systematic review were as follows:

The identified studies compare FOLFOX4 vs CET+FOLFOX4 and FOLFIRI vs CET+FOLFIRI. Therefore, there is a need for indirect comparison. The research team needs to identify studies that compare either FOLFOX4 and FOLFIRI or CET+FOLFOX4 and CET+FOLFIRI. The rationale for this is to identify the most effective choice and to ensure the robustness of results.

Regarding the utility, the research team has compared the utility value from other studies, the value for the stable state are similar but they are negative for the progressive state. There are two more weeks for the utility interviews to finish and therefore the values may change.

Regarding the utility value, there is a limitation on the different approach in interviewing patients with the EQ-5D tool, i.e. cetuximab group used face-to-face interview by 4-5 interviewers while the bevacizumab group used phone interview by only 1 interviewer. However, given the number of samples are limited and the tool used is the same, it will be beneficial to pool the utility value and discuss the difference in data collection approach in limitations.

Next steps for both the teams

Both the teams should identify common parameters between the two groups (cetuximab vs bevacizumab) and explore the possibility of sharing utility data. The teams should reconcile the parameters and decide which ones the research teams would like to use as the base case.

Based on the results, there seems to be a discrepancy in the prescription of cetuximab i.e. it is being prescribed for conditions other than mCRC. Given the circumstances, the best option here would be to

conduct an HTA of cetuximab for other indications such as nasopharynx cancer and to negotiate the lower price for cetuximab. Reviewing more literature would make the results robust. The utility scores for the bevacizumab study and cetuximab study the scores should be pooled.

IV. Side meetings with the Health Technology Assessment Committee (HTAC)

The detailed minutes of the meeting are added in Annexure (d). A summary of the issues discussed are below:

1. Participating in the next HTAsiaLink conference the potential of hosting the HTAsiaLink 2019 or 2020 conference in Indonesia
   HITAP invited HTAC and related organizations like PPJK and University of Indonesia to participate in this year's conference. Global experts have been invited. The Committee was requested to encourage the members and related staff to submit abstracts. Further, the process and methodological guidelines are potential publications and thus abstracts can be submitted, the senior staff are encouraged to submit abstracts on this. The committee proposed to conduct a session in HTAsiaLink 2018 titled "HTA development in Indonesia". This was encouraged, and the committee should submit a concept note to HITAP.
   Lastly, we discussed with them the possibility of hosting the next HTAsiaLink 2019 or HTAsiaLink 2020 either by HTAC, BPJS or University of Indonesia. This will be a very good opportunity for policy advocacy and capacity building.

2. Planning for the two Indonesian scholars to be HITAP's international interns

   Overall, six scholars have been selected for the internship. Two are from Indonesia and their proposed topics and timelines for the project are

	Proposed timeline	Proposed topic
Ery	Jan-Mar 2018 (3 months)	EE on vaccination program (Dengue or Influenza)
Levina	Mar-May 2018 (3 months)	1. EE on diabetes screening strategies for pregnant women 2. EE of community-based HIV intervention program

   HITAP suggested that this internship experience should be able to make an impact once they go back to their home country. They can acquire a variety of skills like setting up an HTA committee in their home country or technical skills etc. Further, the HTAC to consider if the two interns from Indonesia should have the similar or relevant topics so that their work can have a bigger impact. The interns to come to HITAP at the same time so that they can support each other when working. In addition, they will learn how evidence is translated into policy.

   In the last week of the internships, two supervisors from Indonesia will be invited to HITAP to review the progress of the interns and to provide them final support in the study.

3. MOU between Thai MOH and Indonesian MOH

   The draft MOU was shared with the HTAC. This MOU was sent to the MOH, Indonesia to the Minister of the Foreign affair, Indonesia then Ministry of foreign affairs in Thailand finally MOH, Thailand and finally to HITAP. The MOH, Thailand has suggested some edits pertaining to the Intellectual Property Rights. This formal process between the two ministries and the two countries may take several months. Alternatively, a proactive approach to utilize time wisely would be to review the draft internally between Indonesian and Thai MOH. This will help shorten the formal process of finalizing this MOU by May next year. Hopefully, the MOU can be signed during the next HTAsiaLink 2018

4. Dissemination and publication of the Indonesian HTA process and method guidelines, HTA roadmap

   For the process and the methods guidelines. HITAP proposed that the committee should make the guidelines available on the website i.e. BPJK website and GEAR website. Raising awareness for these guidelines amongst other stakeholders in Indonesia such as NITAG, National Drug Committee, domestic research institutes and funders, WHO country office, etc. should be the next agenda. Academic publications could be explored for example summary of suggestions, the process of guideline development in Indonesia. The technical support for drafting the manuscript and support for submission including the publication fee can be provided by the iDSI. It is suggested that publication should be made in an open access journal then the copyright of this product belongs to the HTAC.

