

Chapter 21

Priority-Setting Processes for Expensive Treatments for Chronic Diseases

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INTRODUCTION

Cardiovascular, respiratory, and related chronic disorders are an increasing concern in low- and middle-income countries (LMICs). In 2010, 19 percent (408.7 million) of total disability-adjusted life years (DALYs) and 39 percent (17.0 million) of total deaths in LMICs were attributable to cardiovascular and circulatory diseases, chronic respiratory diseases, diabetes mellitus, and chronic kidney diseases combined. The burden in LMICs accounts for 85 percent and 80 percent of global cardiovascular, respiratory, and related chronic disorder DALYs and deaths, respectively (IHME 2013).

Several treatment options are available for each disease, ranging from generic pharmacologic treatments, such as aspirin for vascular disease, metformin for diabetes, and salbutamol for chronic respiratory disease, to invasive procedures, such as coronary artery bypass graft surgery for vascular disease or kidney transplant for chronic kidney disease. These invasive procedures are often costly and resource intensive, placing a large burden on a country's health care system.

Governments face tough allocation choices for limited public resources across many competing priorities, as each country strives to achieve universal coverage of essential health care services under the Sustainable Development Goals. The large and growing burden of cardiovascular, respiratory, and related chronic disorders forces public

payers to allocate, or at least consider allocating, increasing resources to these diseases and conditions. This chapter explores the difficulty of rationing health resources in LMICs. Governments and public payers may allocate resources using priority-setting policy tools such as essential medicines lists (EMLs), health benefit plans, and health technology assessment (HTA) agencies. Yet, the processes used to arrive at allocation decisions are rarely evidence based, transparent, or participatory.

Furthermore, although the focus of this chapter is on high-cost treatment, the need for a legitimate and evidence-driven priority-setting process applies to all health conditions and diseases, and preventive measures cannot be ignored; the priority-setting process is not complete without considering local evidence on the costs and benefits of both prevention and treatment.

The chapter is divided into three sections. The first section frames the topic of priority setting in health. The second section explores a case study that shows how national essential medicines lists (NEMs) largely fail to influence prescription shares of types of insulin for which marginal cost-effectiveness has not been fully established in several LMICs. The third section examines a second case study that shows the complexity of the priority-setting process in Thailand's decision to include dialysis in the national health insurance (NHI) plan's benefits package.

FRAMING THE ISSUES

A fundamental challenge for all health systems is allocating finite resources across the potentially unlimited demand for health services and technologies. This is a rationing problem, regardless of whether it is explicitly addressed as such, because it requires that choices be made regarding how and when services are provided, to whom, and by what mechanism across many dimensions (Ham and Robert 2003). Inevitably some demand goes unmet, which is one source of the intense pressure to provide more services and newer and more sophisticated technologies within any given resource envelope. Efforts to reduce waste, increase quality, and improve efficiency are all responses to this pressure. Expanding health care costs and spending are indications of the same forces.

Conflicts in priority-setting decisions reflect natural features of all societies, including differences in demographics and disease burden as well as cultural preferences and beliefs. In addition, there are no universal answers to the inevitable policy questions, such as the balance of support between preventive and therapeutic measures, or choices between disease control priorities. Insufficient institutional mechanisms for assessing various proffered priorities, evaluating political and economic constraints, and gathering input from citizens and stakeholders make this problem particularly acute for policy makers in LMICs.

The sheer size of the need for treatments for cardiovascular, respiratory, and related chronic disorders in LMICs forces public resources to be allocated to these conditions and ensures that these diseases will be an important concern for policy makers. Although noncommunicable diseases have traditionally been perceived as a high-income health burden, LMICs are increasingly experiencing these problems. Total DALYs and deaths in LMICs attributable to cardiovascular, respiratory, and related chronic disorders increased substantially from 16 percent of total DALYs (377.8 million) and 36 percent of total deaths (15.14 million) in 2000 to 19 percent of total DALYs and 39 percent of total deaths in 2010 (IHME 2013). Additionally, complications that arise from diabetes affect societies more broadly (van Dieren and others 2010). As cardiovascular, respiratory, and related chronic disorder needs grow, the demand for treatment increases. Consequently, the challenge of rationing becomes greater, and prevention efforts become more critical.

Although technical progress can be cost saving and reduce the relative price of health products and services, new technologies can also be costlier—although, ideally, more effective (Martins and Maisonneuve 2006).

Determining the extent of coverage for an intervention requires analysis of the costs and benefits for health. Most LMICs do not incorporate cost-effectiveness evidence, even when available, in spending decisions. Without an explicit rationing mechanism, many LMICs allocate resources to expensive, novel technologies that benefit a small number of people, while not implementing low-cost, highly effective interventions that would benefit a large number of people and provide greater population health gains (Hutubessy and others 2003). In addition, politics can play a role in the process. Industry leaders, health professional associations, and patients themselves are increasingly pressuring health systems to include novel treatments.

For LMICs, affordability is an important perspective. Although many health technologies may be cost-effective when assessed against a gross domestic product (GDP) per capita threshold (Culyer and others 2007; Johannesson and Weinstein 1993; Weinstein and Statson 1977), they may be unaffordable under a given budget constraint, forcing countries to say “no” to putatively cost-effective technologies—or resort to inequitable, implicit rationing methods. Treatments for chronic diseases can be affordable at one stage of a disease but not at another. For example, treatment at an early stage may be cost-effective to the health system, but it may become unaffordable once the disease has progressed. To that end, considering cost-effectiveness of preventive measures, such as screening, is particularly important.

