Improving Access to Medicines under Universal Health Coverage and Making Progress toward a Regional Network in the Asia Pacific Region

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Chapter 1. Introduction

1. Background and rationale

- Universal Health Coverage (UHC) is to ensure all individuals and communities to receive needed health services of sufficient quality, without excess financial burden.
  - The progress in achieving UHC is largely determined by each country's health insurance scheme and population coverage level (OECD 2016, OECD Korea Policy Centre and Seoul National Univ. Graduate School of Public Health 2015).
  - Variations exist in the current status of UHC among countries in the Asia Pacific region.
    - The major health insurance schemes for the Asia Pacific countries are National Health Service or Social Health Insurance. The population coverage levels vary widely, ranging from 10% to 100% (OECD Korea Policy Centre and Seoul National Univ. Graduate School of Public Health 2015).
- Improving access to medicines is a core component for achieving UHC.
  - World Health Organization (WHO) proposed the access to essential medicines as one of the six building blocks for health systems (WHO, 2010).
  - Previous efforts for improving access to medicines have focused on fragmented and hierarchical approach. However, such efforts have been criticized for their limited, short-term impact. As a result, it has been argued that the solution should be discussed from the health systems perspective (Bigdeli et al. 2013).
  - As the share of pharmaceutical spending in total national health expenditure has been increasing, the effort for improving access to medicines is essential in achieving UHC (Yadav et al. 2012).

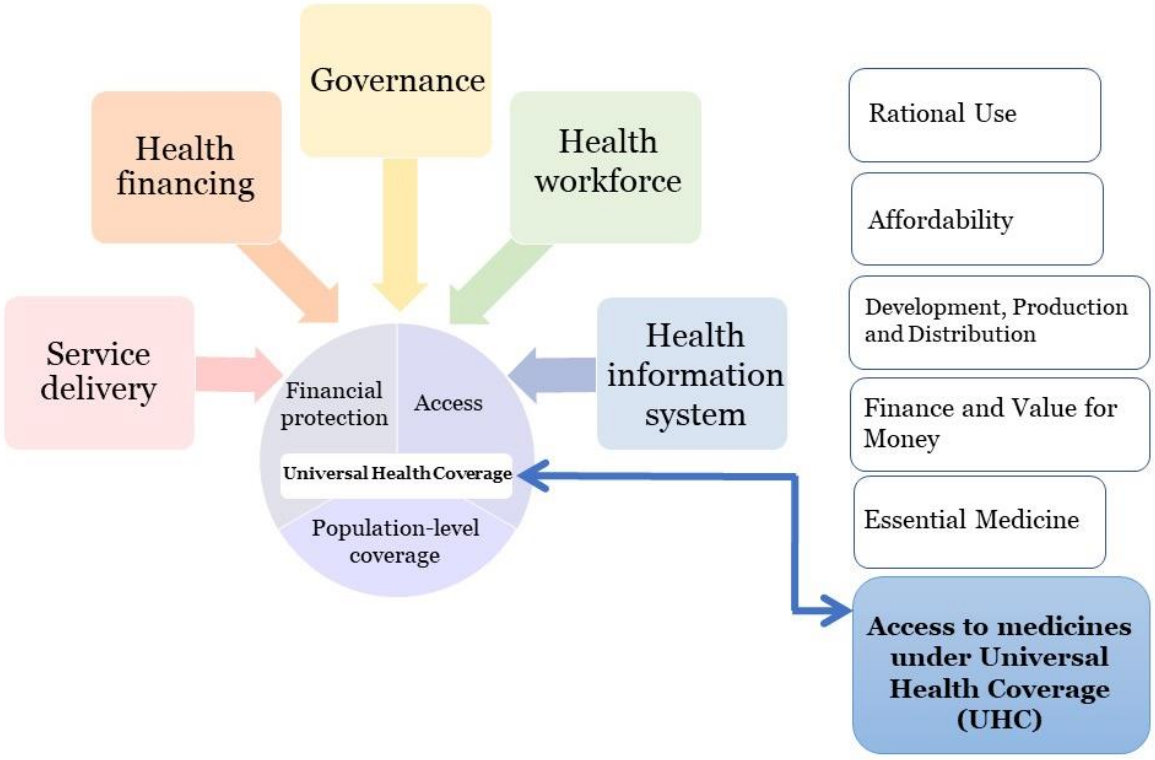

Figure 1. Access to medicines under UHC

- The criteria for evaluating right to health -availability, accessibility, acceptability, quality- are useful for understanding the concept of access to medicines, which has several implications (WHO, 2002C).
  - Availability means the goods and services that determine health should be provided in sufficient quantity.
  - Accessibility indicates non-discrimination, physical accessibility, affordability and information accessibility.
    - Non-discrimination is a general principle of access and intends to ensure that goods and services are available for those in need without any discrimination or barriers. Physical, economic and information access should be ensured to meet this requirement.
    - Physical access indicates that goods and services should be available in a timely manner.
    - Economic access refers to the affordability for goods and services.
    - Information access implies that information about the safety, efficacy and quality

of goods and services should be provided.

- Acceptability means that goods and services should be provided considering biomedical ethics, culture, gender and the different needs at each stage of life cycle.
- Quality indicates that goods and services are scientifically and medically appropriate and outstanding in quality.

- Given wide variations in the current status of UHC among Asia Pacific countries, the levels of access to medicines also vary. Therefore, the prioritization of interim- and long-term agenda for improving access to medicines should take into account the differences among countries.
  - For example, Seiter (2010) suggested core pharmaceutical policy objectives by countries' different income levels.
    - High income countries should focus on the "universal access to all important treatments and support for innovation through research and development (R&D) of new drugs and treatments."
    - Middle income countries should aim for "access to a broader range of medicines, pooled financing mechanisms and industrial development in the pharmaceutical sector."
    - Low income countries should ensure "access to quality essential medicines."
- A shared goal of better access to medicines in the Asia Pacific region should be achieved by strengthening the capacity of a regional network.
  - Pharmaceutical Pricing and Reimbursement Information (PPRI) is an example of a regional network established for discussing pharmaceutical pricing and reimbursement policy and sharing information. PPRI collaborates with more than 90 institutions and actively engage in diverse networking activities such as an annual network conference.
  - PPRI published the research findings funded by the European Commission (2005-2007) and the membership of the network consists of European countries and the

Member States from international organizations such as WHO or OECD (WHOCC, 2016).

- To address the need for a regional network for improving access to medicines in the Asia Pacific region, OECD Korea Policy Centre, WHO Western Pacific Regional Office (WPRO), WHO Collaborating Center for Health System and Financing (Seoul National University Graduate School of Public Health) have hosted the Annual Meeting on Access to Medicines under Universal Health Coverage in the Asia Pacific Region since 2014.
  - At the 4th meeting (2017), measures to improve access to medicines under UHC will be discussed in depth with an aim to promote sustainable and participatory network activities.
  - To that end, it is necessary to thoroughly examine the current status and develop interim- and long-term agenda based on evidence.

2. Purpose

- The purpose of this research is to develop interim- and long-term agenda for improving access to medicines under UHC in the Asia Pacific region considering different circumstances of the countries.
  - To classify the countries based on current status of UHC and national medicine policy.
  - To suggest agenda and outcome indicators based on the country classification.
  - To recommend measures for cooperation and encourage them to be discussed at the Annual Meeting on Access to Medicines under Universal Health Coverage in the Asia Pacific Region.
- Consequently, the interim and long-term agenda can facilitate capacity building for the Asia Pacific regional network.
  - To strengthen cooperation with international organizations including WHO and OECD by discussing interim and long-term agenda and outcome indicators for improving access to medicines under UHC.

3. Overview

- Specific aims and objectives of the research are as follows
  - Classification of Asia Pacific countries
  - Development of level- and staged-based evaluation domains and agenda
  - Suggestion for prioritization and timeline for the agenda (interim-and long-term plan)
  - Development of outcome indicators for evaluation and monitoring

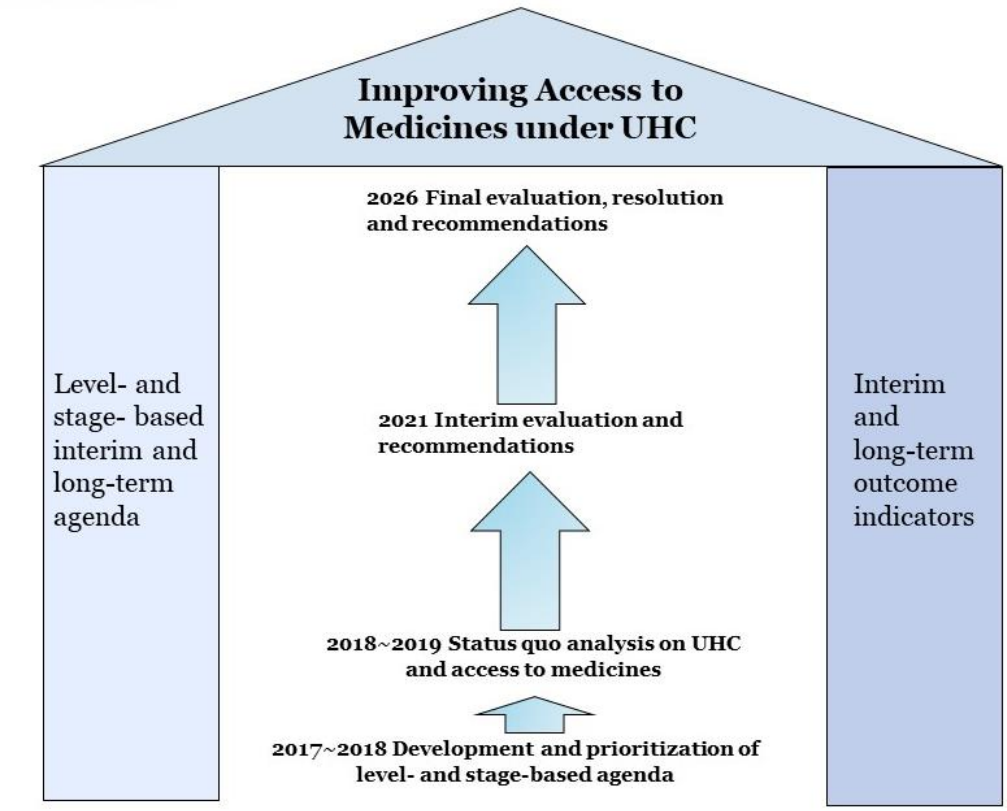

Figure 2. Research overview

- Classification of Asia Pacific countries
  - To examine current status of UHC and access to medicines for the Asia Pacific countries and classify them based on the differences.
  - To compare and investigate each country's capacity for access to medicines based on the essential medicines list developed by WHO.

- Development of level- and staged-based evaluation domains and agenda
    - To understand multi-dimensions of access to medicines and suggest agenda that takes into account the different levels and stages of health system and the medicines delivery process.
    - To develop measures to strengthen the regional network for access to medicines and to promote international cooperation by leveraging the agenda developed from the research.
- Suggestion for prioritization and timeline for the agenda (interim-and long-term plan)
    - 2017 – 2018: Development and prioritization of level- and stage-based agenda
    - 2018 – 2019: Status quo analysis on UHC and access to medicines
    - 2021: Interim evaluation and recommendations
    - 2026: Final evaluation, resolution and recommendations
- Development of outcome indicators for evaluation and monitoring
    - To develop interim- and long-term outcome indicators for evaluation and monitoring of UHC and access to medicines
    - To measure achievement in access to medicines under UHC in the Asia Pacific region and provide feedback.

4. Methods

- Classification of Asia Pacific countries by literature review and web-based data
    - Literature review on the access to medicines under UHC (review articles, case studies, reports from international organizations, etc.)
- Development of agenda and outcome indicators based on the literature review and web-based data
    - To develop level- and stage-based agenda list for improving access to medicines by literature review (review articles, case studies, reports from international

organizations, etc.).

- To generate evidence for policy discussion on the access to medicines under UHC in Asia Pacific region and prioritize the agenda for future directions

- Internal evaluation and selection of agenda and outcome indicators
  - Prioritization of the agenda
    - To classify the countries by high income, upper-middle income, and lower-middle income groups if necessary.
  - Evaluation of importance and feasibility of outcome indicators
    - To suggest outcome indicators for each income group by the classification of Asia Pacific countries.
- Final selection of agenda and outcome indicators
  - Final selection of agenda and outcome indicators by expert consultation
  - The expert panel consists of:
    - Academia: health economics expert, pharmaceutical policy expert, pharmaceutical health services research expert