5. Plan for the current HTA studies

   HTAC has an internal deadline for the completion of this work by December 2017, which was next month. Based on the current progress HITAP suggested that February or March would be best suited. HITAP further explained that the nilotinib and insulin studies were equally important and relatively less technical and would require less time to finish. The nilotinib study will be more informative than an audit could be. An audit would only cover the monetary aspects of technology use. This research will allow us to understand why Nilotinib is being prescribed more than the national formulary suggests it should be and the perceptions of various stakeholders toward this issue. This may uncover some interesting reasons. This information may help inform the best policy design. It may also bring out the need for further HTA studies.

V. Future Actions

Based on the progress of the four studies the consequent visit to Indonesia has planned from the 13 to 15 December 2017. Action points for HITAP are –

- To provide support to the teams in the literature review, data analysis and guide them with the economic modelling.
- To support and encourage the teams to submit abstracts for the up-coming HTAsiaLink conference 2018.
- Regarding the Memorandum of Understanding (MoU), HTAC has identified focal points for this task from the Pusat Pembiayaan Jaminan Kesehatan (PPJK); HITAP & PPJK to work closely to

finalize the MOU and communicate to their own countries' Bureau of International Cooperation within the Ministry of Foreign affairs and aim to get the MoU signed by HTAsiaLink 2018

V. Appendix

a. List of Participants

S.No.	Name	Organisation
2	Prof. dr. Sudigdo Sastroasmoro, SpA(K)	Ketua Komite Penilaian Teknologi Kesehatan
3	drg. Armansyah, MPPM	Kepala Bidang Evaluasi Ekonomi Pembiayaan Kesehatan
5	DR.drg. Mardiati Najib, M.Sc	FKM - Universitas Indonesia / KPTK
8	Dr. Dra. Erna Kristin, Msi, Apt	Lektor Kepala FK. Universitas Gajah Mada
9	Mazda Novi Mukhlisa, SKM	Kasubbid Analisis dan Efisiensi Pembiayaan Kesehatan PPJK
10	Amila Megraini, SE, MBA	FKM - Universitas Indonesia
11	Benjarin Santatiwongchai	H I T A P
12	Rajibul Islam	H I T A P
14	Manushi Sharma	H I T A P
15	Juliet Eames	H I T A P
16	Kittiphong Thiboonboon	H I T A P
17	Thanaporn Bussabawalai	H I T A P
19	Ranti Dewi, SKM	Bidang Penilaian Teknologi Kesehatan
23	dr. Eva Herlinawaty	Bidang Penilaian Teknologi Kesehatan
24	Noventy C. Manik, SKM, MKM	Bidang Penilaian Teknologi Kesehatan
25	Fatma Rahmi	Bidang Analisis Efektifitas dan Efisiensi Pembiayaan Kesehatan
26	Vetty Yulianty	FKM. Universitas Indonesia
27	Hastuti Lestari	FK. Universitas Gajah Mada
28	Rizaldy P	FK. Universitas Gajah Mada
30	Dr. Dwi Endarti, MSc, Apt	Asisten Ahli Fakultas Farmasi Universitas Gajah Mada
31	Dr. dr. Sri Idiani, Sp.KJ	Puslitbang SD Yankes/Peneliti Madya
32	Ery Setiawan, SKM	Bagian Tata Usaha PPJK
33	Septiara P	FKM. Universitas Indonesia
34	Jessica Novia, S.Farm, MSc, Apt	FK. Universitas Gajah Mada
35	dr. Yusuf Subekti	Bidang Evaluasi Ekonomi Pembiayaan Kesehatan PPJK
37	RR. Harshinta, SKM	Bidang Evaluasi Ekonomi Biakes
38	Mukhlissul Faatih, M. Biotech	Puslitbang SD Yankes/Peneliti Muda
39	dr. Levina Chandra, MPH	Fakultas Kedokteran Universitas Indonesia
40	dr. Frans Dany	Peneliti, Puslitbang Biomedis dan Teknologi Dasar Kesehatan
42	Roni Syah Putra, S.Farm, Apt,MKM	Administrasi Kesehatan Ditjen. Kefarmasian dan Alkes
43	Andy Leny Susanty, SSi, Apt, MKM	Puslitbang SD Yankes/Peneliti Muda
44	M Noer Ibtidail	Fungsional Biro KSLN
45	Lilin Riana	Bagian Tata Usaha PPJK
47	Siti Rizny F Saldi, Apt, MSc	Unit CEEBM RSCM - FK. Universitas Indonesia

b. Agenda

iDSI Indonesia HITAP VISIT to Indonesia
Venue: University of Indonesia, Depok, Jakarta