In addition to cost-effectiveness, other values—including fairness, equity, human rights, respect and self-determination, and financial protection—similarly need to be factored into a decision-making framework in an evidence-based way. Although a full discussion is omitted from this chapter, Brock and Wikler (2006) address ethical issues in resource allocation and cost-effectiveness, and the World Health Organization (WHO) Consultative Group on Equity and Universal Health Coverage provides a three-part strategy that countries can use as a guideline for fair, progressive realization of universal health coverage (WHO 2014). Rights-based legal arguments, which have been used in some middle-income countries in Latin America and the Caribbean, have propelled the provision of expensive therapies without directly addressing how much should be spent, how the resources should be used, or what trade-offs might affect equity and health (Kinney and Clark 2004). However, it is important to recognize that many coverage decisions are made with no technical or social goals in mind, no underpinning analysis, and no due process of any kind; this reality is reflected in the case study that follows.

CASE STUDY 1: TYPE 2 DIABETES

This case study examines how NEMs as a priority-setting mechanism often fail to influence prescription shares of insulin analogs. This case study first discusses the burden of disease, treatment, and guidelines. Second, it discusses NEMs as a priority-setting mechanism and analyzes prescription data to gauge the effectiveness of NEMs as a priority-setting tool. It concludes with insights derived from the case study.

Disease Burden and Context

As described in earlier chapters of this volume, diabetes mellitus (type 1 and type 2¹) accounted for 1.9 percent (46.7 million) of DALYs and 2.4 percent (1.28 million) of deaths in 2010. Type 2 diabetes is a growing global concern, especially in LMICs. In 2009, medications for type 2 diabetes constituted the fourth-largest therapeutic class, generating total global sales of US\$30.4 billion (Cohen and Carter 2010). Lower-middle-income countries carry 51.8 percent of the burden of DALYs (24.2 million) and 49.3 percent of deaths (629 million) (IHME 2013). Approximately 90 percent of total diabetes mellitus cases are type 2.

Many pharmacological treatments combat diabetes. Several have been available for many years, such as metformin, which was discovered in the 1950s (Rojas and Gomes 2013). Other agents—such as insulin analogs, which contain small changes to conventional human insulins so that short-acting agents work more rapidly and long-acting agents deliver insulin more slowly—are new and their cost-effectiveness compared with conventional treatments has not yet been established (Cohen and Carter 2010). Newer agents include insulin degludec, an ultra-long-acting insulin analog approved by the European Medicines Agency and the Japanese Pharmaceutical and Medical Devices Agency but rejected by the United States Food and Drug Administration (European Medicines Agency 2014; Japan Pharmaceuticals and Medical Devices Agency 2013; Novo Nordisk 2013). Despite efforts to encourage the use of cost-effective medicines through such instruments as NEMs and clinical practice guidelines, no insulin is continuously accessible in many LMICs (Beran and Yudkin 2010). As a proportion of all prescriptions, prescriptions for treatments for which cost-effectiveness is not proven, such as insulin analogs, remains high in these countries.

The United Kingdom's National Institute for Health and Care Excellence (NICE) publishes clinical guidelines based on the best available evidence for appropriate care. For the type 2 diabetes patient to achieve target glycemic goals, NICE recommends adjustments in lifestyle as a first step.

If blood glucose levels remain unacceptably high or lifestyle management is inadequate, metformin is recommended as an initial pharmacological therapy. If lifestyle intervention and metformin fail to control blood glucose, the next step is to add a sulfonylurea; with further lack of blood glucose control, insulin can be initiated. Other agents, such as thiazolidinediones, glucagon-like peptide-1 agonists (GLP-1s), dipeptidyl peptidase-4 inhibitors, and sodium-glucose linked transporter-2 inhibitors (SGLT-2s), come later in the treatment paradigm or can be used as substitutes for patients for whom the paradigm may need tailoring (NICE 2009). However, these other agents, known as newer hypoglycemic drugs, are still being evaluated for safety and effectiveness (Karagiannis and others 2012; Pinelli and others 2008; Qaseem and others 2012).

Based on review of the available data, NICE recommends long-acting insulin analogs only to a subset of patients and only if one of the following conditions applies:

- The person needs assistance from a caregiver or health care professional to inject insulin, and use of a long-acting insulin analog (such as insulin detemir or insulin glargine) would reduce the frequency of injections from twice to once daily.
- The person's lifestyle is restricted by recurrent symptomatic hypoglycemic episodes, or the person would otherwise need twice-daily Neutral Protamine Hagedorn (NPH) insulin injections in combination with oral glucose-lowering drugs.
- The person cannot use the device to inject NPH insulin (NICE 2009).

Priority-Setting Mechanism: National Essential Medicines Lists

The EML is among the earliest efforts to provide a basis for explicit priority setting in LMICs. Since 1977, the WHO has published a model list with the intent of informing purchasing decisions by national health officials (van den Ham, Bero, and Laing 2011). The medicines on the list are selected based on public health relevance, evidence on efficacy and safety, and—to some extent—comparative effectiveness so that they satisfy the priority health care needs of the population (van den Ham, Bero, and Laing 2011). The model list—updated every two years based on applications from individuals, governments, pharmaceutical companies, and medical associations—is published online. Countries often create their own versions of EMLs, with infrequent updating. As of 2011, 156 countries had adopted versions of the EML (Glassman and Chalkidou 2012).