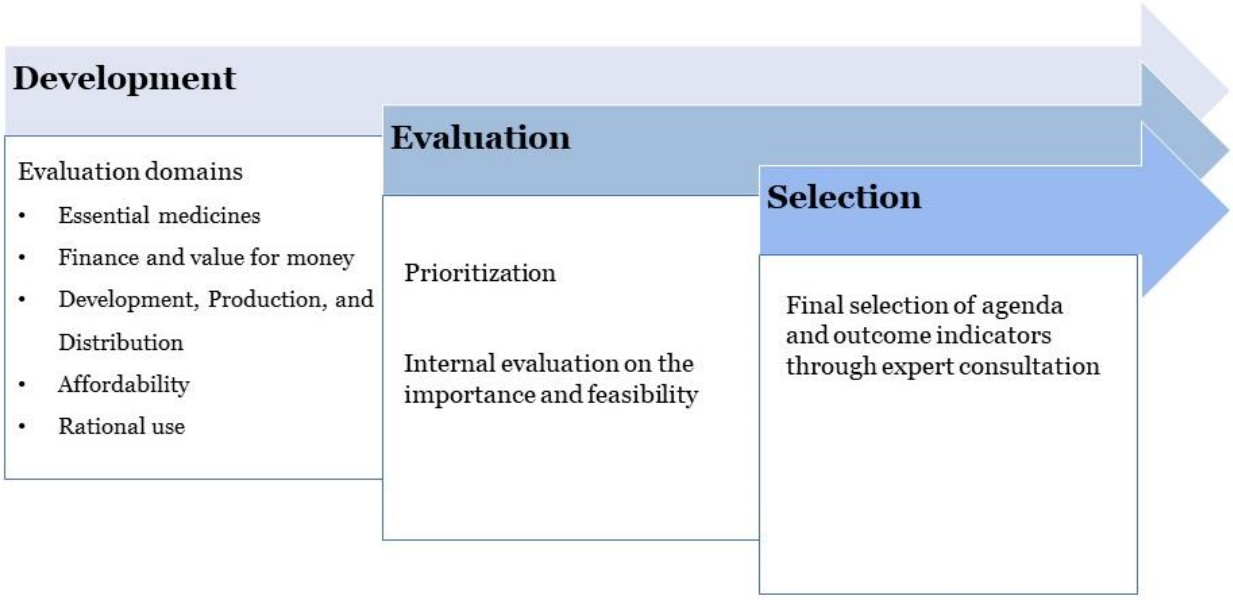

Figure 3. Development process of evaluation domains and outcome indicators

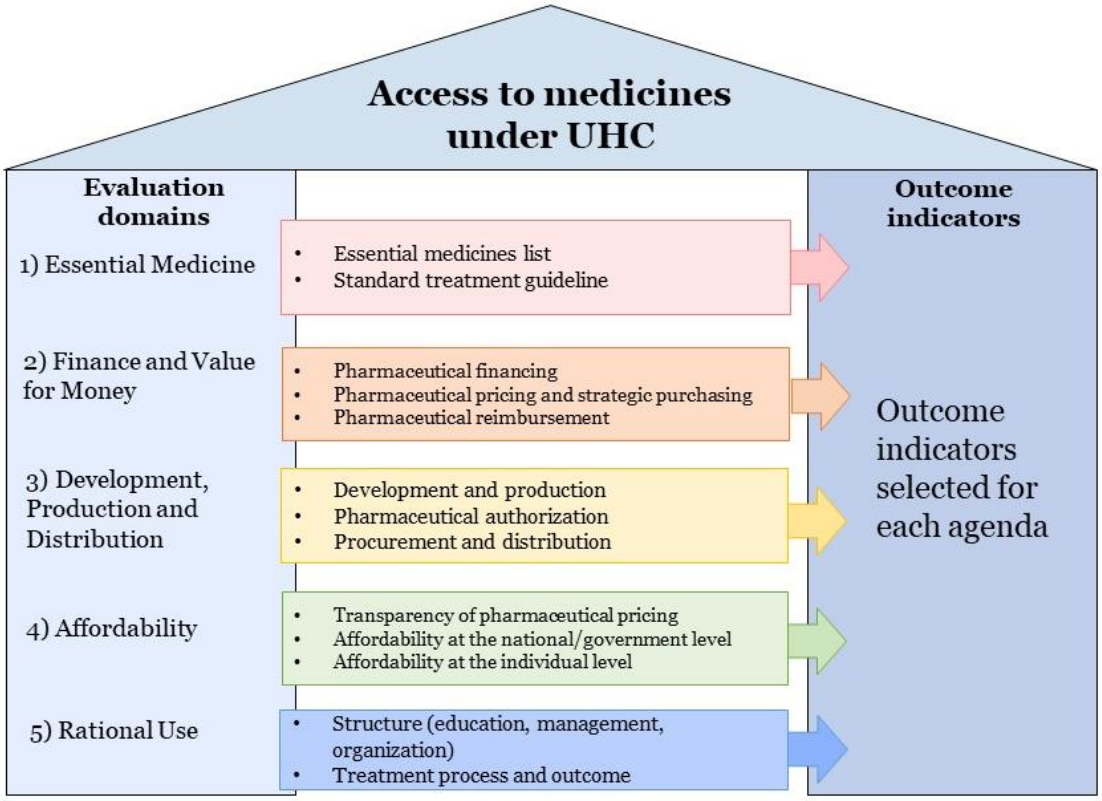

Figure 4. Overview of evaluation domains and outcome indicators

Chapter 2. Classification of Asia Pacific countries

- Classification of 37 WHO WPRO Member States
  - The first grouping was by income level –high income countries, upper-middle income countries, lower-middle income countries– according to the World Bank country classification (World Bank, 2017).
  - The second grouping was dichotomization (A, B) based on the size of population and territory.
- Selection of 14 countries for the focus of this research
  - Excluded 23 countries from the B group that consists of mostly Pacific Island countries and countries with relatively small population and/or territory.
  - 14 countries from the A group were selected: 5 high income countries, 3 upper-middle income countries, 6 lower-middle income countries

	Classification based on the size of population and territory			
Income classification (World Bank)	**A**		**B**	
High income	• Australia • Japan • New Zealand • Republic of Korea • Singapore	**5 countries**	• Brunei Darussalam • French Polynesia • Guam • Nauru • New Caledonia • Northern Mariana Islands	**6 countries**
Upper-middle income	• China • Fiji • Malaysia	**3 countries**	• American Samoa • Hong Kong SAR • Macao SAR • Marshall Islands • Palau • Tuvalu	**6 countries**
Lower-middle income	• Cambodia • Laos • Mongolia • Papua New Guinea • Philippines • Viet Nam	**6 countries**	• Kiribati • Micronesia • Samoa • Solomon Islands • Tonga • Vanuatu	**6 countries**
No data	**14 selected countries**		• Cook Islands • Niue • Pitcairn Islands • Tokelau • Wallis and Futuna	**5 countries**

Figure 5. Classification of Asia Pacific Countries (WPRO 37 Countries)

- Data collection on the characteristics of the 14 selected countries
  - Collected data on the characteristics related to each country's national medicine policy.
  - Specific items collected were as follows: total population, income classification, GNI per capita, OECD membership, legal mandate on the right to health, health insurance, essential medicines list, health technology assessment (HTA) (Table 1).
- The findings are summarized below:
  - Among 14 countries, 4 countries are OECD Member States (Australia, Japan, New Zealand, Republic of Korea).
  - Mongolia, Philippines and Viet Nam has legal mandate on the right to health.
  - Most countries have National Health Service or Social Health Insurance and some countries have mixed or voluntary health insurance. The population coverage rates differ by income level.
    - All high income countries except Singapore has 100% population coverage rate.
    - The population coverage rate for the upper-middle income group is also high, except for Fiji.
    - For lower-middle income countries, wide variations exist in population coverage rates. Mongolia, Philippines, Viet Nam has over 70% population coverage rate while Laos has less than 30%.
  - Most countries have an essential medicines list but some high income countries does not have one (Japan, New Zealand, Republic of Korea).
  - HTA has been conducted mostly in high income countries but some lower-middle income countries (Philippines and Viet Nam) also have HTA agencies.

Table 1. Characteristics of Asia Pacific Countries (WPRO 14 Countries)

No	Country[a]	Population (World Bank 2015)[b]	Income Classification (World Bank 2017)[c]	GNI per capita (2015 current US $)[d]	OECD[e]	Legal mandate[f]	Health insurance (coverage, year)[g]	EML[h]	HTA[i]	HTA agency[j]
1	Australia	23,781,169	High income	60,050	√		National Health Service (100%, 2015)	√	√	Healthpact
2	Japan	126,958,472		38,840	√		Social Health Insurance (100%, 2013)		√	trial basis
3	New Zealand	4,595,700		40,020	√		National Health Service (100%, 2015)		√	Healthpact
4	Republic of Korea	50,617,045		27,450	√		Social Health Insurance (100%, 2014)		√	NECA
5	Singapore	5,535,002		52,090		No data	Mixed (93%, 2012)	√	√	MOH
6	China	1,371,220,000	Upper-middle income	7,900			Social Health Insurance (95%, 2011)	√	√	CNHDRC
7	Fiji	892,145		4,830			Voluntary (No data, 2011)	√		
8	Malaysia	30,331,007		10,570			National Health Service (100%, 2012)	√	√	MaHTAS, PSD
9	Cambodia	15,577,899	Lower-middle income	1,070			Voluntary (24%, 2012)	√		
10	Laos	6,802,023		1,740			Voluntary (15%, 2012)	√		
11	Mongolia	2,959,134		3,870		√	Social Health Insurance (94.6%, 2011)	√		
12	Papua New Guinea	No data		2,240*		No data	Voluntary (No data, 2010)	√		
13	Philippines	7,619,321		3,550		√	Social Health Insurance (87%, 2014)	√	√	NCPAM
14	View Nam	91,703,800		1,990		√	Social Health Insurance (70%, 2014)	√	√	HSPI

a- Selected countries from WPRO Member States
b- ***Source:*** World Bank (2017), Based on World Bank's Atlas method
c,d - ***Source:*** World Bank Atlas method (2017)
Lower-middle income: GNI per capita (2015 current US$) $1,026 ~ $4,035;
Upper-middle income: GNI per capita (2015 current US$) $4,036 ~ $12,475;
High income: GNI per capita (2015 current US$) above $12,476
e- ***Source:*** OECD (2017)
f- ***Source:*** Backman et al. (2008), ***Legal mandate definition:*** Does the state's constitution, bill of rights, or other statue recognize the right to health?
g- ***Sources:*** Van Minh et al. (2014), WHO (2013, 2011), OECD (2016), Yu (2015), Gov't of PNG (2010)
h- ***Sources:*** Backman et al. (2008) and Wirtz et al., (2016), ***EML:*** Essential Medicines List
i, j- ***Source:*** HTAsiaLink, ***HTA:*** Health Technology Assessment
*2014 data

Chapter 3. Development of level- and stage-based agenda and outcome indicators

1. Theoretical framework

- Given multi-dimensions of access to medicines (Wirtz et al. 2016, WHO, 2002C) and the various aspects of national medicine policy (WHO, 2011) and pharmaceutical industry policy (Lee et al. 2014), five evaluation domains were identified.
  - Starting point for the discussion
    - Essential medicines list
  - Higher level: Financing and supply of medicines at the health system level
    - Finance and value for money
      - Considers scarcity of resources
      - Includes the stages of pharmaceutical pricing and reimbursement.
    - Development, production and distribution
      - Includes the process of quality medicines supply and authorization
  - Lower level: Utilization of health services within the health system
    - Affordability
      - Concerned with the actual price that the user pays for, which is related to pricing and reimbursement
    - Rational use
      - Considers physicians, pharmacists, patients and the health system as a whole

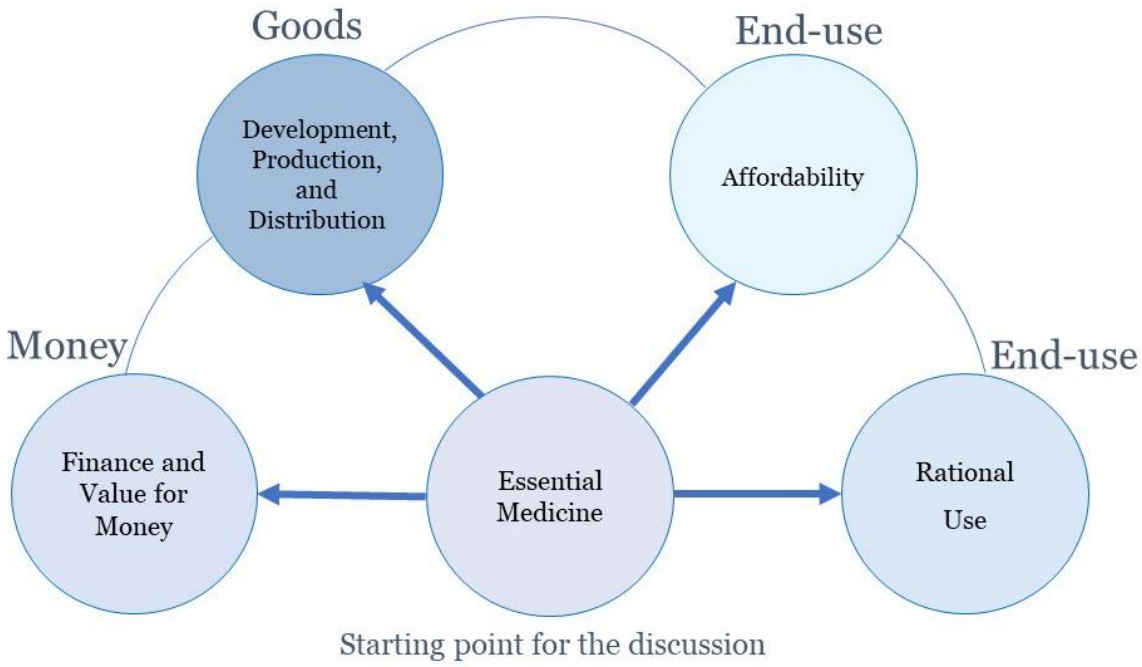

Figure 6. Theoretical framework for agenda and outcome indicators

2. Five evaluation domains for agenda and outcome indicators

2.1 Essential medicines

2.1.1 Introduction

- Discussions about essential medicines have been initiated since the WHO Model List of Essential Medicines in 1977 (Hogerzeil, 2004).
  - WHO Model List has been updated every 2 years and it is intended to be used in low- and middle-income countries.
  - In 2002, essential medicines became an important issue in the field of global health.
    - 156 countries have essential medicines lists and 100 countries have continuously updated the list.
  - The essential medicines list has been utilized by the UNICEF (United Nations Children's Fund) and other non-governmental organizations (NGOs) as well as at the national level.
- WHO defines essential medicines as follows (WHO, 2003; WHO, 2002A):
  - "Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford."
  - The essential medicines can be implemented by each country. Selection of essential medicines is at the discretion of the implementing country.

2.1.2 Implications for access to medicines

- Essential medicines is the starting point for the discussion about access to medicine and the selection of essential medicines involves the following two processes.
  - Scientific evaluation on the medicines and the authorization

- Essential medicines should be evaluated and approved by the national authority for their safety, efficacy and quality.

- The impact of essential medicines on public health
  - Essential medicines are selected from the authorized pharmaceuticals based on comparison among different pharmaceutical products. The comparison is generally based on safety, efficacy and value for money.

- In 2002, WHO reevaluated and updated the WHO Model List rigorously, and one of the important changes was that affordability was recognized as a consequence rather than a precondition for the essential medicines selection.
  - Subsequently, high cost medicines such as antiretroviral medicines for HIV/AIDS were included in the list.

2.1.3 Agenda list

- Essential medicines list
  - Selection process for essential medicines
  - Essential medicines list (EML)
  - Medicines listed on the EML
  - Actual availability of specific medicines
- Standard treatment guideline
  - The process of preparing standard treatment guidelines
  - Standard treatment guidelines

2.1.4 Development of outcome indicators for monitoring and evaluation

(1) Essential medicines list

- Introduction

- The following outcome indicators can be used for essential medicines list.
  - Selection process for essential medicines
  - Essential medicines list (EML)
- Considering various types of pharmaceutical products, specific area should be selected in the first place. For example, disease incidence and prevalence, burden of disease in the geographic locations covered by WPRO can be taken into account.
  - To evaluate whether certain medicines are listed on the EML.
  - To confirm whether certain medicines are actually available.
- The abovementioned approach focuses on the static outcome indicators at a specific time point. The following approach can also be considered for dynamic outcome indicators.
  - To monitor whether the EML is updated routinely.
  - To review whether newly listed medicines from the WHO Essential Medicine List are considered for the EML.

