Adaptive Capacity Building in Utilizing Real-World Data/Evidence for Health Technology Assessment in Indonesia

Arie Rahadi, Ryan R Nugraha, Christian Suharlim

Medicines, Technologies, and Pharmaceutical Services (MTaPS) Program

HEALTH SYSTEMS STRENGTHENING ACCELERATOR

Context

Describe the context in which the activity takes place. What is the health problem that you are trying to solve? What health system challenges contribute to this problem? Which voices were engaged in solving this problem before your activity started? Who was missing from the discussion and what was the impact of that absence?

Indonesia is the largest provider of provider of public health insurance (*Jaminan Kesehatan Nasional* [JKN]) in the world, with over 90% of its population under coverage as of March 2023.[1] Health technology assessment (HTA) is a systematic policy-making process aimed at more equitable and efficient health resource allocation. However, the pace of HTA institutionalization in the country has yet to match the growth in demand for health care services under JKN coverage. An innovative HTA approach that adapts to a rapid need for rational alignment of emerging health technologies is required.

In 2020 the USAID Medicines, Technologies, and Pharmaceutical Services Program (USAID MTaPS) developed and implemented the HTA Roadmap for Low- and Middle-Income Countries,[2] which identified a robust strong demand for utilizing real-world data/evidence (RWD/E) in the HTA process. Responding to this need, in June 2022 USAID MTaPS co-hosted a workshop to integrate RWD/E and other advanced methods in HTA, and thereafter piloted RWD/E integration in a formal cost-effectiveness assessment in a capacity building exercise.

The exercise is conducted with the Indonesian HTA Agent comprising membership from the Ministry of Health (MoH) and Gadjah Mada University, and has the following focus areas:

- **RWD/E integration** in the cost-effectiveness assessment by calibration methods to align cost and outcome projections with the real-world patient data.
- **Decision analysis** using a modelling approach in special software TreeAge Pro.

Using RWD/E USAID MTaPS has strengthened the Indonesian HTA Agent's capacity to incorporate contextually relevant data for decision making. In particular, through this exercise, the country is pioneering RWE calibration methods applied to a cost-effectiveness assessment of cancer drug trastuzumab to improve patient outcomes in early breast cancer.

Activity Description

What systems-thinking approach did you take to address the health problem identified above? What government agencies or other stakeholders did you work with, why did you choose them, and how did you engage them? Describe in detail the process or mechanism used to integrate local, community, sub-national, national, or regional voices, priorities, and contributions into this approach. How did you build community, government/stakeholder ownership or buy-in? It may be useful to describe your theory of change.

USAID MTaPS works closely with the Indonesian HTA Agent, MoH, and expert panels consisting of cancer care providers to formulate policy questions, collaborate in RWD data collection from patients and registries, and conduct the capacity building exercise. The assessment will evaluate whether adding tastuzumab after standard chemotherapy is cost effective for early breast cancer against standard chemotherapy alone in the current practice.

Departing from these policy questions a capacity building program was developed in weekly session encounters of two hours each, of which a majority was conducted via online since September 2022. The exercise was designed to encourage dialogue in understanding economic evaluation objectives and methodologies in an environment that rewards learning. Dearly termed *Reboan*, or 'Wednesday Huddle' (**Box 1**), on the fact that sessions were conducted every Wednesday, core competencies were identified and spread over a flexible curriculum (**Figure 1**) in which topic reiterations, reinforcement, and exploration are encouraged. During each *Reboan* we apportioned time towards the end to discuss the objective of the next encounter. Additionally, we set up a chat group as a medium of learning exchange beyond the allotted session encounters.