In many countries, the adoption of an EML does not lead to the availability of all—or indeed most—of the medicines listed. Surveys undertaken in 36 countries showed that the mean availability of the 15 most frequently surveyed medicines was 38.4 percent in public sector facilities and 64.2 percent in private sector facilities (Cameron and others 2009). The disconnect between the lists, availability, and actual use is likely to be related, at least in part, to the absence of attention and support for an affordability analysis in a specific country's public spending envelope. The WHO's model list includes some hospital and specialist medicines, but many countries seek international advice on how to handle new, higher-cost medications, which—although cost-effective—may be beyond the resources of the health system (PAHO 2010).

The medicines for type 2 diabetes on the 18th WHO EML (updated March 2013) are the following: metformin, NPH insulin, zinc suspension insulin, neutral insulin, glibenclamide, and gliclazide (WHO 2013). Table 21.1 compares the agents on the list with those on the NEMLs of 13 selected countries: Argentina, Brazil, Colombia, the Arab Republic of Egypt, Indonesia, Mexico, Morocco, Pakistan, Peru, the Philippines, South Africa, and República Bolivariana de Venezuela, plus Turkey. The countries were selected based on the availability of IMS MIDAS² medical data. Although IMS MIDAS medical data are available for Turkey, the country does not have an NEML.³

A comparison of antidiabetic medicines on the WHO model list and on NEMLs shows that in most sampled countries, NEMLs conform closely to WHO recommendations. For human insulins, few countries include other medicines on their NEMLs. Indonesia, the Philippines, South Africa, Thailand, and República Bolivariana de Venezuela include premixed (biphasic) insulin on their NEMLs. Only Argentina and Colombia include any insulin analogs. Argentina's NEML includes insulin aspart (a fast-acting insulin analog); Colombia's NEML includes three fast-acting insulin analogs (insulin aspart, insulin glulisine, and insulin lispro) and two long-acting insulin analogs (insulin glargine and insulin detemir). With the exceptions of Argentina and Colombia, the NEMLs conform closely to the WHO's recommendations.

Priority Setting in Action

This section analyzes prescription data to gauge the effectiveness of NEMLs as a priority-setting tool. It finds a high use of products that are expensive or that are not proven to be cost-effective in many countries. Figure 21.1 shows the proportion of each type of treatment out of total insulin retail prescriptions, which includes human

insulins and insulin analogs (Anatomical Therapeutic Chemical Classification System 4 code A10C) for June 2013 from the IMS MIDAS medical database.

Prescription data show high use of insulin analogs in many countries, despite NEML guidance. In several countries, non-analog human insulins make up the vast majority of retail prescriptions, as in Morocco (94.5 percent), Pakistan (90.5 percent), Egypt (79.9 percent), and Peru (75.7 percent).

However, in other countries, insulin analogs make up the majority of the retail prescription market share, even though only Argentina and Colombia include insulin analogs on their NEMLs. Long-acting insulin analogs—insulin glargine and insulin detemir—have the largest share in República Bolivariana de Venezuela (76.2 percent), Brazil (59.3 percent), Mexico (51.7 percent), Colombia (48.5 percent), the Philippines (44.6 percent), and Indonesia (42.8 percent). Fast-acting insulin analogs—insulin glulisine, insulin aspart, and insulin lispro—have the largest share in Turkey (52.3 percent), South Africa (48.7 percent), and Argentina (43.6 percent).

This analysis has several limitations. First, the retail prescription market does not capture the full market and thus does not show the whole picture. However, the results are indicative of extensive use of insulin analogs in a number of countries. Second, not all type 2 diabetes patients undergo insulin therapy, so the analysis captures only part of the patient population. Examining other classes of antidiabetics would be an interesting direction for further research. Third, the data capture only the moving average target of June 2013.⁴ Extending the period may provide a different composition of prescriptions and reveal broader trends in adoption and prescription of insulin analogs. Nevertheless, the current analysis provides a snapshot of the insulin market in LMICs that was not previously available in the literature and provides a starting point for follow-on work.

The case study of insulin analogs for the treatment of type 2 diabetes shows that NEMLs do not restrict the prescribing of medicines. In some countries, an NHI formulary—which is the responsibility of health insurers—can supersede an NEML. For example, in Ghana, both an NEML and an NHI formulary exist, but the two do not contain the same drugs. Countries could benefit from synchronizing the two mechanisms to ensure a more coordinated system for priority setting.