Tuesday, 21st November 2017		
Time	Activity	Speaker
08.30-09.00	Registration	
09.00-09.15	Organizing Committee Report	drg. Armansyah
09.15-09.30	Opening Remark	Head of PPJK
10.00-10.30	Presentation of Goup I (UI): Clinical Effectiveness and Economic Evaluation of Cetuximab Therapy for Patient with Metastatic Colorectal Cancer (mCRC)	UI Team
10.30-11.00	Presentation of Group II(UGM): Economic Evaluation of Adding Bevacizumab to Chemotherapy Regiment for Patient with Metastatic Colorectal Cancer (mCRC)	UGM Team
11.00-12.00	Discussion on Study Progress	HTA Committee, HITAP/Mahidol & Teams
12.00-13.00	**Lunch**	
13.00 - 13.30	Presentation of Group III: Contributing Factors of Imatinib and Nilotinib Utilization For Chronic Myeloid Leukemia in JKN Program	Imatinib Team
13.30 - 14.00	Presentation of Group IV : Systematic Review of Insulin Clinical Effectiveness for Diabetes Type 2 Treatment	Insulin Team
14.30 - 15.00	Discussion on Study Progress	HTA Committee,HITAP/Mahidol & Teams
15.00 - 15.15	**Coffee Break**	
15.15 - 16.00	Discussion	HTA Committee,HITAP/Mahidol & Teams
Wednesday, 22nd November 2017		
Time	Activity	Speaker
09.00-12.00	Discussion on Colected Data	HITAP/Mahidol , HTA Committee, Study team
12.00 - 13.00	**Lunch**	
13.00 - 15.30	Data Analysis	HITAP/Mahidol, HTA Committee, Study team
15.30 - 15.45	**Coffee Break**	
15.45 - 17.30	Discussion & plan for report writing	HITAP/Mahidol, HTA Committee, Study team
Thursday, 23rd November 2017		
Time	Activity	Speaker
09.00 - 10.30	Discussion on next step plan	HITAP/Mahidol, HITA Committee, Study team
10.30 - 11.00	Meeting Conclusion	HITAP/Mahidol, HTA Committee
11.15 - 11.30	Closing Remark	Head of PPJK
11.30 - ...	Lunch	

C. Risk register

Researchers and HITAP team discussed and listed out the risk associated with all the studies. This is to help researchers and HTAC to control the risks in the project. No significant differences could be found between the risk register described in the previous visits in April risk registers of today. The table below presents the updated risk assessment.

Table 1: Project a - The process of approving nilotinib reimbursement and pattern of treatment for chronic myeloid leukaemia treatment in Indonesia

Sl.	Risk	Importance of the risk	Likelihood of the risk	Severity of impact	Proposed solutions
1	The risk that HTAC will call an end to the study	Termination of the conduct of the study and that there will be no strong evidence to inform policy change regarding on over-prescription of nilotinib	**Moderate**	**High**	HITAP and the group will work to explain to the committee that HTA studies can be qualitative and how this study will provide important evidence for policymakers. Also, explain that it might uncover the need for further HTA studies in the area.
2	The inadequate full-time staff of the local technical team	Delay in the conduct of the study	High	High	There is three staff from PPJK and Litbangkes involved and it seems that none of them can work up to 20% of their FTEs. More staff needed or the current staff may allocate more time to this work
3	Researchers not familiar with this type of study	Delay in the conduct of the study, lack of confidence and difficulties in moving the study forward	High	High	Keep in close contact with the HITAP team and ensure that they ask HITAP when they are unsure how to proceed or need guidance or support.
4	Budget cuts for this study	Impact the quality of the study	High	Moderate	Different survey designs have been developed for different budget situations so that this should not impact the timing of the surveys. HITAP has helped draw up the best research design possible in a limited funds scenario.
5	Low survey response rate due to a current	Impact the quality of the study	Low/Moderate	Moderate	The team will draw up a confidentiality statement making clear that respondents and hospitals will be totally

Sl.	Risk	Importance of the risk	Likelihood of the risk	Severity of impact	Proposed solutions
	clamp down on malpractice				anonymous and explain the purpose of the research. Additional mechanisms may need to be initiated in order to ensure a high response rate. HITAP will follow up with this proactively.