Box 1. *Reboan* core values

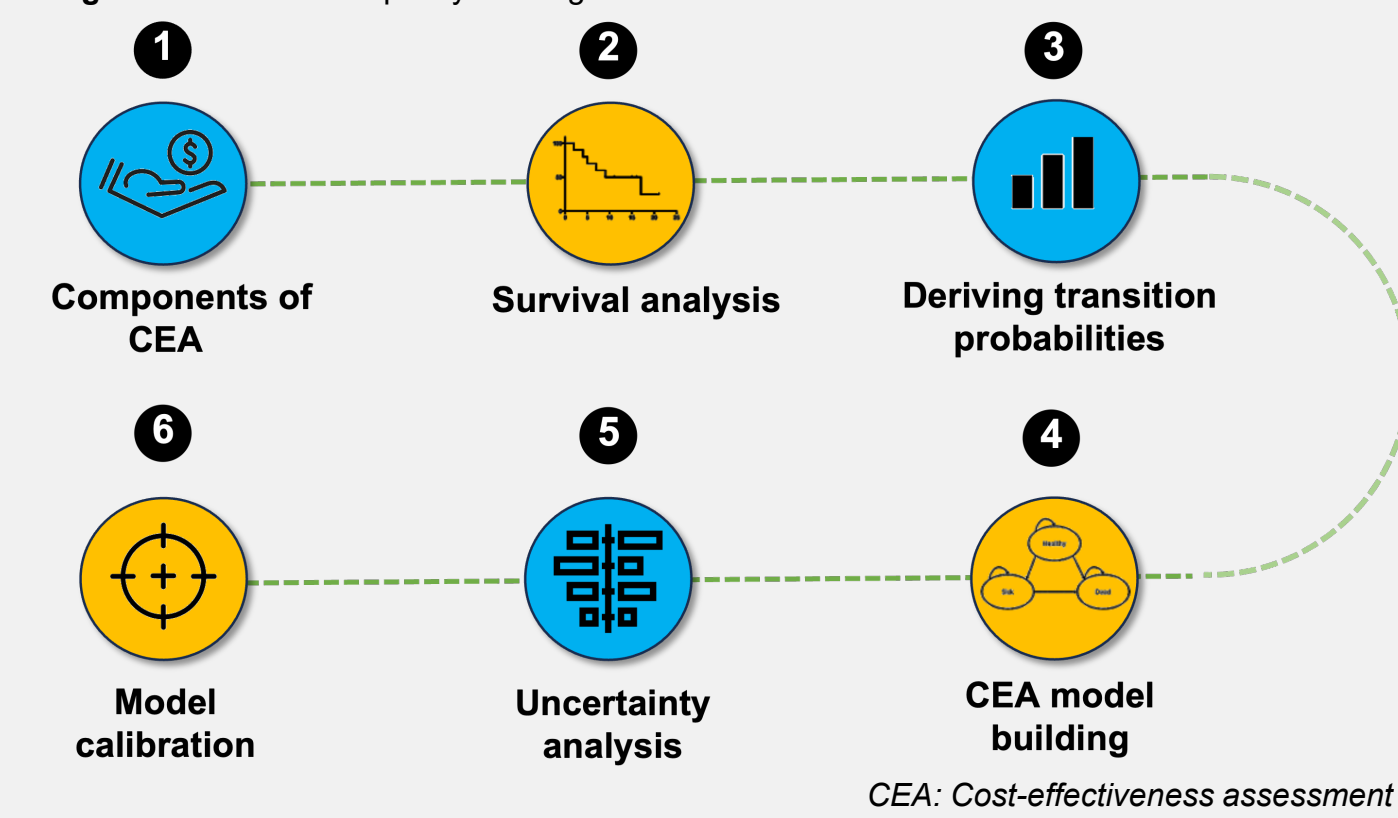|	*Reboan* in context
	Reboan (Wednesday Huddle) aims to build capacity in HTA with a strong emphasis on dialogue and was founded on the following values:
Needs-based learning	At the outset we collaboratively identified core competencies to implement model calibration in HTA. The unique approach we took was that members of the team was free to recommend relevant literature or exploration into sub-competencies. Material for a subsequent encounter, given its relevance to the core competencies, is decided collectively at the end of each encounter.
Inclusivity	We motivated learning by giving an option for self-paced learning and harmonizing the understanding in tutorial encounters. This approach gives an equal space to members of the Indonesian HTA Agent to build their competencies and be confident to have a greater role in the cost-effective assessment.
Learning by doing	Our approach also utilizes practice sets in which team members trained on analysis by using dummy data and pre-programmed statistical procedures. Incoming RWD was then used as they became acquainted with the analysis.
Cultivating leadership	As they gained more competencies, the Indonesian HTA Agent took more prominent roles in facilitating session encounters and continued to build on these in mentoring to lead production of activity outputs in reports and other scientific publications.