NEMLs and NHI formularies should be synchronized for available agents as well as for new products. The insulin analog case study is one example showing that countries would benefit from reviewing both available and novel interventions. A joint report by the International Insulin Foundation and the Health Policy Analysis Centre, with the support of the International Diabetes Federation,

Table 21.1 Antidiabetic Treatments on the WHO and National Essential Medicines Lists

	WHO (2013)	Argentina (2005)	Brazil (2010)	Colombia ^a (2015)	Egypt, Arab Rep. ^b (2006)	Indonesia (2008)	Mexico (2010)	Morocco (2008)	Pakistan (2007)	Peru (2010)	Philippines (2008)	South Africa (2008)	Turkey (No NEML)	Venezuela, RB (2004)
<i>Human insulins and analogs</i>														
Insulin, NPH (isophane)	X	X	X	X	X	X	X	—	X	X	X	X	—	X
Insulin, zinc suspension	X	X	—	X	X	—	X	—	X	—	X	—	—	—
Insulin, soluble (neutral)	X	X	X	X	X	X	X	—	X	X	X	X	—	X
Insulin, premixed (biphasic)	—	—	—	X	—	X	—	—	—	—	X	X	—	X
Insulin aspart	—	—	—	X	—	—	—	—	—	—	—	—	—	—
Insulin detemir	—	—	—	X	—	—	—	—	—	—	—	—	—	—
Insulin glargine	—	—	—	X	—	—	—	—	—	—	—	—	—	—
Insulin glulisine	—	—	—	X	—	—	—	—	—	—	—	—	—	—
Insulin lispro	—	X	—	X	—	—	—	—	—	—	—	—	—	—
<i>Sulfonylureas</i>														
Glibenclamide	X	X	X	X	X	X	X	X	X	X	X	X	—	X
Gliclazide	X	—	X	—	—	—	—	X	—	—	X	X	—	—
Glimepiride	—	—	—	—	—	—	—	X	—	—	—	—	—	—
Glipizide	—	X	—	—	—	X	—	—	—	—	X	—	—	—
<i>Biguanides</i>														
Metformin	X	X	X	X	X	X	X	X	X	X	X	X	—	X
<i>Alpha-glucosidase inhibitors</i>														
Acarbose	—	X	—	X	—	—	—	X	—	—	X	—	—	—

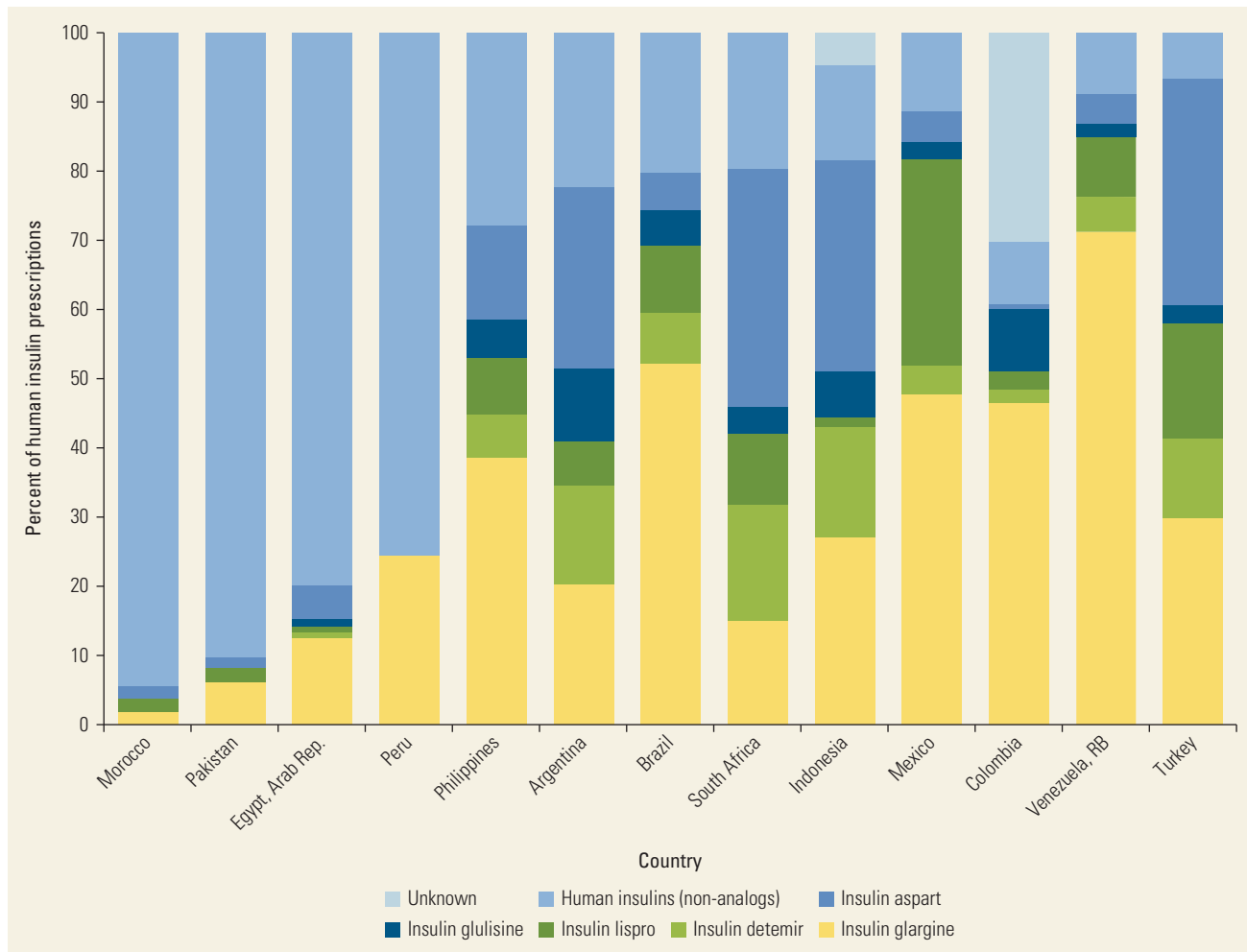
Source: Country-specific national essential medicines lists, available at http://www.who.int/selection_medicines/country_lists/en/.