    - Specific outcome indicators
- Selection process for essential medicines
  - Organization for selecting essential medicines
  - Committee for selecting essential medicines
  - Transparency in selecting essential medicines
- Essential medicines list (EML)
  - Existence of essential medicines list
  - Existence of essential medicines list for children
    - Separate essential medicines list is necessary for children to take into account the

different priorities. WHO also stipulated separate essential medicines lists for children and adults.

- Amendment of the EML and the amendment cycle

- Medicines listed on the EML
  - This outcome indicator reviews if specific medicines are listed on the EML.
  - Specific essential medicines can be identified from the WHO essential medicines list.
- Actual availability of specific medicines
  - This outcome indicator evaluates if the patient can purchase a certain prescribed medicine at the pharmacy.
  - Cherny et al. (2016) proposed the following framework to evaluate the actual availability of a certain medicine.
    - Always available.
    - Usually available.
    - Available half the time.
    - Available occasionally.
    - Never available.
  - Additionally, the actual availability can consider the following aspects.
    - Public and private
    - Community
  - The available product type should be also considered.
    - Original
    - Generic

(2) Standard treatment guideline

- Introduction

- The following outcome indicators can be used for standard treatment guidelines.
  - The process of preparing standard treatment guidelines
  - Standard treatment guidelines
- The abovementioned approach focuses on the static outcome indicators at a specific time point. The following approach can also be considered for dynamic outcome indicators.
  - To monitor whether the standard treatment guideline is updated routinely.

- Specific outcome indicators

- The process of preparing standard treatment guidelines
  - Organization for preparing standard treatment guidelines
  - Committee for preparing standard treatment guidelines
- Standard treatment guidelines
  - Validity in preparing standard treatment guidelines
  - Existence of standard treatment guidelines (for essential medicines)
  - Amendments of guidelines (for essential medicines)

2.1.5 Recommendations

- The following should be considered.
  - A comprehensive database to manage Member States' essential medicines list is needed.
    - WHO organized a database for managing essential medicines lists for some low- and middle-income countries.
      - http://www.who.int/selection_medicines/country_lists/en/

- It is necessary to select specific areas or diseases for an evaluation.
  - Recent studies have discussed chronic diseases such as asthma, arthritis, diabetes, hypertension (Joshua et al. 2016) and cancer drugs (Cherny et al. 2016; Bazargani et al. 2015).

- WHO/HAI[1] (2008) recommended to select maximum of 50 medicines in measuring price, availability and affordability.
  - 14 global core list of medicines (global level)
  - 16 regional core list of medicines (regional level)
  - 20 medicines of supplementary list (national level)
- Global, regional core medicines were selected based on the following criteria.
  - Burden of disease and disease prevalence
    - Cardiovascular disease
    - Diabetes
    - Asthma
    - Respiratory infection
    - Mental illness
  - Evidence-based medicine
    - First-line therapy
  - Availability
  - Significance
- Global core list of medicines is as follows.

[1] Health Action International

Table 2. Global core list of medicines from WHO/HAI (2008)[2]

	Disease	Name[a]	Strength	Dosage form
1	Asthma	Salbutamol[b]	0.1 mg/dose	inhaler
2	Diabetes	Glibenclamide	5 mg	cap/tab
3	Cardiovascular disease	Atenolol	50 mg	cap/tab
4	Cardiovascular disease	Captopril	25 mg	cap/tab
5	Cardiovascular disease	Simvastatin	20 mg	cap/tab
6	Depression	Amitriptyline	25 mg	cap/tab
7	Infectious disease	Ciprofloxacin	500 mg	cap/tab
8	Infectious disease	Co-trimoxazole	8+40 mg/ml	suspension
9	Infectious disease	Amoxicillin	500 mg	cap/tab
10	Infectious disease	Ceftriaxone	1 g/vial	injection
11	CNS	Diazepam	5 mg	cap/tab
12	Pain/inflammation	Diclofenac	50 mg	cap/tab
13	Pain/inflammation	Paracetamol[c]	24 mg/ml	suspension
14	Ulcer	Omeprazole	20 mg	cap/tab

[a] Medicine names may be spelt differently in different countries. Consult the HAI web site[1] for alternative spellings of global and regional core medicines.
[b] Also called albuterol.
[c] Called acetaminophen in some countries.

- Regional core list of medicines was excluded from the 2016 updated list. As a result, 50 medicines consist of 14 global level and 36 national level list of medicines.
  - National level medicines should be selected considering each country's circumstances and should include the following.
    - If medicines on the global core list of medicines are not available in a country, different doses or dosage form.
    - If medicines on the global core list of medicines are not available in a country, a substitute should be included.

[2] As of May 2016, Atenolol 50mg tab/cap was replaced with Bisoprolol 5mg tab/cap. Glibenclamide 5mg tab/cap was replaced with Metformin 500mg tab/cap.

2.2 Finance and value for money

2.1.1 Introduction

- Healthcare financing consists of 3 major functions (McIntyre and Kutzin, 2012).
  - Firstly, revenue collection can be divided into public (national health insurance fund, other public funding) and private sources of financing (out-of-pocket payment, other private funding).
  - Secondly, pooling is to provide health coverage through taxation or premiums, especially for population-level health insurance coverage.
  - Thirdly, purchasing is an important function for making health services available for the population through healthcare financing.
- Likewise, pharmaceutical financing can be divided into public (national health insurance fund, other public funding) and private sources of financing (out-of-pocket payment, other private funding).
  - The public funding can be either National Health Service through taxation or Social Health Insurance through premium or in other cases, the both can be mixed.
  - In Asia, most countries adopted the mixture of taxation and Social Health Insurance, rather than pure taxation or pure Social Health Insurance (Kwon, 2011).
  - The private funding is mostly from private insurance or out-of-pocket payment. The higher the out-of-pocket payment is, the more likely an individual is to become vulnerable to catastrophic health expenditure. Also, it can lead to inequity in access to medicines.
- To achieve financial sustainability for medicines, not only the sufficient funds but also the balance between public and private sources of financing is important.
  - This is because the impact of different sources of financing on the equity and efficiency can vary (Kwon, 2011).
  - The amount and public-private mix of financial resources can be influenced by national income, the level of economic development, political will and efficiency in resource allocation (Kwon, 2011).

- To put it simply, pharmaceutical expenditure depends on the public and private sources of financing. According to Wirtz et al. (2016), 61% of pharmaceutical expenditure for high income countries were from public sources while 62% of pharmaceutical expenditure came from private sources for low- and middle-income countries (Wirtz et al. 2016).
  - Tackling high out-of-pocket payment is an important agenda for low- and middle-income countries (Wirtz et al. 2016; Nguyen et al. 2015).
  - In this context, the figure below illustrates the government share of pharmaceutical expenditure for 13 out of 14 selected countries for this study. The public share is generally higher for high income countries compared to upper-middle and lower-middle income countries.

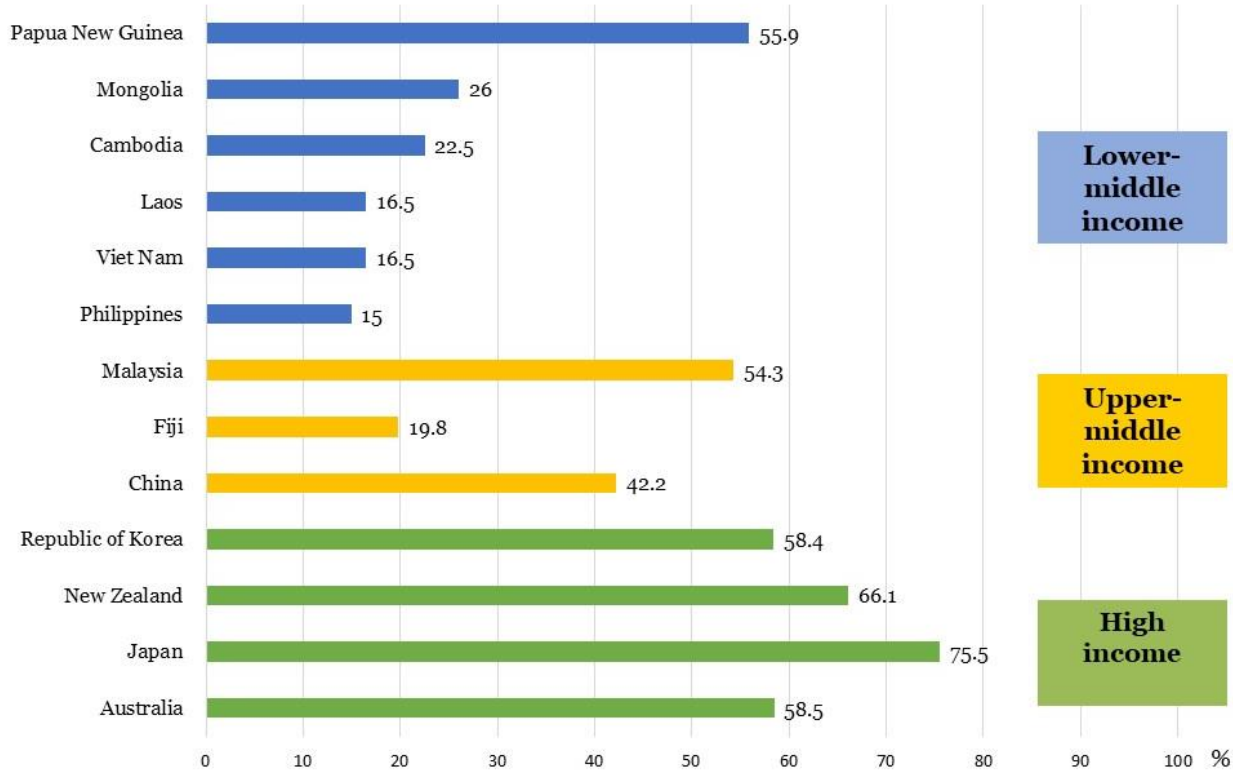

Figure 7. Government share of pharmaceutical expenditure for 13 Asia Pacific countries (2014)

Source: OECD/WHO(2016) OECD Health at a Glance: Asia/Pacific 2016

- Value for money asks if the benefits from the expenditure exceeds the costs, rather than reduction in spending (OECD Korea Policy Centre, 2011).

- High cost medicines sometimes offer high value that can justify the cost while low cost medicines can generate little benefits and value. Therefore, cost and value should be distinguished from each other (Owens et al. 2011).
- The management policy by the government or reimbursement authority is essential because the third party payer often acts as an agent and pays for the medicines, especially those covered by insurance.

- Competitive purchasing strategy should be established in addition to sufficient funding and management policy by reimbursement authority to maximize value for money.
  - Strategic purchasing plays a key role in linking secured funds to the efficient distribution of quality medicines (Mathauer, 2015).
  - Purchasing refers to the process of paying for health services including medicines and there are three types of purchasing (WHO the World Health Report, 2010).
    - Integration of purchasing and provision: government makes a direct payment to the providers from the government budget or health insurance funds.
    - Purchaser-provider split: institutionally separated reimbursement authority makes a payment on behalf of the purchaser.
    - Direct payment by individuals: individuals make a direct payment to the providers.

2.1.2 Implications for access to medicines

- According to Kanavos (1999), there is a principal-agent relationship in pharmaceutical financing due to the involvement of a number of third parties between consumers and producers.
  - Third-party payers: government, insurers, etc.
  - Wholesalers: interested in acquiring pharmaceuticals at the lowest price when distributing pharmaceutical products.
  - Prescribing physicians: make a decision on behalf of the patients.

- Dispensing pharmacists: usually follow physicians' instructions but their behavior can be influenced by payment methods or type of products

- Consequently, pharmaceutical policy should take into account this intrinsic mechanism of differing interests.

- Following criteria can be considered to use available resources efficiently and ensure sustainability of pharmaceutical financing (Management Sciences for Health, 2012C).

  - Access to medicines: how does the financing mechanism contribute to improving access to medicines?

  - Rational use of medicines: does the financing mechanism create incentives for overuse, underuse of misuse of medicines? (financing through insurance can encourage effective balance if it increases patients' demand for medicines by improving access and at the same time, promotes standard treatment guidelines for providers.)

  - Efficiency: does the financing mechanism maximize output and benefits?

  - Equity: who pays and who benefits from it?

  - Sustainability: will a reasonable level of funding be sustained? (dependence on donor funding can impede sustainability.)

  - Administrative and managerial requirement: does administrative and managerial policy exist to operate financing mechanism?

- TRIPS (Trade-related Aspects of Intellectual Property Rights) has a direct impact on financial accessibility for medicines and the debate on TRIPS is still ongoing.

  - World Trade Organization (WTO) and UN has led the discussion on other measures to facilitate access to medicines such as TRIPS Flexibilities, but different views exist on such measures (Diependaele et al. 2016; Wirtz et al. 2016; Nicol et al. 2013).

  - Leisinger et al. (2012) proposed corporate responsibilities for access to medicines in low- and middle income countries and suggested the following framework (Leisinger et al. 2012).