Figure 1. *Reboan* cacapacity building curriculum

1. Components of CEA
2. Survival analysis
3. Deriving transition probabilities
4. CEA model building
5. Uncertainty analysis
6. Model calibration

CEA: Cost-effectiveness assessment

This learning methodology helps us customize learning content that dynamically caters to the current needs of the Indonesian HTA Agent. Several highlights of this dynamic process are as follows:

- In familiarizing with modelling software TreeAge Pro, a hands-on manual with step-by-step instructions was created to allow self-paced learning to help establish a principal understanding and transition to tutorial encounters.
- In analysis of RWD on patient survival, we utilized dummy data and programmed all statistical procedures for replication with incoming RWD from cancer registries, which incrementally built confidence of the Indonesian HTA Agent to lead the analysis.
- In synthesis of treatment effects from clinical trials, the Indonesian HTA Agent voiced to propose an examination of possible differential health benefits by chemotherapy regimens in step with current evidence.[3] This proposal provided justification to modify the objective of the cost-effectiveness assessment.
- Prior to the calibration process the Indonesian HTA Agent assembled four sets of model parameters, discussed the merit and drawbacks of each, and finalized on one that the team felt best reflected the current practice and epidemioiogical setting of Indonesia.

The activity was documented in manuals, analysis documentation, and video-recorded encounters to preserve learning and facilitate further knowledge transfer.
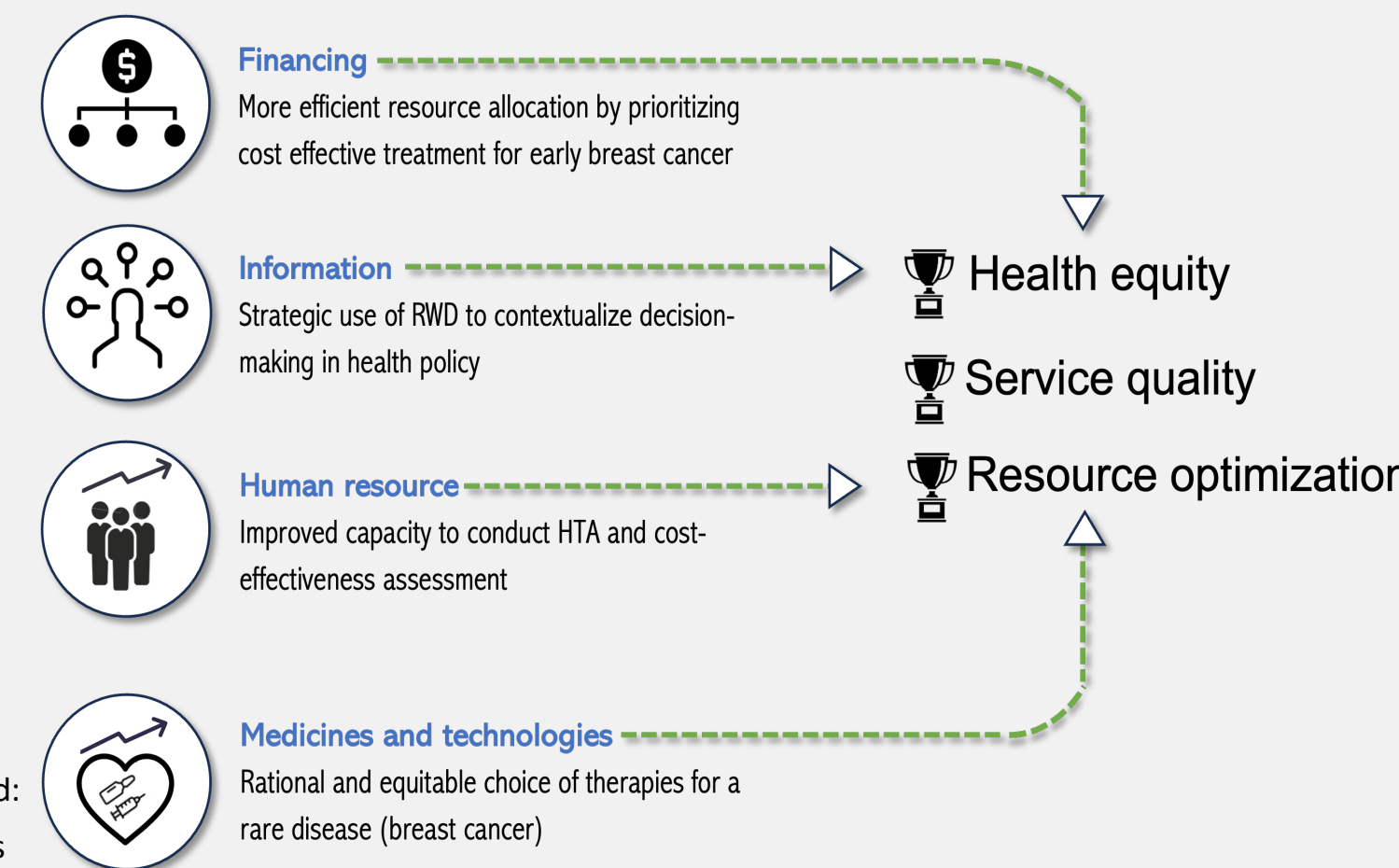
Activity Impact

How did this activity strengthen the health system? Which components of the health system did you act on (for example, did you support improvements in financing, cross-sectoral coordination, governance, local ownership, information, human resources, behavior of health system actors, service delivery, or medical products, vaccines, or technologies)? How does this activity contribute to health equity, quality or resource optimization? Be sure to explain the causal pathway by which your engagement of new voices contributed to this impact.