Note: NPH = Neutral Protamine Hagedorn; WHO = World Health Organization. — = medication is not on the respective WHO or national essential medicines lists.

a. Colombia included insulin analogs in 2011, all others (NPH, zinc, neutral) were included in 2006.

b. For the Arab Republic of Egypt, insulins are listed as Human Insulin Short Acting, Human Insulin Intermediate Acting, and Human Insulin Long Acting.

Figure 21.1 Percentage of Total Human Insulin Retail Prescriptions by Treatment by Country, 2013



Source: IMS Health 2013.

finds that 57 percent of the Kyrgyz Republic’s insulin expenditure goes to insulin analogs. Based on their analysis, switching from an insulin analog to a human insulin could release enough resources to treat twice as many people (Abdraimova and Beran 2009).

Review of available technologies may lead to disinvestment, a process that has traditionally received little attention. Disinvestment involves withdrawing resources, either partially or entirely, from interventions—practices, procedures, pharmaceuticals, or medical devices—that are not cost-effective and do not lead to efficient resource allocation (Elshaug and others 2007). Interest in disinvestment is growing because of budget constraints in countries across all levels of development.

One of NICE’s tools for disinvestment is its “do not do” recommendations, a database of clinical practices that NICE’s independent advisory board compiles during the process of guidance development, because of

evidence that the practice is not beneficial or lack of evidence to support its continued use (NICE 2012). The database includes several recommendations for type 2 diabetes.

From guidance TA203: Liraglutide (a GLP-1 agonist) 1.8 milligrams daily is not recommended for the treatment of type 2 diabetes.

From guidance CG66: Exenatide (a GLP-1 agonist) is not recommended for routine use in type 2 diabetes.

From guidance TA288: Dapagliflozin (an SGLT-2 inhibitor) in a triple therapy regimen in combination with metformin and a sulfonylurea is not recommended for treating type 2 diabetes, except as part of a clinical trial.

Despite efforts to promote disinvestment, it is difficult to know the extent to which “do not do” lists are implemented given that there is no mandate to adopt the recommendations. A challenge for the United Kingdom’s National Health Service is the lack of data on usage beyond the primary care level as well as indication-specific precision (Garner and Littlejohns 2011). Drug utilization studies are critical. In addition, independent information interventions directed at clinicians and patients can reinforce messages of what to do and what not to do. Without these data and interventions, the health system cannot fully determine variations in care and the potential savings from disinvestment.

Case Study Insights

Despite policy makers’ attempts to use the NEML as a mechanism to promote cost-effective treatments, insulin analogs make up the majority of retail prescriptions and are purchased in significant quantities by public payers in some countries, with Colombia as a clear example (see also box 21.1). A number of lessons can be drawn from the case study.

Affirming the Role of Cost-Effectiveness Analyses in the Priority-Setting Process

The WHO model list is composed of treatments based on public health relevance, efficacy, safety, and comparative cost-effectiveness, yet the type 2 diabetes treatments on the NEMLs of many countries differ from the model list. In Morocco, the NEML does not include non-analog human insulins, which have been proven cost-effective; the NEMLs of Argentina and Colombia include insulin analogs, which have not been proven to be cost-effective for broad use, at least at the prices currently obtained by different purchasers.

Several reasons could contribute to the discrepancy, such as lack of awareness of the WHO model list or failure to update the NEML to reflect the best available evidence. However, another contributing factor could be that the model list does not reflect country-level cost-effectiveness analyses, and thus cannot be reconciled with the country’s public spending envelope. When governments seek to set priorities for the use of limited health resources, including updating an NEML, a global or regional reference is crucial but is only a starting point.

Comparing Priority-Setting Mechanisms and Processes in Similar Countries

Based on the analysis of the 13 NEMLs in this case study, NEMLs differ from each other as well as from the WHO model list. In addition, a comparison of human insulin prescriptions in retail markets shows vastly different

compositions across countries, at least of those captured in the IMS MIDAS database. Non-analog insulins make up more than 90 percent of human insulin prescriptions in Morocco and fewer than 10 percent of human insulin prescriptions in Turkey, despite similar epidemiological profiles with respect to population characteristics and diabetes prevalence.

Each country can learn from the priority-setting mechanisms and processes of other countries with similar characteristics, such as region, development status, burden of disease, or health system. In addition to the WHO model list, other countries’ NEMLs and processes could serve as good benchmarks when selecting treatments to include on an NEML or in a health benefits package. Data on actual use are helpful to understanding how prescribing levels of various treatments differ between similar countries. NEMLs are easy to obtain online, but obtaining data on actual use is more difficult. It may be costly to obtain use data from a third party; comparing data captured internally by governments requires a large amount of coordination among countries. These data need to be more readily available to enable countries to compare their own priority-setting mechanisms and processes with those in similar countries.

Staying Up to Date on the Market Authorization Process

The case study shows that the composition of human insulin treatment prescriptions is vastly different across countries. Since discrepancies occur between NEMLs and actual prescribing, the prescribing differences between countries are not simply the result of differences in medications listed but can be driven by the entry of new products as part of each country’s market authorization process. Once a new product comes to market, the pressure to publicly subsidize it increases.