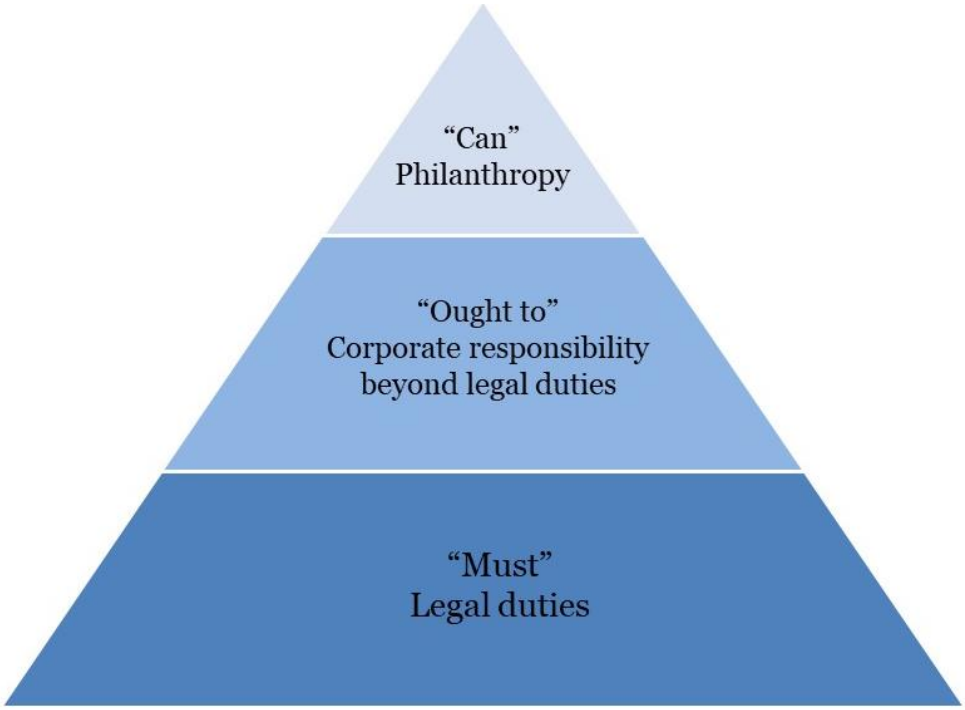

Figure 8. The hierarchy of corporate responsibility

Source: Leisinger et al. (2012)

- In case of low- and middle-income countries, introducing third party payers such as reimbursement authority can be a valuable strategy to improve access to medicines, and can result in increased consumption of medicines (World Bank, 2010).
  - However, substantial increase in consumption may lead to increase in cost. Therefore, reimbursement list should be systematically managed by reimbursement authority.
- In case of OECD countries, various policy measures have been introduced to maximize value for money (OECD Korea Policy Centre, 2011).
  - Price regulation
  - International benchmarking
  - Therapeutic referencing
  - Pharmacoeconomic assessment
  - Product-specific pricing agreements (volume-price agreements, agreements to limit budget impact, coverage with evidence development, risk-sharing agreements, etc.)
  - Efforts to develop generic markets

- From a systematic research on comparing value for money of medicines, Simoens (2012) revealed that the majority of medicines provided value for money in Europe.
- However, few studies have examined value for money in the context of low- and middle-income countries and the countries that perform HTA at the national level are concentrated mostly in high income countries.
- For an efficient resource allocation, strategic purchasing (price and quality maker) should be adopted as opposed to passive approach (price and quality taker) (Mathauer, 2015).
- For strategic purchasing, government or purchasing agency should play an active role.
    - Management of revenue and expenditure
    - Decision on which medicines to buy based on population needs, health priorities of a country and cost-effectiveness
    - Decision on provider selection and price negotiation
    - Decision on the methods and amount of payment
    - Monitoring and evaluation on pharmaceutical expenditure, provider performance, volume and quality

2.1.3 Agenda list

- Discussion on the strategies for sustainability of pharmaceutical financing
    - Sustainable financing for pharmaceuticals has significant implications on the reduction in medical expenditure, improvement in population health and productivity, and risk management such as pandemic. In this context, Burci et al. (2017) viewed public financing for pharmaceuticals as social and economic investment to improve access to medicines (Burci et al. 2017).
- Discussion on the strategies for development and management of reimbursement list
    - Development and management of reimbursement list based on each country's circumstances and essential medicines list is important for improving value for money.

- Discussion on the strategies for pharmaceutical pricing and purchasing applicable for each country
  - From the study on pharmaceutical pricing and purchasing policy for low- and middle-income countries, Nguyen et al. (2015) suggested that there is no one-size-fits-all strategy but each country should choose policy options according to the policy context and pharmaceutical system (Nguyen et al. 2015).
  - Management and control of pharmaceutical price can be discussed in terms of pricing and purchasing.
  - Examples of pharmaceutical pricing strategies include reference pricing, the use of pharmacoeconomic evaluation, cost-plus pricing, price premium, etc.
  - Examples of purchasing strategies include positive list, negative list, price volume agreement, pooled procurement system, etc.

2.1.4 Development of outcome indicators for monitoring and evaluation

- Introduction

- The following aspects can be considered for outcome indicators.
  - Pharmaceutical financing
  - Pharmaceutical pricing and strategic purchasing
  - Pharmaceutical reimbursement
- Data from the OECD Health at a Glance Asia Pacific, which is a biennial report, can be utilized for monitoring outcome indicators.
- WHO Country Profiles for Asia Pacific countries were published in 2012-2013 but these are mostly for Pacific Island countries and no updates have been published online. The profiles were published for the following countries:
  - Cook Islands, Fiji, Papua New Guinea, Kiribati, Palau, Solomon Islands, Tuvalu

- Specific outcome indicators

- Pharmaceutical financing

- Pooling: National health insurance scheme and population level coverage
- Revenue collection: sources of pharmaceutical financing

- Pharmaceutical pricing and strategic purchasing
  - Pharmaceutical price
  - Strategic purchasing
- Pharmaceutical reimbursement
  - Reimbursement authority
  - Reimbursement process
  - Reimbursement management

2.1.5 Recommendations

- Following approach can be recommended for strengthening capacity for pharmaceutical financing in low- and middle-income countries.
  - As for the pharmaceutical pricing and strategic purchasing, the agency relationships in pharmaceutical financing can be considered: supply side, proxy demand side, demand side.

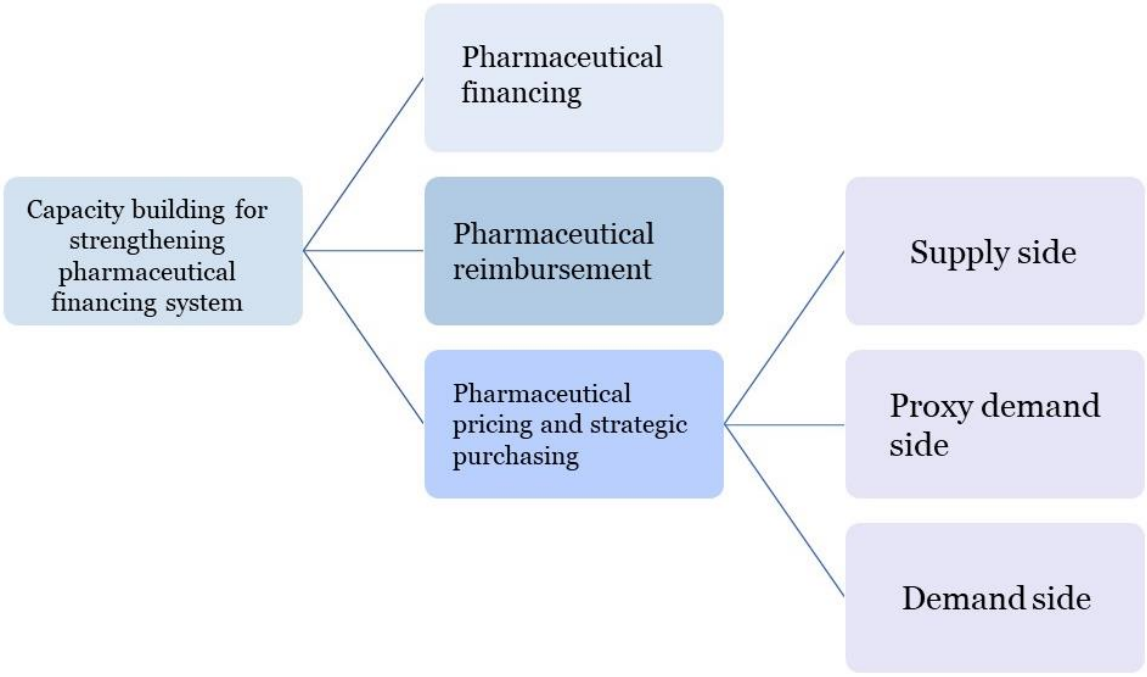

Figure 9. Capacity building for strengthening pharmaceutical financing system

- Supply side (pharmaceutical company, government, reimbursement authority, third party payer, etc.)
  - Free pricing
  - Price regulation by government
  - Pricing methods such as negotiation, estimation, international price comparison, etc.
  - Risk sharing
  - Reference pricing
  - Reimbursement policy (positive list, negative list)
  - Profit control for pharmaceutical company
  - Pharmacoeconomic evaluation
- Proxy demand side (physicians, pharmacists, etc.)
  - Ex post management of pharmaceutical price
  - Regulation on use and prescription

- Promotion of the use of generics
- Systematic disease management

- Demand side (patients)
  - Out-of-pocket payment
  - Use of over the counter (OTC) medicines
  - Setting expenditure limits
  - Demand side will be discussed in more detail in affordability domain.

- Strategies for maximizing value for money should be identified from diverse perspectives. National Medical Supplies Fund suggested the following directions:
  - Use of therapeutically equivalent generics
  - Pharmacoeconomic analysis
  - Evidence-based selection of essential medicines
  - Price control measures
  - Rational use of medicines
  - Management of adherence to treatment regimens
  - Prohibition of unethical promotion by pharmaceutical companies
  - Reduction in medication errors and adverse drug reactions
  - Promotion of responsible self-medication
  - Responsibility of clinical pharmacy services
  - Pooled procurement
  - Improvement in safety, efficacy and quality of medicines
  - Management of medical devices

- Among a wide range of policy options for strengthening pharmaceutical financing system, the following cyclic approach can be recommended.

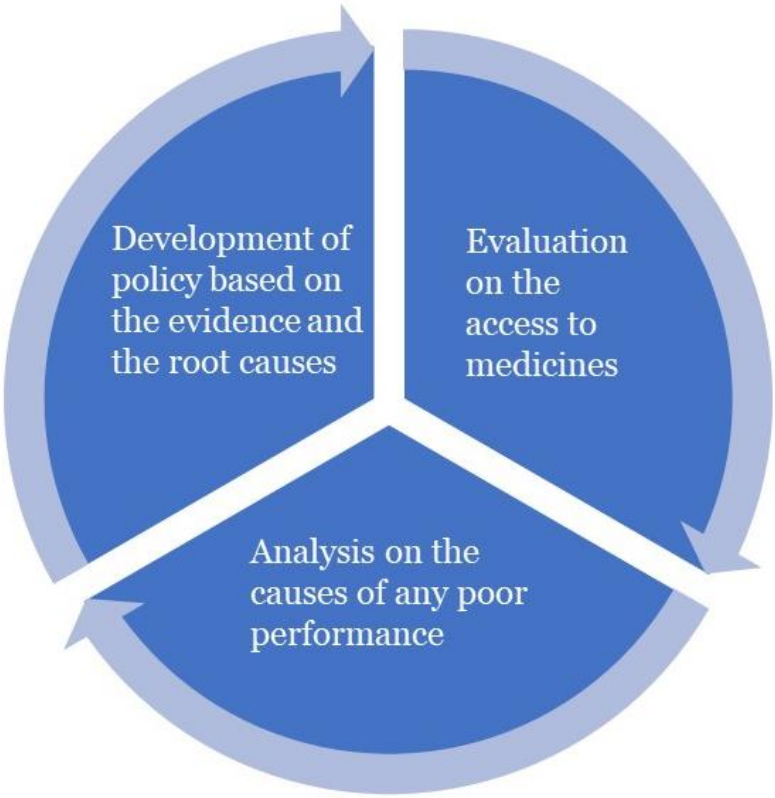

Figure 10. A cyclic approach to national policy for strengthening pharmaceutical financing

2.3 Development, production and distribution

2.1.1 Introduction

- Development, production and distribution of pharmaceutical products examines the access to medicines from the supply side, which focuses on providing quality-assured, low-cost pharmaceuticals (Management Sciences for Health, 2012A).
- Recently, the term medicine value chain has been used to encompass development, production, distribution and use of medicines (IMS Institute, 2014).
  - Development
    - R&D, authorization by the authority, production
  - Distribution to prescribing health facilities
    - Refers to an intermediate process between production and prescription of medicines (usually at pharmacy or dispensary). Distribution process depends on whether medicines are produced or imported and where the pharmacy or hospitals are located.
  - Dispensing
    - Providing appropriate medicines in a convenient and timely manner. During this process, information should be provided on the adverse drug reactions or drug-drug interaction.
  - The focus of this section will be development, production and distribution and dispensing will be discussed in the rational use section.

2.1.2 Implications for access to medicines

(1) Development and production

- During the 1970s and 1980s, some international organizations and governments argued for the local production of pharmaceutical products in developing countries because it would (Management Sciences for Health, 2012B).
  - Increase self-sufficiency in pharmaceutical supply
  - Improve the quality of medicines

- Improve balance of trade through exports of domestically manufactured medicines and replace imported medicines
- Create new job opportunities

- However, some researchers said that the idea of local manufacturing was not feasible in most developing countries due to economies of scale and technological needs (Lashman, 1986).
  - Lashman discussed that given the size of local markets and the technological capacity for producing Active Pharmaceutical Ingredient (API), Argentina, Brazil, China, Egypt, India, Mexico and Thailand are the examples of developing countries capable of local production.

- The progress in pharmaceutical industry can be evaluated from many different angles.
  - Ballance et al. (1992) proposed the following categories to explain each country's level of progress in pharmaceutical industry in the 1990s.
    - Type 1: Countries with capacity for research, development and production
      - United States, United Kingdom, France, Germany, Japan, Switzerland, Italy, Belgium, The Netherlands, Sweden
    - Type 2: Countries with previous experience in producing at least one innovative pharmaceutical products
      - Argentina, China, India, Mexico, Russia, Serbia, Montenegro
    - Type 3: Countries with no capacity for R&D but those that have capability to produce API and finished pharmaceuticals
    - Type 4: Countries with no capacity for R&D but those that have capability to produce finished pharmaceuticals (but not API)
    - Type 5: Countries with capacity for neither R&D nor production of finished products
  - Similarly, Management Sciences for Health (2012B) categorized the production of pharmaceuticals as follows.

- Primary production: API production
- Secondary production: Finished pharmaceuticals manufacturing from API
- Tertiary production: Packaging and labelling

○ As the previous research suggested, pharmaceutical industry can be divided into R&D and production. Production consists of API production and finished pharmaceuticals manufacturing.

□ Recent studies report the progress according to medicine value chain (Ethiopia Ministry of Health and Ministry of Industry, 2015).