Table 2 - Project b: Economic evaluation of human insulin and insulin analogues for type 2 diabetes a Systematic Literature review

Sl.	Risk	Importance of the risk	Likelihood of the risk	Severity of impact	Proposed solutions	Current Status (Nov 2017)
1	BPJS or HTA committee require more evidence e.g. economic evaluation or budget impact	The research team might not be able to respond to the demand due to time constraint and limited capacity	High	Moderate	- Research team submit the proposal to BPJS and HTA committee for review - The research team may arrange additional stakeholders consultation meeting to present the proposal - The decision about the study scope should be made very soon and before the study conducted	-The team finalized the study topic to be "Insulin analogues vs human insulin" -Submitted the proposal for review to HTAC and the related stakeholders such as Association of Internal medicine and Association of Endocrinologists. Also, had a consultation meeting.
2	Commitment from researchers in the team	Few persons have a contribution to the study	High	Moderate	- The research team should have a clear agreement on contribution and task allocation	This is still a major risk and has contributed towards delay in the study.
3	Inadequate skills among researchers to carry out systematic review and meta-analysis	The study is delayed or not completed	Moderate	high	- Researcher(s) with experience in conducting a systematic review and meta-analysis is added to the research team or identified as a supervisor	The study is delayed owing to the inadequacy of technical skills amongst the staff.

4.	Research question does not reflect the real situation/problem e.g. there might be other factors (apart from efficacy or price) attributed to the use of insulin analogue	Research findings might not influence the policy change.	Moderate	Moderate	- The research team should review more in-depth of the background of the research problem. - Research team submit the proposal to BPJS and HTA committee for review - Research team arrange a stakeholders consultation meeting to present the proposal	After finalization of the topic. The team conducted a literature review and stakeholder consultation. The team will conduct a situational analysis of the insulin market in Indonesia.by three approach ➢ Historical data on the price of both types of insulin ➢ Compare for the prices in other countries. ➢ Investigate the price of insulin in private hospitals. Thus, the research findings are important as they give crucial information to policy makers.

Table 3 – Project c & d: Clinical Effectiveness and Economic Evaluation of Cetuximab Therapy for Patient with Metastatic Colorectal Cancer (mCRC) and Economic evaluation of bevacizumab as an addition to chemotherapy for metastatic colorectal cancer (mCRC) in Indonesia

Sl	Risk	Point of Risk Assessed	Importance of the risk	Likelihood of the risk	Severity of impact	Proposed solutions
1	The study may not be completed in the planned timeline (because of the data collection process).	-Hospitals take a long time to give the permission for collecting the data. - The medical records: Some hospitals keep/record the patient's data only for the previous three years, so the data before that period cannot be obtained. The states of the patients are not identified in the medical records, so the team needs to ask clinicians. Also, the cause of death is not recorded in the medical record. -Delay in data collection as the patient's interview cannot be done during hospital audit (JCI)	The HTA committee will not have any evidence for proposing any policy improvement regarding the mCRC treatment by the end of 2017. Potential conflict on Donor regulation that we have to finalize the study report by the end of December 2017.	High	High	It would be faster if the proposal of collecting the data is from PPJK with a recommendation letter from the Ministry of Health. Discuss with the clinician (Dr.Ronald) Extend the time for data collection

2	Cannot access full-text articles, so the team need to ask for help from outside	Have to exclude some eligible articles	We will have a potential bias since we do not get the all existing evidence because of the accessibility of some articles.	Moderate	Moderate	Take help from HITAP
3	Perform a network meta-analysis	Don't have prior experience on network meta-analysis	A potential bias on network meta-analysis result	low	Moderate	Get some consultation to HITAP team who has a good experience on performing network meta-analysis

d. Other relevant material

- Project a – The process of approving nilotinib reimbursement and pattern of treatment for chronic myeloid leukaemia treatment in Indonesia
  Presentation - https://1drv.ms/p/s!AgWJO9PqiPQogdEvCF0C73uP3dThlw
  Analysis of the BPJS claims data - https://1drv.ms/p/s!AgWJO9PqiPQogdEvCF0C73uP3dThlw
- Project b: Economic evaluation of human insulin and insulin analogues for type 2 diabetes a Systematic Literature review
  Presentation 1 - https://1drv.ms/p/s!AgWJO9PqiPQogdEyNXj0BI6Mtg6vAg
  Presentation 2 - https://1drv.ms/p/s!AgWJO9PqiPQogdExKFcvW9QjiN6fJw
- Project c: Clinical Effectiveness and Economic Evaluation of Cetuximab Therapy for Patient with Metastatic Colorectal Cancer (mCRC)
  Presentation 1 - https://1drv.ms/b/s!AgWJO9PqiPQogdEwF3W6zvs_wNUQVA
  Presentation 2 - https://1drv.ms/p/s!AgWJO9PqiPQogdE0onK10Fw7Qg-DkA
- Project d: Economic evaluation of bevacizumab as an addition to chemotherapy for metastatic colorectal cancer (mCRC) in Indonesia
  Presentation - https://1drv.ms/p/s!AgWJO9PqiPQogdEuu_wlDC_IVrtDQQ
- Minutes of the side meeting with the HTAC (Topic IV): https://1drv.ms/b/s!AgWJO9PqiPQogdE1So7q_FiuwoBRXQ