The capacity building of USAID MTaPS with trastuzumab has the following targets and impacts on the following health system building blocks (see also, **Figure 2**):

- **Financing:** Cancer ranks the second in health expenditure among the cluster of catastrophic illnesses.[4] Adjuvant trastuzumab holds potential to imrove chemotherapy outcomes and save a portion this expenditure by reducing out-of-pocket expenditures.
- **Information:** Existing RWD can be used to better inform decision-making in health policy. The calibration methods applied in this serial capacity building exercise has made use of hospital-based cancer registries to provide RWD on patient survival against which we calibrated our cost and outcome projections to contextualize decision-making.
- **Human resource:** The exercise strengthens the capacity of the Indonesian HTA Agent in calibration methods and these can be applied to other health areas with a modest requirement for RWD.
- **Medicines and technologies:** A novel treatment for breast cancer that is widely accessible to those in need under JKN coverage means improved equity in health as consideration of its benefit in the national formulary is often overlooked due to its relatively rare cases compared to other diseases.

Figure 2. The target health system blocks and intermediate outcomes

- **Financing:** More efficient resource allocation by prioritizing cost effective treatment for early breast cancer
- **Information:** Strategic use of RWD to contextualize decision-making in health policy
- **Human resource:** Improved capacity to conduct HTA and cost-effectiveness assessment
- **Medicines and technologies:** Rational and equitable choice of therapies for a rare disease (breast cancer)

→ Health equity
→ Service quality
→ Resource optimization

In this current phase of activity, the following have been achieved:

- A finalized decision model to assess the cost effectiveness of adjuvant trastuzumab vs. chemotherapy alone.
- Completed analyses of RWD on patient survival for target calibration and of treatment effect estimates by chemotherapy regimens.
- Calibrated survival rates and other model parameters for use in the subsequent cost-effectiveness assessment.

Evidence

What evidence do you have that the integration of local, community, sub-national, national, and regional voices, priorities, and contributions in this approach was successful? What evidence do you have that this approach led to health or health system impacts? How can you best show what your activity accomplished? How do you know that you met your goals? Is the evidence able to be measured? Graphs or charts may be useful here to show this evidence.

On average 12 members, of whom 80% are female, of the Indonesian HTA Agents participated in *Reboan* encounters since September 2022. On occasions we invited clinical experts and professional organizations to seek inputs to the activity and comment on progress. The exercise focused on practical skills building to boost confidence in the capacity of the Indonesian HTA Agent to lead the engagement.

Leadership

Key achievements to date have been presented at the prestigious International Society for Pharmacoeconomics and Outcomes Research (ISPOR) 2023 conference and accepted for oral presentation this coming September at the HTAsiaLink 2023, a regional forum of 25 HTA agencies in Asia-Pacific, to be held in Malaysia (**Figure 3**). The presentation topics showcase the capacity of the Indonesia's HTA Agency in harnessing existing RWD/E and calibration methods for economic evaluation in oncology.

Figure 3. Indonesian delegate speaking at ISPOR 2023 in Boston

Analysis outputs

The exercise has completed the following in terms of analysis outputs:

- A finalized decision model with calibrated parameters for cost-effectiveness assessment (**Figure 4**)
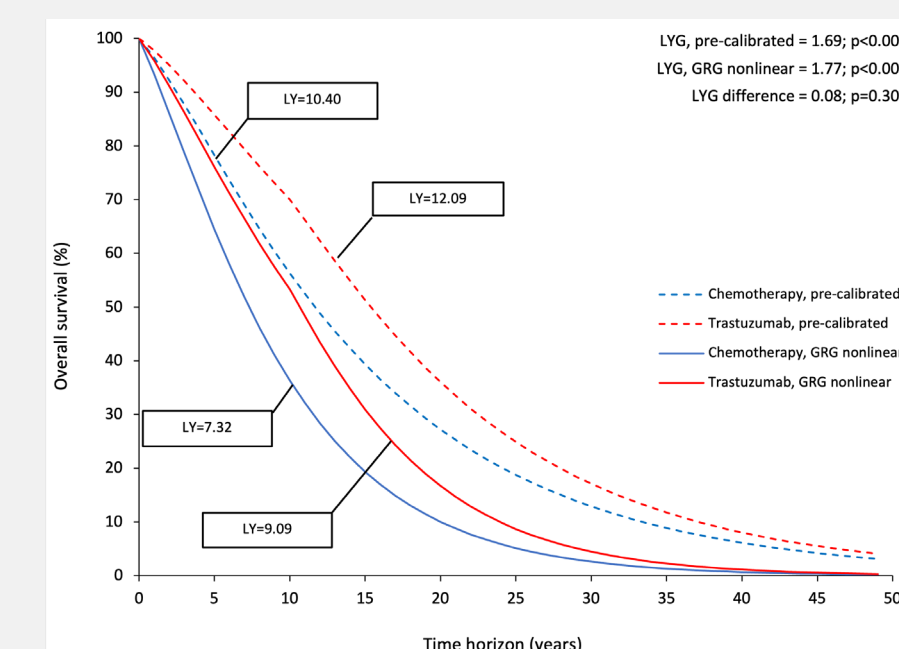- Projected survival rates and gains in life years resulting from adjuvant trastuzumab (**Figure 5**).

Figure 5. Projected survival

Projected survival in proportions and duration of life years (LY) is presented for standard care chemotherapy (blue lines) and adjuvant trastuzumab (red lines). Pre-calibrated (dotted lines) and calibrated projections (solid lines) are also shown in the figure. The generalized reduced gradient (GRG) nonlinear optimization method was used in calibration along with two other methods: Nelder-Mead, Bound Optimization BY Quadratic Approximation (not shown here).
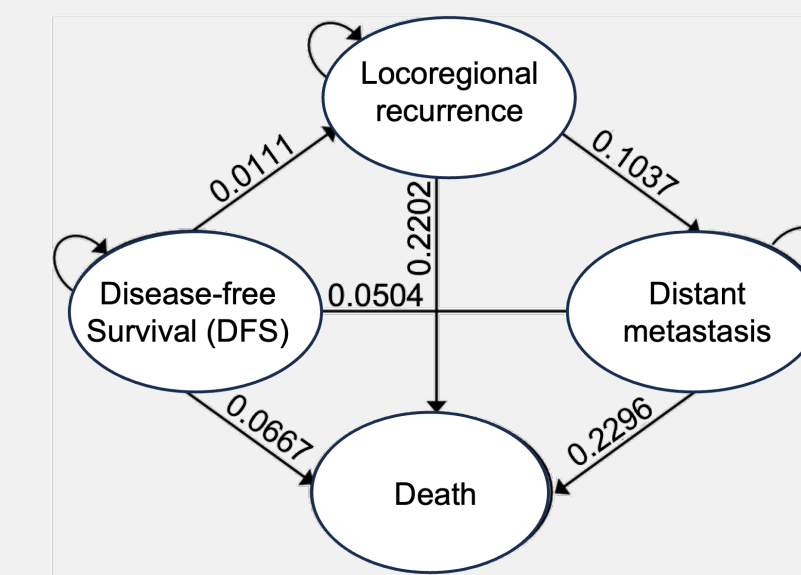
Figure 4. Decision model

The model comprises of four 'health states' around which a cohort of simulated patients cycle according to the specified probability parameters from calibration as denoted by the fractions.

Facilitators

What aspects of the health system, context, or external partner support helped make this successful? For example, were there existing working groups in place that enabled efficient coordination between stakeholders on this activity? Did you use a tool or knowledge resource from a global partner like WHO or UNICEF to help inform your activity?

Key facilitators of success include:

- **Political ownership:** Strong commitment of the Indonesian HTA Agency as adjuvant trastuzumab in early cancer is among the priority technologies to be formally assessed for coverage decision under JKN.
- **Stakeholder engagement:** High participation and retention from the Indonesian HTA Agency in weekly *Reboan* and enthusiasm for involvement among other stakeholders such as cancer hospitals in facilitating data collection and access to disease registries.
- **Effective coordination:** Continual engagement of USAID MTaPS and the USAID Mission in related activities with MoH which allows effective coordination among the stakeholders and keeps track of progress as well as inter-activity resource sharing.
- **Collaborative learning:** Session materials are designed to address fundamental bases of a methodology while leaving much room for interactions and problem solving around its practical aspects in model design, collection of RWD from patients and registries, analysis, and model calibration.
- **Flexible curriculum:** Topic reiterations or exploration around the six core competencies are allowed, which motivates learning and peer mentoring. This approach stands in contrast with common capacity building activities where the curriculum is linearly designed and often delivered as a short course.