It is important to be aware of market authorization processes, not only for a single treatment but for the treatment class as a whole. Understanding the market authorization process for classes of drugs in neighboring or similar countries can be useful for managing the pressures on and anticipating the changes to prescribing patterns.

Communicating Priority-Setting Processes and Decisions

In many countries, the actual priority-setting process—for example, exactly how or why a drug is included or excluded from an NEML—is not clear to the public.

Public awareness of the decision-making process and dissemination of the supporting evidence compels a payer or listing entity or the drug regulation entity to remain accountable for its decisions. Accountability mechanisms,

Box 21.1

Analog Insulin Pricing and Sales in Colombia

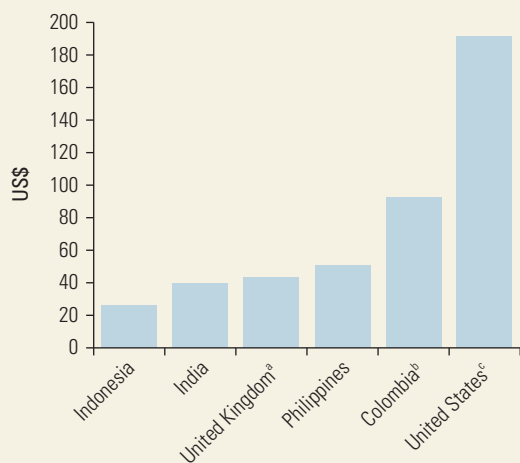
In June 2013, the price per package of Lantus, or insulin glargine, in Colombia was more than twice that in the United Kingdom and several middle-income countries (figure B21.1.1). In 2013, the Colombian government announced that it would regulate several hundred medications based on the international reference price, which benchmarks against the prices of countries such as Argentina, Brazil, Chile, Ecuador, France, Panama, and Spain. Under regulated pricing, the price per package of Lantus is US\$45.38; the unregulated price is US\$92.23 per 10 milliliter unit. The regulated price is closer to the price in the United Kingdom, although it is still higher than that in other countries.

In 2011, several insulin analogs were included in Colombia's publicly funded health benefits plan, which uses a national essential medicines list as a

reference to define the included medicines. Since then, government spending on insulin analogs has accelerated. All insulin analogs except insulin degludec are included in Colombia's national essential medicines list.

Industry- and wholesaler-reported data from a mandatory Ministry of Health system indicate sales to the public sector. These data show rapidly increasing sales of insulin analogs from 2010 to 2013 and a slight decrease in 2014 due to changes in regulation to change the reimbursable price for insulin analogs (figure B21.1.2). Total sales of fast- and long-acting insulin analogs increased by 102 percent and 143 percent, respectively, before 2010 and after the benefits plan was updated in 2012. Long-acting insulin analogs had sales of US\$55 million in 2013, more than five times the sales of fast-acting insulin analogs. In the past several years, insulin glargine—a long-acting insulin analog—has had the highest sales among insulin analogs, with US\$48 million in 2013, an increase from US\$13 million in 2010.

Figure B21.1.1 Price per Package (10 milliliter) of Lantus (Insulin Glargine), 2014



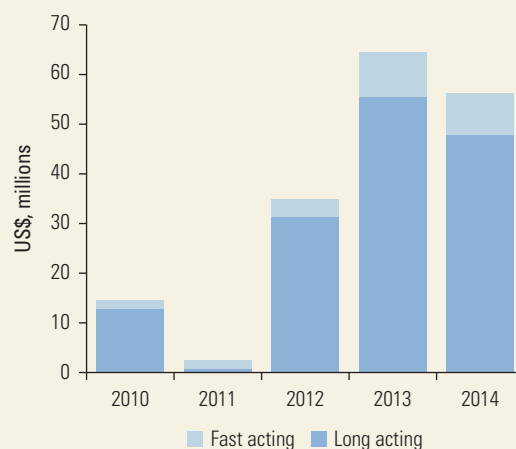
Sources: Colombia: Ministerio de Salud y Protección Social Colombia 2014; Indonesia, India, and the Philippines: MIMS 2014; United Kingdom: British Medical Association and the Royal Pharmaceutical Society of Great Britain 2011; United States: Truven Health Analytics 2014.

a. 2011.

b. Regulated price.

c. Wholesale acquisition cost.

Figure B21.1.2 Insulin Analog Sales to the Institutional Chain, 2010–14



Source: Ministerio de Salud y Protección Social Colombia 2014; SISMED 2014.
Note: Using the average 2013 exchange rate, 1 Col\$ = US\$0.0005.

such as the appointment of an independent, multidisciplinary committee or the establishment of an appeals process, are discussed in the next section (WHO 2011). These mechanisms reduce the influence of marketing pressures on priority-setting decisions; even if such pressures do have an impact, the mechanisms allow regulators to subsequently manage and minimize the risk of poor prescribing decisions.

The processes for selecting which drugs are on each country's NEML are not clear, especially when they deviate from the WHO model list. For example, Morocco's NEML does not include any non-analog human insulins. Colombia's NEML includes three fast-acting and two long-acting insulin analogs, but Argentina's NEML only includes one insulin analog. Several countries' NEMLs include acarbose, an alpha-glucosidase inhibitor, and glipizide, a sulfonylurea, neither of which are on the WHO model list.