○ The medicine value chain includes the following areas

- Import
- Packaging and labelling
- Finished pharmaceuticals manufacturing
- API manufacturing
- R&D

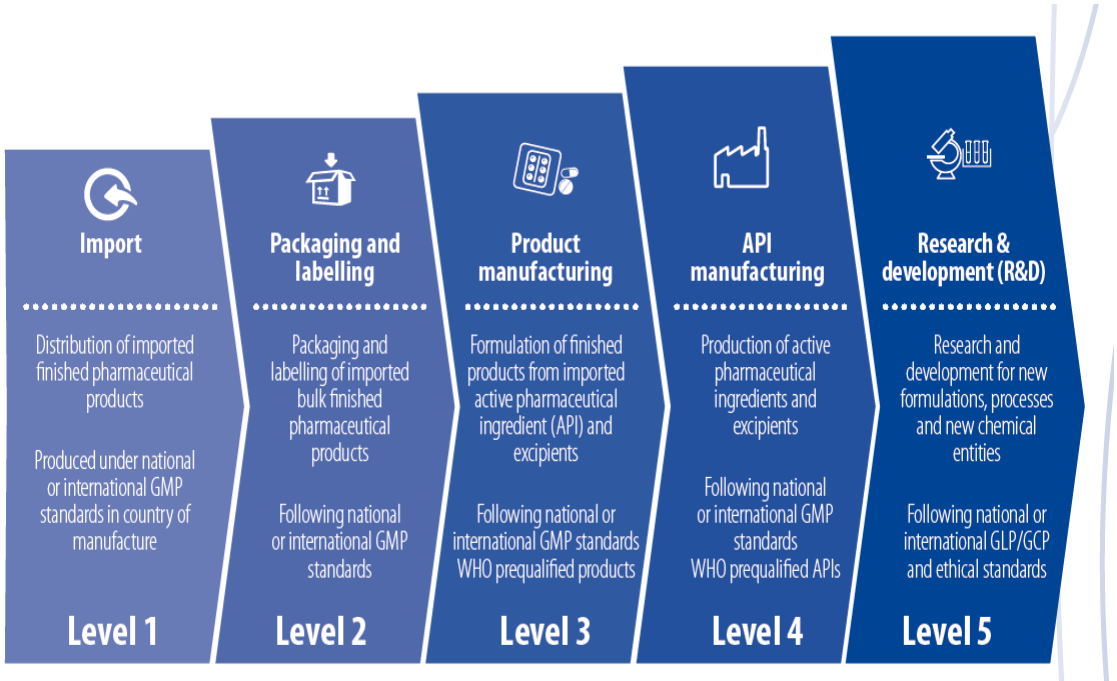

Figure 11. The levels of development by medicine value chain

Source: Ethiopia Ministry of Health and Ministry of Industry (2015)

(2) Procurement and distribution

- Pharmaceutical procurement should consider the following (WHO, 1999)
  - Decision on the cost-effectiveness and appropriate quantity of medicines
  - Selection of reliable providers
  - Timely delivery
  - Management of pharmaceutical expenditure
- Distribution of pharmaceutical products should be linked to prices of each process. WHO and HAI proposed the following stages for prices at each process (WHO/HAI, 2008)
  - Manufacturer's selling price
  - Import tariffs and freight
  - Importers' margin
  - Wholesalers' margin
  - Retailers' margin
  - Tax
- During the distribution of pharmaceuticals from manufacturers or importers to wholesalers and retailers, margins are added.
  - A: Manufacturers' selling price or importers' importing costs
  - B: Wholesalers' margin
  - C: Retailers' margin

2.1.3 Agenda list

- Development and production (Import)
  - Pharmaceutical value chain
    - R&D, production and import
  - Pharmaceutical manufacturing development

- Pharmaceutical authorization
  - Pharmaceutical regulatory authority
  - Pharmacovigilance and monitoring of adverse drug reactions
  - Guidelines regarding pharmaceuticals
  - Substandard and falsified medical products (SF)
- Procurement and distribution
  - Pharmaceutical procurement
  - Pharmaceutical distribution

2.1.4 Development of outcome indicators for monitoring and evaluation

- Introduction

- The following outcome indicators can be considered for development and production
  - Pharmaceutical value chain
  - Pharmaceutical manufacturing development
- The following outcome indicators can be considered for pharmaceutical authorization.
  - Pharmaceutical regulatory authority
  - Pharmacovigilance and monitoring of adverse drug reactions
  - Guidelines regarding pharmaceuticals
  - Substandard and falsified medical products (SF)
- The following outcome indicators can be considered for procurement and distribution
  - Procurement system in public sector
  - Price variations of specific medicines among various supply chains
    - Manufacturers' selling price
    - Importers' margin

- Wholesalers' margin
- Retailers' margin

- Specific outcome indicators

(1) Development and production

- Pharmaceutical value chain
  - The number of pharmaceutical importers
  - The number of packaging and labelling based manufacturers
  - The number of manufacturers
  - The number of active pharmaceutical ingredient (API) manufacturers
  - The number of R&D-based manufacturers

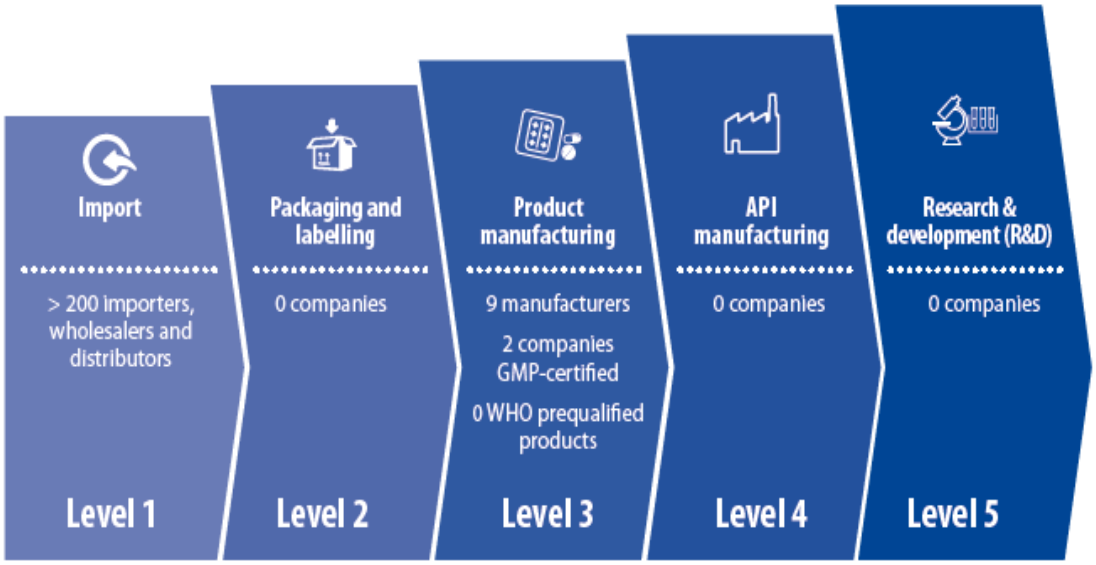

Figure 12. Case study on the levels of development by medicine value chain_ Ethiopia

Source: Ethiopia Ministry of Health and Ministry of Industry (2015)

- Pharmaceutical manufacturing development
  - Packaging and labelling of bulk finished pharmaceuticals
  - Finished pharmaceuticals manufacturing from API

- API manufacturing
- Research and development

(2) Pharmaceutical authorization

- Pharmaceutical regulatory authority
  - Pharmaceutical regulatory authority
  - List of pharmaceuticals approved by the authority
- Pharmacovigilance and monitoring of adverse drug reactions
  - Pharmacovigilance
  - Monitoring of adverse drug reactions
- Guidelines regarding pharmaceuticals
  - Presence of Good Manufacturing Practices (GMP)
  - Presence of Good Distributing Practices (GDP)
  - Presence of Good Pharmacy Practice (GPP)
- Substandard and falsified medical products (SF)
  - Monitoring SF
  - Sanctions against SF

(3) Procurement and distribution

- Pharmaceutical procurement
  - Procurement system in public sector
  - Public procurement system for essential medicines
- Pharmaceutical distribution
  - Price and margin variations among various supply chains

- Specific medicines for price variations and margins can be derived from the core list discussed previously.
  - Price variations from manufacturers or importers
  - Price or margin variations from wholesalers
  - Price or margin variations from retailers

2.1.5 Recommendations

- Decisions regarding producing or importing pharmaceuticals in low-and middle-income countries are complex due to different levels of national capacity and related policies (Management Sciences for Health, 2012B).
  - Human resources and physical infrastructure are required.
  - Production of pharmaceuticals is closely related to industrial policy and health policy, and the two policy areas sometimes have conflicting values.
    - In order to encourage production, setting high prices may be necessary. At the same time, affordability is another important criteria considering access to medicines for the population.
  - In addition, market factors, regulation and related policy, economic incentives and public-private relations should be taken into account.
- Management Sciences for Health (2012B) provided the evaluation guidelines for decision making.
  - Human resources and physical infrastructure
    - Are technical specialists or skilled production staff available?
    - Is there an educational system for trained workers?
    - What are the cost and reliability of water, power, construction, equipment and other resources?
    - Are there financial resources available to retain skilled workers and to support the maintenance of infrastructure?
  - Market factors
    - What are the population size, geographic distribution and income levels in the

country?

- Is there existing local production capacity?
- What are the barriers to imported products?
- Can the size, reliability and preference of the public sector market ensure economies of scale?
- Is there predictable demand for medicines?

- Regulatory environment
  - What is the status of laws on pharmaceutical registration?
  - What is the status of product and process patent protection?
  - Does the regulatory agency have systems and capacity to assure product quality through GMPs and enforcement of standards?
  - Are there generic labeling, prescribing and dispensing laws and practices?
- Investment and industrial development environment
  - How strong is the country's financial sector (banking and nonbanking activities)?
  - Is there sufficient access to capital?
  - Are tax or other investment incentives available?
  - Are industrial development funds available (access to start-up capital)?
  - What are the ownership requirements (limits on foreign ownerships, requirements of local ownership)?
  - Are there restrictions on repatriation of profits (foreign investors)?
- Economic incentives
  - Does the government enforce price controls?
  - Is there access to foreign exchange?
  - Are there export incentives (economic and noneconomic)
- Duties and import controls
  - Are there duties or import controls on-
    - Active pharmaceutical ingredients?
    - Inactive pharmaceutical ingredients and other raw materials?
    - Packaging materials?
    - Specialized/nonspecialized pharmaceutical equipment?

- Pharmaceutical production for high income countries and low-and middle-income countries should be discussed in different contexts (World Bank, 2005).

- Subsidiaries of large multinational companies
- Generics manufacturers operating globally
- Generics companies with predominantly national operations
- Small-scale local manufacturers

- Managing and monitoring produced pharmaceuticals can be more important than production.
  - Medicines are closely related to health. Quality medicines contribute to the prevention, diagnosis and treatment but substandard medicines may threaten population health. Therefore, pharmaceutical products should be rigorously managed from the production stage.
  - A number of low- and middle-income countries lack capacity for monitoring, managing and regulating pharmaceutical productions. Measures to mange and monitor production should be implemented in advance so that the quality of medicines should not be compromised.

2.4 Affordability

2.1.1 Introduction

- Bors et al. (2015) defined affordability for medicines as the ability to purchase medicines "without unduly compromising their ability to meet other essentials, such as housing, education and food" (Bors et al. 2015).
- Also, the concept of affordability is distinguished from the value that medicines offer.
  - A specific medicine can provide high level of benefits or value, but have low level of affordability (e.g. hepatitis C medicines).
  - On the other hand, some medicines can have high affordability but offer low level of value.
- Comparison for the evaluation on the affordability of medicines among countries has not been possible due to lack of data and standardized measurement methods (Niens, 2013).
  - Two general approaches to measuring affordability of medicines are 1) to calculate the proportion of the population that falls below a relevant poverty line as a result of purchasing medicines or 2) to calculate the proportion of the population that pays more than a certain percent of their income to purchase medicines.
  - These two methods take into account the income distribution because they attempt to measure impoverishment and catastrophic payment in relation to the population income.
  - WHO and Health Action International (HAI) proposed an alternative method to evaluate affordability by measuring the number of days' wages that the lowest paid unskilled government worker (LPGW) should pay to purchase medicines for a particular disease.
- The following policies have been implemented to improve affordability of medicines in health systems.
  - Differential pricing
  - Monopsonies
  - TRIPS Flexibilities

- The proportion of out-of-pocket payment for medicines is higher in low- and middle-income countries than the high income countries.
  - According to a World Bank report, cash market may result in market failure and overpayment by patients (Seiter, 2010).
- There is a considerable difference in the levels of pharmaceutical expenditure per capita between high income countries and low- and middle-income countries in the Asia Pacific region.
  - Low- and middle-income countries have shown low levels of pharmaceutical expenditure per capita but relatively high out-of-pocket payment compared to high income countries (Yadav et al. 2012).
  - High out-of-pocket payment is one of the important causes for catastrophic health expenditure.
- Evidence and policy research are important in improving access to medicines.
  - Through a systematic review, Gray et al. (2015) evaluated the extent to which the published evidence on pharmaceutical policy is applicable to low- and middle-income countries and found the policy research is mostly conducted in the context of high income countries.
  - However, as low- and middle-income countries move towards UHC which separates financing from service provision, policies related to pharmaceutical pricing and reimbursement will be more applicable for these countries as well.

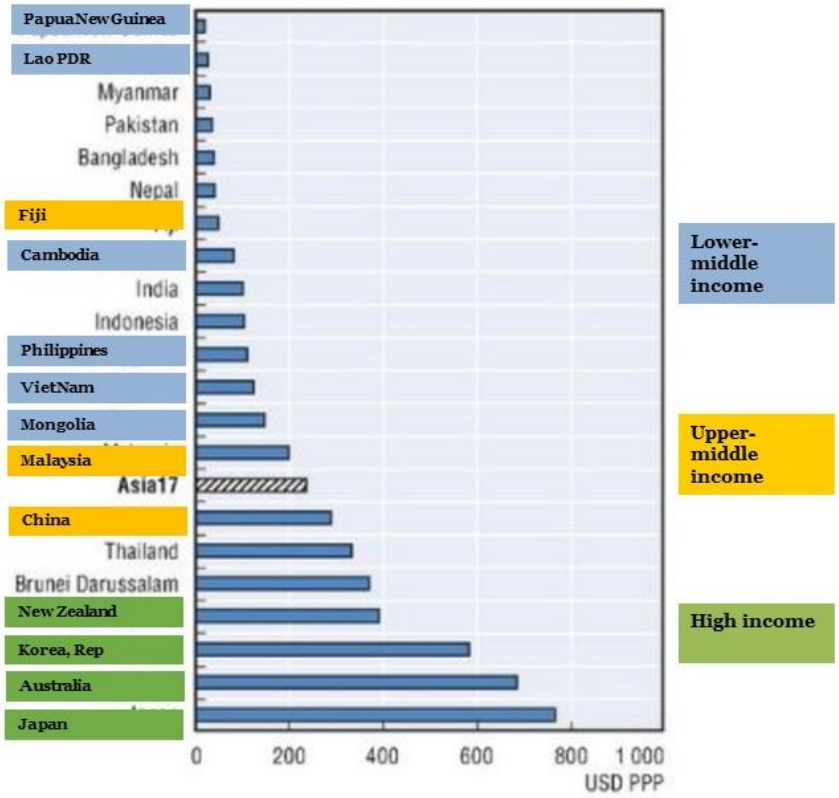

Figure 13. Pharmaceutical expenditure per capita, international dollars (USD PPP) (2014)

Source: OECD/WHO(2016) OECD Health at a Glance: Asia/Pacific 2016

2.1.2 Implications for access to medicines

- Srivastava et al. (2014) estimated a country's price elasticity of government demand for medicines in low income countries, and found that it is generally elastic (price elasticities at the government level range between -1 and -2). They also suggested that the information on pharmaceutical pricing should be transparent to secure access to medicines in low income countries.
  - Lack of information on pharmaceutical prices can prevent individuals and health systems from making rational decisions for pharmaceutical purchasing.
  - According to Wirtz et al. (2016), most countries have not responded to repeated surveys on pharmaceutical prices and no data has been collected for the affordability of medicines based on income level.
  - Collecting data on pharmaceutical prices is relatively easy for single payer, government operation system but continuous update is challenging due to price

variations.