Challenges

What were some problems or challenges that you faced during your activity implementation? Did you expect these challenges or were they unanticipated? How did you respond to these challenges?

Several notable challenges encountered during the activity:

- **Competing priorities:** Engagement outside scheduled encounters was difficult for some members who also had competing priorities in other HTA areas or beyond. As there was no dedicated staff in this activity, team members had multiple functional roles and balancing commitments became an issue. A usual approach to tackle this challenge was to reschedule the encounter to a different time slot or day acceptable to all members of the Indonesian HTA Agency.
- **Bureaucratic process:** Red tapes in organizing procurement of RWD from hospital registries caused a setback in timeline, which was later resolved strategically by inviting greater participation in the activity from the care providers.
- **Patient eligibility:** A limited number of patients available in specific stages of cancer progression for data collection on patient costs and quality of life slowed progress in the conduct of the cost-effectiveness assessment. Currently, we are expanding our data collection sites to other major hospitals to expedite completion by end of June 2023.
- **Sustainability:** The ability of *Reboan* to deconstruct traditional learning process while demonstrating results in the current activity may not be easy to replicate in future undertakings to build new competencies in HTA. First, *Reboan* seems prolonged in duration to prioritize flexibility and adaptability in the learning process. This distinction may appeal poorly to public institutions which place a great emphasis on completion in their performance measures. Second expertise in advanced HTA methods may be scarce, and the ability to decode this expertise in palatable learning portions means an extra investment likely unaffordable to many public employees.

Lessons Learned

What lessons have you learned while you implemented this activity? How will this impact future activities or approaches? What advice would you give to other implementers and health systems actors in other countries that might want to adapt your approach?

Targeting competencies in HTA advanced methods or similarly complex skills builds on realistic expectations and demands adapting to the current needs of the stakeholders who participate in the exercise. In our case, *Reboan* taps into the aspirations of the Indonesian HTA Agency in how they perceived a learning process to which we adapt and shift priorities as the need arises. *Reboan* also has other features (e.g., commitment, collaboration) that a review found are critical success conditions for capacity building programming in international development.[5] It is likely that *Reboan* will continue to contribute to the learning process up to completion of the cost-effectiveness assessment of adjuvant trastuzumab in September 2023.

Other lessons include:

- Investments in team dynamics is critical to promote meaningful participation and leadership in capacity building.
- A flexible curriculum not only enhances a methodological understanding but also gives opportunity to reflect on related policy questions to target. In our exercise, a concern over varying effects of adjuvant trastuzumab by chemotherapy regimens was voiced and the team accordingly proposed to expand the objective of the cost-effectiveness assessment.
- Synergies with other program activities helps to maintain the momentum of the capacity building exercise and integrate activities.

References

1. Firmansyah MJ. BPJS kesehatan claims nearly 91% Indonesians covered by JKN-KIS. Tempo.Co [Internet]. 2023 Mar 14 [cited 2023 June 9]. Available from: https://en.tempo.co/read/1702469/bpjs-kesehatan-claims-nearly-91-indonesians-covered-by-jkn-kis
2. Castro HE, Kumar R, Suharlim C, Guzman J, Gilmartin C, Amaris AM, et al. A Roadmap for Systematic Priority Setting and Health Technology Assessment (HTA): A Practical Guide for Policy Action in Low- and Middle-Income Countries. Arlington, VA: USAID/MSH; 2020.
3. Early Breast Cancer Trialists' Collaborative Group. Anthracycline-containing and taxane-containing chemotherapy for early-stage operable breast cancer: a patient-level meta-analysis of 100 000 women from 86 randomised trials. Lancet. 2023;401(10384):P1277-92.
4. BPJS Kesehatan. Info BPJS Kesehatan – Edisi 104. Jakarta: BPJS Kesehatan; 2021.
5. Ika LA, Donnelly J. Success conditions for international development capacity building projects. Int J Proj Manag. 2017;25(1):44-63.

USAID | RESULTS FOR DEVELOPMENT | HEALTH STRATEGY AND DELIVERY FOUNDATION | ICF | BILL & MELINDA GATES foundation