Most countries lack explicit decision-making mechanisms of any kind, but progress has been made. Policy makers in LMICs are increasingly adopting policy instruments that explicitly define, limit, control, or guarantee the particular health technologies, interventions, and benefits that are to be funded and sometimes provided by the government. One approach to explicit priority setting has been to establish HTA entities to assess new and current medical technologies.

CASE STUDY 2: DIALYSIS IN THAILAND

This case study explores Thailand's decision to include dialysis in the benefits package of an NHI plan. First, it discusses the burden of disease, treatment, and

health coverage. Second, it discusses HTA agencies as priority-setting mechanisms. Then it examines Thailand's decision to include dialysis using a peritoneal dialysis (PD)—first policy in the Universal Coverage Scheme's (UCS) (box 21.2) benefits package. It concludes with insights from the case study.

Disease Burden and Context

The burden of kidney disease has increased as risk factors such as diabetes and high blood pressure have increased. In LMICs, the DALYs attributable to chronic kidney disease increased by 55 percent between 1990 and 2010 (from 11.0 million to 17.1 million); the number of deaths increased by 87 percent in the same period (from 0.29 million to 0.54 million) (IHME 2013). The increasing trend is notable, although the actual burden-of-disease values, as recognized earlier in this volume, for acute kidney injury, chronic kidney disease, and end-stage renal disease are understudied.

In Thailand, the burden has increased at an accelerated pace—the incidence of end-stage renal disease was 122 per million population (about 8,000 cases) in 2004 and 160 per million population (more than 100,000 cases) in 2007 (Tantivess and others 2013).

Patients with chronic kidney disease require lifetime renal replacement therapy through PD or hemodialysis,⁵ if not transplantation—and all interventions come at a high cost. Hemodialysis costs US\$12,000 per year, four times higher than the cost per quality-adjusted life year threshold for cost-effectiveness set by the National Health Security Office (NHSO) (Treerutkuarkul 2010). PD costs US\$7,300 per year. Instead of receiving treatment as

Box 21.2

Health Coverage in Thailand

In Thailand, nearly all citizens have health insurance coverage through three main schemes:

- Social Security Scheme (SSS)
- Civil Servant Medical Benefit Scheme (CSMBS)
- Universal Coverage Scheme (UCS).

SSS and CSMBS cover private and public employees; UCS—launched in 2001 through a reform to Thailand's public health financing system—covers the poor and near-poor. UCS gives each of its 48 million

members free care at health centers in their home districts, as well as at contracted hospitals and referrals to second- or third-level hospitals in urban areas.

UCS makes a comprehensive benefits package available to its members. Like SSS, UCS covers outpatient and inpatient care; accident and emergency services; dental and other high-cost care; and diagnostics, special investigations, medicines, and medical supplies. UCS also focuses on prevention by covering clinic-based preventive and health-promotion services in health centers.

prescribed, patients make do through other strategies, such as reducing the frequency of treatment, or they take other measures to fund treatment, such as borrowing money at high interest rates, a common occurrence in poor households (Tantivess and others 2013).

Priority-Setting Mechanism: Health Technology Assessment Agencies

HTA is the systematic appraisal of the properties, effects, or impacts of health technology through a wide range of research methods. In particular, value for money derived from comparative clinical and economic evaluation analysis (cost-effectiveness) is the major component of HTA. Many high-income countries have long used HTA to guide public reimbursement or coverage decisions. Almost all countries have national HTA agencies that prepare evidence dossiers, including cost-effectiveness analyses, as part of the application process for including new medicines for public reimbursement. Since 2005, HTA agencies or units have been established in upper middle-income or new high-income countries, including Brazil, Chile, Colombia, Croatia, Estonia, the Republic of Korea, Malaysia, Poland, Thailand, and Uruguay—and are increasingly influential in providing a basis for the uses of public funding.

The Health Intervention and Technology Assessment Program (HITAP) in Thailand is an autonomous arm of the Ministry of Public Health that provides evidence to support coverage decisions for the UCS benefits package. HITAP is a leader in its use of evidence to manage explicit priority-setting decisions. A highlight of Thailand's health system is that decisions for inclusion or exclusion in the UCS health benefits package are made using an ongoing, explicit priority-setting process by an HTA agency. Thailand's HITAP is sophisticated relative to its counterparts in other middle-income countries for several reasons: a scope beyond the assessment of pharmaceuticals, a deliberative process around HTA, the establishment of a locally relevant cost-effectiveness threshold, and formal stakeholder participation.

Priority Setting in Action

Generally, the UCS benefits package mirrors that of the Social Security Scheme (SSS). However, the SSS and the Civil Servant Medical Benefit Scheme benefits packages have included PD and hemodialysis since 1985 and 1990, respectively, while UCS did not, even though all three schemes rely on public funds. UCS patients—who are typically poor or near-poor—would receive a kidney disease diagnosis and learn that the treatment that

their life depends on would have to be self-financed (Treerutkuarkul 2010).