- Obtaining information on the actual price paid by patients can be difficult for low- and middle-income countries with high out-of-pocket payment and wide variations in the actual price.

- As pharmaceutical expenditure is continuously increasing along with health expenditure, developing strategies to maximize the value is urgent.
  - Nguyen et al. (2014) defined pharmaceutical expenditure as a function of medicine price, consumption volume and the interaction between the two (Nguyen et al. 2014).
  - Mousnad et al. (2014) conducted a systematic review to analyze the cost drivers for pharmaceutical spending and explained that the important cost drivers are the increase in the utilization of medicines and the introduction of new medicines. Also, they proposed the following policy alternatives.
  - Educational strategies: practice guidelines, continuing education programs, drug committees and patient information packages
  - Managerial strategies: positive and negative lists, reference pricing systems, reimbursement schemes, disease management strategies, practice guidelines and the regulation of marketing and commercial information
  - Financial strategies: fixed budgets for prescribing, price regulation, price/volume agreements, copayment schemes, financial incentives for pharmacists to improve the quality of pharmacy services, promotion of generic drugs
- The following two levels should be considered to define affordability.
  - Affordability of national health system at the population level
  - Affordability of patients at the individual or household level
- The following issues can be addressed for improving macro-level affordability or the affordability at the health system level.
  - Developing a reimbursement list as a component of UHC is directly related to the affordability of medicines.
  - Since the majority of countries depend on imported medicines, countries should

monitor if tariffs or other trade barriers are used against affordability of medicines.

- Strategies to promote competition by the introduction of generics can be an option to improve affordability of medicines.

- Micro-level affordability or pharmaceutical expenditure by individuals should be maintained at the reasonable level.
  - If supply of medicines and quality control in public sector are insufficient, individuals have no choice but to pay out-of-pocket to purchase medicines in public sector, and in such cases, the price tends to be higher than in public sector.
  - High out-of-pocket payment can lead to inequity in access to medicines both for low- and middle-income countries and high income countries.

2.1.3 Agenda list

- Discussion on the measures to share information on pharmaceutical policy and pricing for securing transparency.
  - The importance of creating national or regional level network for information sharing has been emphasized, and an example of such a network is Pharmaceutical Pricing and Reimbursement Information (PPRI) in Europe.
- Discussion on the prioritization strategies to improve affordability at the national/government level
  - Prioritization of health system through reasonable approach to pharmaceutical expenditure can be examined from multiple perspectives.
  - Some of the examples include the approaches based on epidemiology and disease burden, evidence-based medicine, health economics approach, etc.
- Discussion on the measures to reduce the share of out-of-pocket payment to improve individual-level affordability.
  - Specifically, low- and middle-income countries have high level of out-of-pocket payment, which can lead to a vicious cycle of increase in pharmaceutical spending, misuse/abuse of medicines, etc.

2.1.4 Development of outcome indicators for monitoring and evaluation

- Introduction

- For monitoring and evaluation of affordability of medicines, the outcome indicators in terms of the following three dimensions can be considered.
  - Transparency of pharmaceutical pricing
  - Affordability at the national/government level
  - Affordability at the individual level

- Specific outcome indicators

- Transparency of pharmaceutical pricing
  - Information collection: information collection on the pharmaceutical pricing, expenditure and consumption.
  - Information sharing: information sharing on pharmaceutical price and policy.
- Affordability at the national/government level
  - Decision on pricing: decision making on pharmaceutical pricing and related policy.
  - Pharmaceutical financing: budget management for pharmaceutical spending.
- Affordability at the individual level
  - Consumption: public acceptance for the use of generics.
  - Price: price level for the patients.
  - Expenditure: pharmaceutical expenditure per capita and total pharmaceutical expenditure.

2.1.5 Recommendations

- The efforts to make pharmaceutical pricing more transparent are prerequisite for ensuring affordability of medicines.
  - An example of such collaborative effort is Pharmaceutical Pricing and

Reimbursement Information (PPRI), which has operated a network on pharmaceutical pricing and reimbursement policy since the European Commission's project in 2005. The following activities of PPRI can be useful.

Table 3. Key activities of PPRI

Activities	Objective
Networking	To facilitate an exchange of information among policy makers of different countries.
Needs assessment	To explore information needs related to pharmaceutical policies for policy makers and stakeholders.
Indicators	To develop indicators to compare pharmaceutical systems
Country report	To conduct a survey for collecting comprehensive information and data on each country's pharmaceutical system in a comparable format.
Ad-hoc queries	To promote access to specific country information.
Benchmarking	To perform cross-country comparisons.
Glossary	To facilitate mutual understanding and language.
Policy monitoring	To conduct a survey on major changes in pharmaceutical policies among European countries.
Policy analysis	To investigate the impact of pharmaceutical policies.
Dissemination- conferences and other activities	To disseminate PPRI and its outcome to stakeholders and the public.

Source: Vogler et al. (2014)

- The policy directions to improve affordability should focus on a country's burden of disease, especially chronic diseases.
  - Khatib et al. (2016) investigated the affordability for the most frequently used cardiovascular disease and estimated that 0.14% of high income countries, 25% of upper-middle income countries, 33% of lower-middle income countries and 60% of low income countries could not afford these medicines (Khatib et al. 2016).
  - Cameron et al. (2008) performed a study for 36 developing countries and suggested

that the affordability of medicines for common chronic diseases such as ulcer, asthma and type 2 diabetes tends to be low in private sector.

- Another study on insulin prices for 20 low- and middle-income countries found that the insulin costs from 1.1 to 13.7 days of wages in these countries (Health Action International, 2016).

- Countries should take into account various aspects such as health system, national priority, available resources, human rights and ethical issues when implementing a policy for improving affordability (Wirtz et al. 2016).
  - Specifically, the directions for policy development and implementation should depend on whether the medicines supply and health service delivery take place mostly in public or private sector.
- Recent discussion on high cost medicines should go beyond the context of high income countries and the early discussion on high cost medicines for low- and middle-income countries is recommended.
- Political will and the investment for routine data collection and monitoring should be supported to improve affordability of medicines.

2.5 Rational use

2.1.1 Introduction

- WHO defined rational use of medicines as follows (WHO, 1987).
  - "The rational use of drugs requires that patients receive medicines appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and the community."
  - Rational use refers to the use of medicines to meet the clinical needs in appropriate doses, for an adequate period of time, and at low cost.
    - Irrational use of medicines can be detrimental to the patients' health, health financing and environment.
  - However, it was reported that 50% of medicines were inappropriately prescribed, dispensed and used (WHO, 2002B).
- The rational use of medicines is an integral part of National Drug Policy (WHO, 2001).
  - WHO proposed accessibility, quality and rational use as the main objectives of National Drug Policy.
    - Accessibility indicates equitable access and affordability of essential medicines.
    - Quality refers to the safety, efficacy and good quality of all medicines.
    - Rational use means the use of therapeutically sound and cost-effective drugs by health professionals and consumers.
- The irrational use of medicines can be caused by various factors, thus requiring policy intervention from diverse perspectives.
  - A number of previous studies suggested that overprescribing, polypharmacy, long-term prescribing with high strength medicine, prescribing without clinical evidence, unnecessary prescription of antibiotics and injections, misuse/abuse of medicines are examples of irrational use of medicines.
  - Key types of irrational use and the associated factors are summarized below.

Table 4. Types of irrational use and related factors from the perspectives of prescribers and patients

Types of irrational use	Prescriber-side	Patient-side
General over-prescribing	Meeting patient expectations Obtaining financial incentives	Having false perceptions that "more is better" Limited opportunity to see doctor
Over-use of antibiotics and injections	Having difficulty in diagnosis The patient may not be compliant with other treatments	Expecting a strong effect and quick relief with false perception
Use of expensive drugs despite lack of evidence	Influenced by pharmaceutical industry such as promotion and economic incentive	Having false perceptions that "expensive is better"
Non-use of generics	Having false perceptions that "generics is bad"	Prescribing patterns of prescribers Having false perceptions that "generics is bad"
Under-use of treatments for chronic disease	Limited opportunity to see doctor	Perceptional barriers in chronic disease

Source: WHO(2001)

2.1.2 Implications for access to medicines

- The rational use and affordability of medicines deal with the actual prescription and dispensing of medicines.
  - Essential medicines, finance and value for money, development, production and distribution can be discussed at the national or higher level whereas the rational use and affordability can be discussed at the lower level relating to the actual use of health services by consumers.
  - Various factors can be associated with health service utilization by consumers. Therefore, measures to promote quality use of medicines should be discussed at both higher and lower levels. A single policy intervention may result in unintended consequences.

- The factors that impede rational use of medicines include conflicting interests, lack of information or information asymmetry, inappropriate drug promotion, unrestricted use of medicines (WHO, 2001).
  - Conflicting interests
    - Depending on the payment system, prescribers and pharmacists may have a financial interest in prescribing more drugs or high cost medicines.
    - Producers can provide financial incentives to physicians or pharmacists to increase sales.
    - Consumers may believe that the rational use of medicines is intended to cut costs rather than to improve the quality of therapy.
  - Lack of information
    - In many low- and middle-income countries, the access to drug information is limited and it is dependent on commercial sources of information from pharmaceutical companies.
  - Inappropriate drug promotion
    - Irrational use of medicines can have a potential for harm and therefore, the promotion of medicines requires special controls to protect the public.
    - Scientific accuracy and balance of information, improper inducements to prescribers or dispensers, lack of full product information, misleading presentations by medical representatives and promotional activities disguised as educational or scientific exercises should be regulated.
  - Unrestricted use of medicines
    - In some countries, medicines that require medical supervision and a prescription are freely used from pharmacies or other sellers. Medicines without interventions from health professionals can lead to inappropriate use and hamper correct diagnosis and treatment.
- Educational, managerial and regulatory strategies can be recommended for promoting rational use of medicines (WHO, 2001).

- Education is needed for all participants to encourage rational use of medicines. However, it is important to note that adequate knowledge does not always lead to appropriate behavior.
  - Training for health professionals
    - "Guide to good prescribing" by WHO can be a good reference source.
  - Education for the public
- Some managerial strategies can contribute to policy implementation.
- Regulations may be needed for enforcement purposes.
- In addition, standard treatments, essential medicines lists and hospital pharmacy and therapeutics committee can be effective in promoting rational use of medicines (Laing et al. 2001).
  - Standard treatments and essential medicines lists suggest the list of necessary medicines and desirable prescribing behavior.

2.1.3 Agenda list

- Agenda list for rational use can be suggested in terms of structure, process and outcomes.
  - Structure can be understood as policy and measures to encourage rational use of medicines.
    - Education, management and organization are included in the structure.
  - Process can be viewed as behavior of physician, pharmacists and patients for rational use of medicines.
  - Outcomes can be interpreted as the actual achievement of rational use by means of policy and relevant measures.

2.1.4 Development of outcome indicators for monitoring and evaluation

- Introduction

(1) Structure (education, management, organization)

- Holloway and Henry (2014) proposed policy options for rational use of medicine such as national medicines policy (NMP), educational policies, managerial policies, economic policies, regulatory policies, structural policies and human resource polices.
  - NMP and monitoring quality use of medicines
    - NMP document
    - NMP implementation plan
    - NMP integrated into national health plan
    - National strategy to contain antimicrobial resistance
    - National prescribing audit in the last 5 years
  - Educational policies
    - Undergraduate training of doctors, nurses, pharmacists and paramedics on the essential medicines list
    - Undergraduate training of doctors, nurses, pharmacists and paramedics on the standard treatment guidelines
    - Continuing medical education of doctors, nurses, pharmacists and paramedics
    - Public education on antibiotics
    - Public education on injections
  - Managerial policies
    - National essential medicines list updated in the last 5 years
    - National essential medicines list updated in the last 2 years
    - Public insurance drug coverage limited to national essential medicines list
    - National standard treatment guidelines updated in the last 2 years
    - National formulary updated in the last 5 years
    - Generic prescribing in public sector
    - Generic substitution in public sector

- Economic policies (payment scheme)
  - Some drugs covered by public health insurance
  - Coverage of some of the population by public health insurance
  - Dispensing prescribers in public sector
  - Revenue for prescribers from drug sales
  - Provision of essential medicines free at the point of care to all patients
  - Provision of essential medicines free at the point of care to patients <5 years of age
  - Provision of essential medicines free at the point of care to pregnant women
  - Provision of essential medicines free at the point of care to elderly patients
- Regulatory policies
  - Antibiotics not available over-the-counter
  - Injections not available over-the-counter
  - Active monitoring of adverse drug reactions
  - Joint regulation of drug promotion by government and industry
- Structural policies
  - National Ministry of Health unit promoting rational use of medicines
  - Drug and therapeutics committees at the hospital level
  - National reference laboratory for antimicrobial resistance
  - National task force to contain antimicrobial resistance
  - Presence of national drug information center
- Human resource policies
  - Prescribing by doctors in public primary care
  - Prescribing by nurses in public primary care

- No prescribing by untrained staff in public primary care

□ Indicators described above represent diverse aspects and some of them overlaps with dimensions discussed in this study.

○ Essential medicines lists and standard treatment guidelines discussed in NMP and managerial policies are included in essential medicines domain suggested in this study. Economic policies touch upon some aspects of universal health coverage, finance and value for money.

○ This is because rational use of medicines is related to diverse factors and closely linked to health systems.

□ Considering the relationships with other evaluation domains, tis study selected the following outcome indicators from structural policies.

○ Organization

- National unit promoting rational use of medicines
- National drug information center

○ Education

- Education for health care professionals on the essential medicines list, standard treatment guidelines and generic prescribing and substitution
- Public education on the use of antibiotics and injections

○ Management

- National strategy to contain antimicrobial resistance
- National strategy for enhancing generic medicines

(2) Treatment process and outcome

□ In the 1990s, WHO and INRUD developed core drug use indicators to evaluate the use of medicines in the primary care setting. The indicators can be categorized as prescribing indicators, patient care indicators and health facility indicators (WHO, 1993; WHO, 2002B).

- Prescribing indicators[3]
  - Average number of drugs per encounter (1.6-1.8)
  - Percentage of drugs prescribed by generic name (100)
  - Percentage of encounters with an antibiotic prescribed (20.0-26.8)
  - Percentage of encounters with an injection prescribed (13.4-24.1)
  - Percentage of drugs prescribed from essential drugs list or formulary (100)
- Patient care indicators
  - Average consultation time (≥10 mins)
    - Process indicator
  - Average dispensing time (≥90 secs)
    - Process indicator
  - Percentage of drugs actually dispensed (100)
  - Percentage of drugs adequately labelled (100)
  - Patients' knowledge of correct dosage (100)
- Health facility indicators
  - Availability of copy of essential drugs list (100)
  - Availability of key drugs
- Other indicators have been used for previous studies. These belong to prescribing indicators described above.
  - Percentage of patients with an antibiotic prescribed
  - Percentage of acute diarrhea patients with an antibiotic prescribed
  - Percentage of acute diarrhea patients given hydration measures

[3] Values in the parentheses indicate the optimal value.

- Percentage of medicines prescribed from the essential medicines list
- Percentage of medicines prescribed entirely from generics
- Percentage of patients with an injection prescribed
- Percentage of pneumonia patients with an appropriate antibiotic prescribed
- Percentage of upper respiratory infection patients with an antibiotic prescribed
- Percentage of patients treated in compliance with standard treatment guidelines

• Specific outcome indicators

(1) Structure (education, management, organization)

- Organization
  - National unit promoting rational use of medicines
    - If present, what are the activities of the organization?
  - National drug information center
    - If present, what are the activities of the center?
- Education
  - For health care professionals (doctors, nurses, etc.)
    - Essential medicines list
    - Standard treatment guidelines
    - Generic prescribing and substitution
  - For public (patients)
    - Antibiotics
    - Injections
    - Generic prescribing and substitution

- Management
  - National strategy to contain antimicrobial resistance
  - Generic substitution
    - Generic substitution permitted in public sector
    - Measures to enhance generic substitution
    - Generic substitution permitted in private sector

(2) Treatment process and outcome

- Prescription
  - Percent of prescribed drugs belonging to essential medicines list
  - Percent of drugs prescribed by generic name
  - Percent of patients prescribed antibiotics
  - Percent of patients prescribed injections
- Treatment
  - Percent of patients treated in compliance with standard treatment guidelines

2.1.5 Recommendations

- Problems and solutions related to rational use of medicines are interconnected with diverse factors. Governments should take an active role in setting a clear policy agenda. In addition, measures for promoting rational use of medicines should be specific, comprehensive and embrace behavior patterns of prescribers and consumers. To that end, the following stages should be taken into account.
  - Awareness, measurement and understanding on the irrational use of medicines
    - WHO manual titled “How to investigate drug use in health facilities” can be a reference source to evaluate the quality of prescription and dispensing.

        - This will in turn facilitate cross country comparison.
    - WHO and International Network for the Rational Use of Drugs (INRUD) provides an education program for rational use of medicines.
- Measures to establish and achieve goals
    - Once the problems are identified, measures to tackle them can be suggested in terms of education, management and regulation. These need to be designed to complement each other.

Chapter 4. Discussion and conclusion

1. Establishment of interim- and long-term plans

1.1 Evaluation domains and prioritization

- This study suggested five evaluation domains concerning multi-dimensions of access to medicines (Wirtz et al. 2016; WHO, 2002C) and the comprehensiveness of national medicines policy (WHO, 2001) and pharmaceutical industry policy (Lee et al. 2014).
  - Essential medicines list
  - Finance and value for money
  - Development, production and distribution
  - Affordability
  - Rational use
- Under each of the five evaluation domains, specific agenda has been suggested for future discussion. The five evaluation domains and the agenda are listed below.

Essential medicine	Finance and value for money	Development, production and distribution	Affordability	Rational use
Essential medicines list	Pharmaceutical financing	Development and production	Transparency of pharmaceutical pricing	Structure (education, management, organization)
Standard treatment guideline	Pharmaceutical pricing and strategic purchasing	Pharmaceutical authorization	Affordability at the national/government level	Treatment process and outcome
	Pharmaceutical reimbursement	Procurement and distribution	Affordability at the individual level	

Figure 14. Agenda list for 5 evaluation domains

- Additionally, this study classified Asia Pacific countries into high income, upper-middle income and lower-middle income groups.
  - Establishing common priorities can help lead a discussion on the agenda more

efficiently. Therefore, this study proposed the common prioritization of evaluation domains.

- However, separate prioritization was proposed for each agenda under five evaluation domains according to the country's income level.

- In other words, this study selected and prioritized the common five evaluation domains regardless of income level.

  - However, heterogeneity among different income groups has been addressed for evaluation domains requiring special attention to the income levels.

  - Also, the prioritization for the agendas under five evaluation domains are presented separately for each income group since heterogeneity derived from income levels is still an important factor.

- Firstly, recent discussion on the access to medicines and universal health coverage at the international level has centered around financing.

  - Considering this trend, finance and value for money was recommended as the first priority for discussion.

  - Finance and value for money focus on securing sources of financing at the higher level, while the affordability is assessed within the health system level. Therefore, finance and value for money and affordability should be discussed together.

- Secondly, development, production and distribution deals with the supply of medicines, which corresponds to the sources of financing. Some lower-middle income countries are having difficulty in the supply of medicines and their pharmaceutical industry is still at an early development stage. Therefore, this vulnerability should be taken into consideration.

  - However, the issue of development, production and distribution has low priority in high income countries or upper-middle income countries.

- Thirdly, adequate financing and supply should precede the discussion on the rational use of medicines.

  - Consequently, the rational use has higher priority than development, production and

distribution in high income countries. However, the rational use has lower priority than development, production and distribution in lower-middle income group context.

- Even though this study viewed rational use as lower priority than other domains, it is still an important issue.

- Finally, essential medicines have held an important position in the field of global health since 2002.
  - In 2002, 156 countries established essential medicines lists and approximately 100 countries update the list continuously.
  - Also, a large proportion of low- and middle-income countries have essential medicines lists (Backman et al, 2008).
  - The concept of essential medicines is worth the attention as a starting point of discussion but many countries have already achieved the targeted goal and thus essential medicines can be considered as lower priority than other domains.
    - Even though essential medicines are relatively lower priority compared to other evaluation domains, the implications of the concept are still important.

- As was suggested by the above discussion, this study proposed the shared prioritization of the five evaluation domains.
  - Finance and value for money, affordability, rational use
  - In addition to these, development, production and distribution, essential medicines were suggested as priorities for lower-middle income countries.

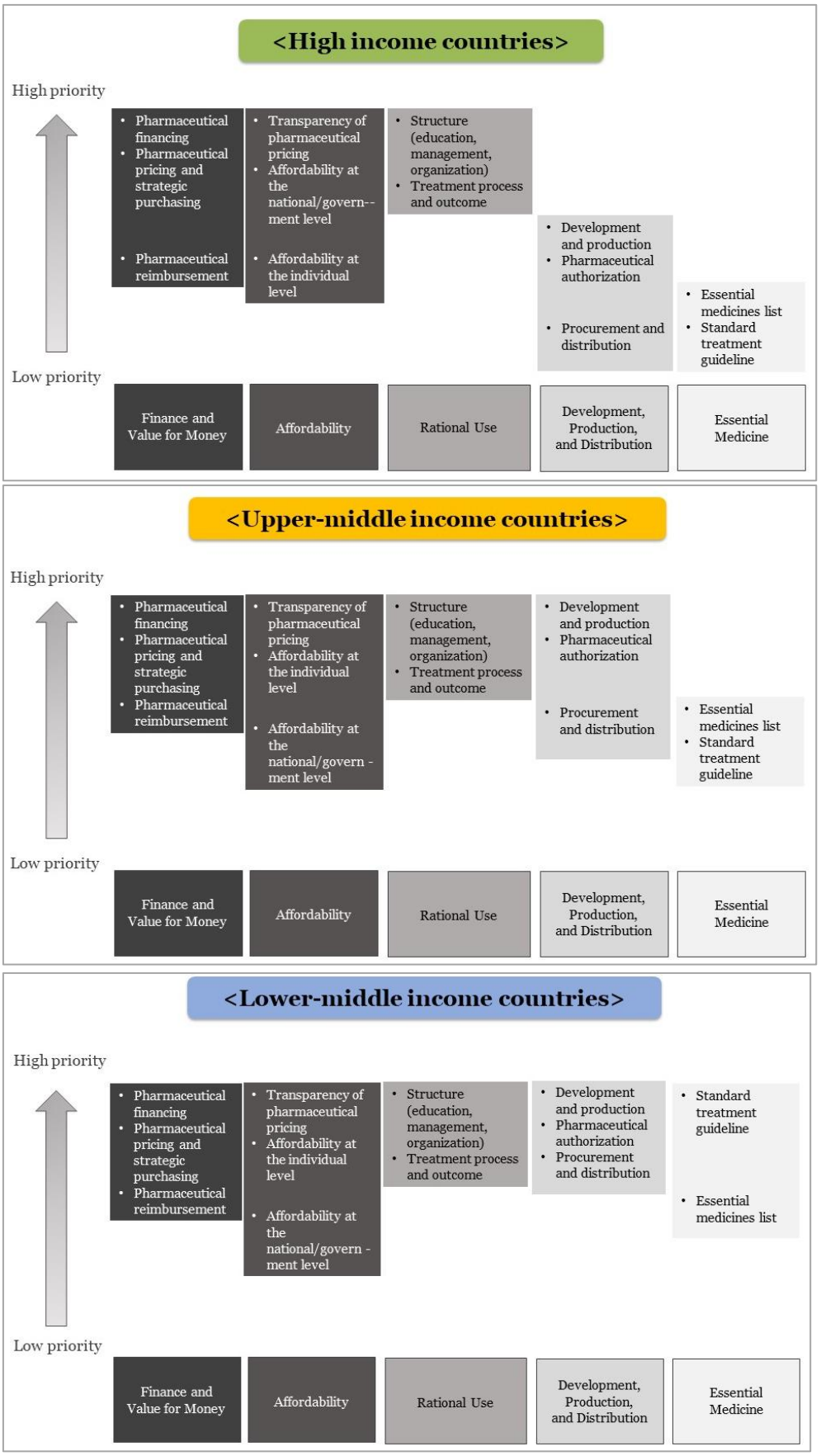

Figure 15. Prioritization of the agenda for 5 evaluation dimensions by income level

1.2 Agenda under evaluation domains and prioritization

- This study proposed different prioritizations of the agenda under five evaluation domains by income level to promote an effective discussion.

- Prioritized agenda under finance and value for money domain is discussed below.
  - Regardless of income levels, countries have high priority in the agenda for 1) pharmaceutical financing and 2) pricing and strategic purchasing.
  - Considering high income countries, the priority of pharmaceutical reimbursement is at the intermediate level.
    - The reimbursement authority, reimbursement process and reimbursement management were selected as the outcome indicators for pharmaceutical reimbursement

- Prioritized agenda under affordability domain by different income levels is discussed below.
  - Regardless of income levels, countries have high priority in the agenda for transparency of pharmaceutical pricing.
  - Upper- and lower-middle income countries have higher priority for the affordability at the individual level than that at the national/government level.
    - This reflects the current situation of upper- and lower-middle income countries with high out-of-pocket payment.
  - High income countries have higher priority for the affordability at the national/government level than that at the individual level.

- Prioritized agenda under development, production and distribution domain by different income levels is discussed below.
  - The gaps among different income groups are considerable for the agenda under development, production and distribution domain.
    - This is due to the different levels of pharmaceutical industry development, the capacity of pharmaceutical regulatory authority and pharmaceutical procurement

and distribution among different income groups.

- High income countries have low priority for the development, production and authorization and intermediate level of priority for procurement and distribution.
- Upper-middle income countries have high priority for the development, production and authorization and intermediate level of priority for procurement and distribution.
  - Development and production of medicines in upper-middle income countries should take active pharmaceutical ingredient (API) into account.
- Lower-middle income countries have high priority for all agenda items under development, production and distribution domain.
  - Development and production of medicines in lower-middle income countries should consider not only API production but the production of finished products, import and other issues more broadly.

□ Prioritized agenda under rational use domain by different income levels is discussed below.

- Regardless of income levels, all countries have high priority for structure (education, management, organization) and treatment process and outcome.
  - Specifically, education on generics and generics substitution are on the high priority regardless of income levels.

□ Prioritized agenda under essential medicines domain by different income levels is discussed below.

- As for essential medicines list, upper-middle income and lower-middle income countries have intermediate level of priority while high income countries have low priority.
- As for standard treatment guidelines, lower-middle income countries have high level of priority but upper-middle income countries and high income countries have intermediate and low level of priority respectively.

Table 5. Prioritization of agenda list by income level

Evaluation domain	Agenda	High income countries	Upper-middle income countries	Lower-middle income countries
Essential medicines	Essential medicines list			
	Standard treatment guideline			
Finance and value for money	Pharmaceutical financing			
	Pharmaceutical pricing and strategic purchasing			
	Pharmaceutical reimbursement			
Development, production and distribution	Development and production			
	Pharmaceutical authorization			
	Procurement and distribution			
Affordability	Transparency of pharmaceutical pricing			
	Affordability at the national/government level			
	Affordability at the individual level			
Rational use	Structure (education, management, organization)			
	Treatment process and outcome			

Note: Darker shades indicate higher priority.

1.3 Agenda and outcome indicators for evaluation domains

- Under each agenda item, the outcome indicators and specific outcome indicators were developed. The importance and feasibility of specific outcome indicators were presented to facilitate actual evaluation.
  - The importance of outcome indicators were categorized as A, B and C.
    - A: Recommended for the use as core indicators.
    - B: Appropriate for the use as core indicators.
    - C: Can be used as core indicators, if necessary.
  - The importance of outcome indicators was presented separately for each income level (high income, upper-middle income, lower-middle income).
  - The feasibility of outcome indicators was evaluated from the perspective of the relevant government official and categorized as I and II.
    - I: High level of feasibility based on previous studies.
    - II: Additional effort is required based on previous studies.
  - The feasibility of outcome indicators was determined by literature search of the research team and the actual feasibility of a country is subject to change.
    - Therefore, the feasibility of outcome indicators should be further discussed at the Annual Meeting on Access to Medicines under Universal Health Coverage in the Asia Pacific Region.

Table 6. Agenda and outcome indicators_ Essential medicines

Agenda	Outcome Indicators	Specific Outcome Indicators		Importance			Feasibility
				High-income	Upper middle-income	Lower middle-income	
Essential medicines lists	Selection process for essential medicines	Organization for selecting essential medicines		C	B	B	I
		↳If present,	Specific organization	C	B	B	I
		Committee for selecting essential medicines		C	C	C	I
		↳If present,	Composition of the committee	C	C	C	I
		Transparency in selecting essential medicines (information sharing regarding the selection of essential medicine)		C	B	B	II
	Essential medicines list(EML)	Essential medicines list		C	B	A	I
		↳If available,	Amendments of the list	C	B	A	I
		↳If available,	Amendment cycle	C	B	A	I
		Essential medicines list for children		C	B	A	I
		↳If available,	Amendments of the list	C	B	A	I
		↳If available,	Term of amendments	C	B	A	I
	Medicines listed on the EML	Coverage of the EML (compared to WHO model lists of essential medicines)		C	B	A	I
	Actual availability of specific medicines	Actual availability of specific medicines in public area		C	B	A	II
		Actual availability of specific medicines in private area		C	B	A	II
		Generics availability of off-patented medicines		B	A	A	II
Standard treatment guidelines	The process of preparing standard treatment guidelines	Organization for preparing standard treatment guidelines		C	B	A	I
		↳If present,	Specific organization	C	B	A	I
		Committee for preparing standard treatment guidelines		C	C	C	I
		↳If present,	Composition of the committee	C	C	C	I
		Validity in preparing standard treatment guidelines (evidence for preparing guidelines)		C	B	A	II
	Standard treatment guidelines	Standard treatment guidelines in specific disease areas		C	B	A	I
		↳If available,	Amendments of guidelines	C	B	A	I
		↳If available,	Amendment cycle	C	B	A	I

Importance- A: Recommended for the use as core indicators, B: Appropriate for the use as core indicators, C: Can be used as core indicators, if necessary.
Feasibility- I: High level of feasibility based on previous studies, II: Additional effort is required based on previous studies

Table 7. Agenda and outcome indicators_ Finance and value for money

Agenda	Outcome Indicators	Specific Outcome Indicators		Importance			Feasibility
				High-income	Upper middle-income	Lower middle-income	
Pharmaceutical financing	Pooling	National/government level health insurance system (tax-based health service, social insurance, mixed)		B	A	A	I
		Percentage of population coverage by national/government level health insurance		B	A	A	I
	Revenue collection	Government share of total pharmaceutical expenditure		A	A	A	I
		Out-of-pocket spending as a share of total pharmaceutical expenditure		A	A	A	I
Pharmaceutical pricing and strategic purchasing	Pharmaceutical price	National/government level authority for pharmaceutical pricing, regulation and management		A	A	A	I
		↳If present,	Price negotiation policy	A	A	A	I
			Ex post management of pharmaceutical price (Update on the drug reimbursement list, reevaluation of the drug prices, etc.)	A	A	A	I
	Purchasing and monitoring	Evidence on purchasing decision (review, evaluation, results, etc.)		B	B	B	II
		Methods for leveraging government purchasing power (e.g. tender, pooled procurement)		B	B	B	II
Pharmaceutical reimbursement	Reimbursement authority	National/government level authority for pharmaceutical reimbursement		C	B	A	I
		Publicly available information on the drug reimbursement list		C	B	A	I
	Reimbursement process	Principles on the reimbursement decision making process (e.g. cost-effectiveness, medical need and therapeutic value, humanitarian value)		B	A	B	I
		Policy for pharmacoeconomic evaluation or health technology assessment (HTA)		B	A	B	I
	Reimbursement management	Information system at the national/government level for monitoring pharmaceutical expenditure		B	B	B	I
		Total number of medicines on the reimbursement list (or those excluded from the reimbursement)		B	A	A	II

Importance- A: Recommended for the use as core indicators, B: Appropriate for the use as core indicators, C: Can be used as core indicators, if necessary.
Feasibility- I: High level of feasibility based on previous studies, II: Additional effort is required based on previous studies

Table 8. Agenda and outcome indicators_ Development, production, and distribution

Agenda	Outcome Indicators	Specific Outcome Indicators		Importance			Feasibility
				High-income	Upper middle-income	Lower middle-income	
Development and production (import)	Pharmaceutical value chain	The number of pharmaceutical importers		C	B	A	I
		The number of packaging and labelling based manufacturers		C	B	A	I
		The number of manufacturers excluding packaging based manufacturers		C	B	A	I
		The number of GMP certified manufacturers		C	B	A	I
		The number of active pharmaceutical ingredient(API) manufacturers		B	A	A	I
		The number of research and development based manufacturers		A	A	B	I
	Pharmaceutical manufacturing development	Packaging and labelling of bulk finished pharmaceuticals		C	B	A	I
		Finished pharmaceuticals manufacturing from API		C	B	A	I
		API manufacturing		B	A	A	I
		Research and development		A	A	B	I
Pharmaceutical authorization	Pharmaceutical regulatory authority	Pharmaceutical regulatory authority		C	B	A	I
		List of pharmaceuticals approved by the authority		C	B	A	I
	Pharmacovigilance and monitoring of adverse drug reactions	Pharmacovigilance		A	A	A	I
		↳If available,	Specific measures	A	A	A	II
		Monitoring of adverse drug reactions		A	A	A	I
		↳If available,	Specific measures	A	A	A	II
	Guidelines regarding pharmaceuticals	Presence of Good Manufacturing Practices(GMP)		C	B	A	I
		↳If available,	Implementation of GMP	C	B	A	II
		Presence of Good Distributing Practices(GDP)		C	B	A	I
		↳If available,	Implementation of GDP	C	B	A	II
		Presence of Good Pharmacy Practice(GPP)		C	B	A	I
		↳If available,	Implementation of GPP	C	B	A	II
	Substandard and falsified medical products(SF)	Monitoring SF		A	A	A	I
		↳If available,	Specific measures	A	A	A	II
		Sanctions against SF		A	A	A	I

		↳If available,	Specific measures	A	A	A	II
Procurement and distribution	Procurement	Procurement system in public areas such as hospitals		C	B	A	I
		Public procurement system for essential medicines		C	B	A	I
	Distribution	Margins among various supply chains such as wholesalers, retailers, and pharmacy level		C	B	A	I
		Price variations of specific medicines among various supply chains		C	B	A	I

Importance- A: Recommended for the use as core indicators, B: Appropriate for the use as core indicators, C: Can be used as core indicators, if necessary.
Feasibility- I: High level of feasibility based on previous studies, II: Additional effort is required based on previous studies

Table 9. Agenda and outcome indicators_ Affordability

Agenda	Outcome Indicators	Specific Outcome Indicators	Importance			Feasibility
			High-income	Upper middle-income	Lower middle-income	
Transparency of pharmaceutical pricing	Information collection	Information system at the national/government level for collecting real-time information on the price, volume and expenditure	A	A	A	I
		Routine tracking of price information for the medicines on the reimbursement list	B	A	A	II
		Routine tracking of volume information for the medicines on the reimbursement list	B	A	A	II
		Routine tracking of expenditure information for the medicines on the reimbursement list	B	A	A	II
	Information sharing	Publicly available information on the final rules and regulations for the pricing	A	A	A	I
		Establishment of a network for sharing pharmaceutical pricing information within a region	A	A	A	I
Affordability at the national/government level	Decision on pricing	Price negotiation method for medicines procurement in public sector	B	B	A	II
		Policy for lowering the price of original medicines	B	B	B	I
	Pharmaceutical financing	Budget for medicines on the essential medicines list	C	B	A	I
		Management of pharmaceutical expenditure at the national/government level (e.g. Total pharmaceutical expenditure management, post management of expenditure for individual medicines)	A	A	B	I
Affordability at the individual level	Consumption	Public acceptance level on the use of generic medicines	A	A	A	II
	Price	Price level for the patients for a specific medicine (a list of medicines can be selected for this indicator based on the burden of disease in the Asia Pacific region)	A	A	A	II
	Expenditure	Percentage of pharmaceutical expenditure as a share of total health expenditure	A	A	A	I
		Average annual expenditure on medicines for an individual	A	A	A	I
		Percentage of average pharmaceutical expenditure as a share of GNI per capita	A	A	A	I

Importance- A: Recommended for the use as core indicators, B: Appropriate for the use as core indicators, C: Can be used as core indicators, if necessary.
Feasibility- I: High level of feasibility based on previous studies, II: Additional effort is required based on previous studies

Table 10. Agenda and outcome indicators_ Rational use

Agenda	Outcome Indicators	Specific Outcome Indicators		Importance			Feasibility
				High-income	Upper middle-income	Lower middle-income	
Structure for organization, education, and management	Organization	National unit promoting rational use of medicines		A	A	A	I
		↳If present,	Specific organization	A	A	A	I
		↳If present,	Specific measures	A	A	A	II
		National drug information center		C	B	A	I
		↳If present,	Specific measures	C	B	A	II
	Education	For health care professionals	Regarding essential medicines list	C	B	A	I
			Regarding standard treatment guidelines	A	A	A	I
			Regarding generic prescribing and substitution	A	A	A	I
		For patients	Regarding antibiotics	B	B	A	I
			Regarding injections	B	B	A	I
			Regarding generic prescribing and substitution	A	A	A	I
	Management	National strategy to contain antimicrobial resistance		A	A	A	I
		National strategy for enhancing generic medicines		A	A	A	I
		In public sector	Generic substitution	A	A	A	I
			Specific measures to enhance generic substitution	A	A	A	I
		In private sector	Generic substitution	A	A	A	I
			Specific measures to enhance generic substitution	A	A	A	I
Treatment process and outcome	Prescription	Percent of prescribed drugs belonging to essential medicines list		C	B	A	II
		Percent of drugs prescribed by generic name		A	A	A	II
		Percent of patients prescribed antibiotics		B	A	A	II
		Percent of patients prescribed injections		B	A	A	II
	Treatment	Percent of patients treated in compliance with standard treatment guidelines		B	A	A	II

Importance- A: Recommended for the use as core indicators, B: Appropriate for the use as core indicators, C: Can be used as core indicators, if necessary.
Feasibility- I: High level of feasibility based on previous studies, II: Additional effort is required based on previous studies

2. Practical applications of research findings

2.1 Applications for agenda and outcome indicators

- This study developed interim and long-term agenda for improving access to medicines and making progress toward a regional network in the Asia Pacific region.
  - The classification of countries were suggested according to each country's current status of UHC and national medicine policy.
  - Additionally, level- and stage-based agenda and outcome indicators were suggested based on the multi-dimensions of access to medicines, health system and the delivery of medicines.
- This study proposed the following interim- and long-term plan.
  - 2017 – 2018: Development and prioritization of level- and stage-based agenda
  - 2018 – 2019: Status quo analysis on UHC and access to medicines
  - 2021: Interim evaluation and recommendations
  - 2026: Final evaluation, resolution and recommendations
- The agenda and outcome indicators suggested in this study should be discussed at the Annual Meeting on Access to Medicines under Universal Health Coverage in the Asia Pacific Region. The potential discussion points are given below.
  - Domain level
    - Specific evaluation domains and the prioritization
  - Agenda level
    - Specific agenda and the prioritization
  - Outcome indicator level
    - Specific outcome indicators
    - The importance of outcome indicators
    - The feasibility of outcome indicators

- Each Member State should take responsibility for the first draft of the status quo analysis based on the outcome indicators (2018-2019). WHO Collaborating Center for Health System and Financing (Seoul National University Graduate School of Public Health) can provide technical support for data collection if necessary.
    - To minimize Member State's burden on data collection and evaluation, the importance of outcome indicators should be presented.
    - Member States should play an active role in reviewing outcome indicators that have low level of feasibility but high level of importance.
    - Furthermore, evaluation and monitoring for the 23 excluded countries should be performed in the future.
- The outcome of this study can be used to suggest future directions of the Annual Meeting on Access to Medicines under Universal Health Coverage in the Asia Pacific Region and to outline resolutions and recommendations.
    - Based on the discussion at the meeting, the measures for global-level cooperation as well as recommendations specific to country groups can be suggested.

2.2 Capacity building for the regional network

- Establishing an effective network based on the classification of Asia Pacific countries
    - As presented in this study, the classification of Asia Pacific countries can be useful to develop agenda and effective cooperation plan through group networks based on the current status of UHC and access to medicines.
    - When establishing a network, it is important to assess policy needs for access to medicines because each country may have different needs depending on different circumstances.
- Planning and organizing activities for evidence generation
    - As WHO EVIPNet (Evidence-Informed Policy Network), and Europe's Pharmaceutical Pricing and Reimbursement Information (PPRI) exemplifies, a cross-border network can help facilitate systematic policy development though organized

collection and sharing process of policy evidence .

- Member States should cooperate with the sharing, collection and analysis of national data.

- Continuous policy monitoring and interactions within a network
  - Since improving access to medicines under UHC is a long-term agenda, strategies for the management of long-term network should be developed.
  - Policy monitoring and interactions within a network on a regular basis can be helpful for systematic operation of the network.
  - Publication of country reports, dissemination of the research and conference can be useful tools for achieving long-term goals.

3. Recommendations

3.1 Asia Pacific countries

- Each Member State should actively participate in the evaluation and collection of information to assess current situation of UHC and access to medicines.
  - This study suggested the prioritization of the outcome indicators based on the importance and feasibility to promote efficient data collection and minimize Member State's burden.
  - Routine data can be important source of evidence for monitoring and evaluation of future policy.

- Since different countries have different priorities for improving access to medicines, this study suggested the prioritized evaluation domains by income levels.
  - Firstly, high income countries have high priorities for finance and value for money, affordability and rational use.
  - Secondly, upper-middle income countries have high priorities for finance and value for money, affordability, rational use, development, production and distribution.
  - Thirdly, lower-middle income countries have high priorities for all evaluation

domains: finance and value for money; affordability; rational use; development, production and distribution; essential medicines.

3.2 Asia Pacific regional network

- A regional network should play an active role in evidence generation and policy development.
  - Examples of activities include networking, publication of country report, conferences, policy analysis, monitoring, evaluation, benchmarking and needs assessment.
- As suggested previously, interim- and long-term plan for the network can be summarized as follows.
  - 2017~2018: Development and prioritization of agenda and outcome indicators
  - 2018~2019: Status quo analysis on UHC and access to medicines
  - 2021: Interim evaluation and recommendations
  - 2026: Final evaluation, resolution and recommendations
- The shared agenda and outcome indicators derived from this research can facilitate the policy recommendations within the regional network.
  - This study suggested the prioritization of agenda and outcome indicators based on income level, but it is recommended that more specific prioritization should be developed after assessing each country group's situation within a network.

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