In the early 2000s, nephrologists and patients made a strong push for inclusion of dialysis in the UCS benefits package on the basis of the equity and financial protection goals of the UCS (Tantivess and others 2013; Treerutkuarkul 2010). At the time, patient groups had not participated in the HTA process; however, for dialysis, an organization called the Thai Kidney Club received support from the HIV/AIDS (human immunodeficiency virus/acquired immune deficiency syndrome) and cancer patient networks, as well as from the Thai Nephrologists Association (Tantivess and others 2013; Treerutkuarkul 2010). Newly in office following a government coup, public health minister Mongkol Na Songkhla sought to identify what forms of therapy should be made available and how dialysis could be financed in a sustainable way.

In response, the NHSO commissioned policy researchers and nephrologists to evaluate the value for money of dialysis. The study found that neither PD nor hemodialysis was cost-effective relative to Thailand's threshold. However, compared with hemodialysis, providing PD would be a relatively cost-effective option. Based on the study's estimates, PD would cost 466,000–497,000 Thai baht (US\$15,000) per life year saved or 667,000–700,000 Thai baht (US\$21,400) per quality-adjusted life year gained, depending on the patient's age (Teerawattananon, Mugford, and Tangcharoensathien 2007). The infrastructure and human resources needed to treat patients using hemodialysis were concentrated in urban centers, making the treatment inaccessible to rural populations, while PD had a home treatment option (Tantivess and others 2013). Based on the results of the study, the NHSO decided in 2007 to offer PD as a first-line therapy in the UCS benefits package—the PD-first policy.

To make the policy feasible in the long term, the burden of kidney disease had to be controlled. The Ministry of Public Health implemented community screening programs, with financial incentives for community health workers, to boost early detection and treatment of hypertension and diabetes. This effort was accompanied by knowledge strengthening and training to provide information throughout the continuum of care (Tantivess and others 2013).

Despite the measures taken to reduce the burden of kidney disease, the sustainability of this policy is in question. Over the course of 2007–09, the annual incidence of hemodialysis increased by 8 percent (Tantivess and others 2013); the incidence of PD increased by 150 percent (Praditpornsilpa and others 2011). Since 2008, many more patients have received PD—the number of patients grew from less than 1,000 before 2008

to nearly 8,000 per quarter in 2011 (Tantivess and others 2013). By 2012, the number of dialysis units had increased from 23 to 160 and plateaued at this level, with each unit taking on an increasing number of patients (Tantivess and others 2013). Annual budget allocations for dialysis started at US\$5 million (160 million Thai baht), or 0.2 percent of the total NHSO budget in 2008, but grew to US\$115 million (3.9 billion Thai baht), or 3.4 percent of the total budget in 2012 (Tantivess and others 2013). With continuing increases in the burden of diabetes and hypertension, and most likely kidney disease, the budget for dialysis is likely to increase. Some experts expect that the dialysis budget could be as high as 12 percent of the total budget once access is at full scale (Treerutkuarkul 2010).

Case Study Insights

Thailand is a leader in the universal health coverage movement as evidenced by its early success in reforming the country's health financing system to provide nearly

every citizen with health insurance. This health system is supported by a sophisticated HTA agency that sets priorities through an explicit and evidence-driven process. This case study explores the process of including dialysis in the UCS benefits package and some of the considerations involved (a parallel example on South Africa is provided in box 21.3). A few lessons can be drawn from this example.

Acknowledging the Importance of Equity- and Ethics-Related Commitments

Cost-effectiveness and value for money are often key concerns when considering particular interventions to be included or excluded from a benefits package. The decision to include PD in the UCS benefits package was deliberate, based on results from economic evaluations but also considering equity- and ethics-related factors.

The equity-based argument for inclusion of dialysis compared the relative coverage between the UCS and the other two schemes, given that all are supported by public funds. In addition, the UCS aims to reduce catastrophic

Box 21.3

Dialysis in South Africa

South Africa's experience with dialysis highlights the challenges with treatment rationing—a difficult decision-making process faced by all countries because the demand for dialysis far exceeds the available resources. Only one of five patients with health insurance or those who are wealthy enough to pay out of pocket for the US\$20,000 per year treatment receives dialysis. The remainder rely on public health insurance coverage under a system that has to allocate money to other health priorities.

A dialysis selection committee at each hospital decides which patients will receive coverage for dialysis treatment; there is no explicit decision-making system. Even though apartheid ended in South Africa in 1994, a study finds that white patients were more likely to be accepted for dialysis treatment than nonwhites at Tygerberg between 1988 and 2003. Patients who were to be covered by health insurance for dialysis were selected on the basis of “social worth”—such as income and criminal record—as judged by medical practitioners.

South Africans are working on making the priority-setting process more equitable and transparent. Until 2010, medical staff made decisions based on what they perceived to have been economically beneficial to the hospitals with no involvement by hospital managers. In 2010, provincial officials and medical professionals worked together to create official guidelines for patient selection. A more explicit and accountable system was created. Patients were classified based on medical factors, such as age and body mass index, as well as social factors, such as access to running water and electricity and evidence of financial means to afford transport to a renal unit.

Still, hospitals have to turn away patients. Physicians struggle with the priority-setting process for deciding which patients can receive treatment as well as where they can receive treatment; in addition, they bear the burden of telling the patient.

Sources: Fink 2010; Renal Services Task Team 2010.

expenditures on health for the Thai poor and near-poor. For those who needed dialysis, having to pay large out-of-pocket sums meant that the UCS did not deliver on its promise of financial protection. This case study shows that HTA goes beyond the numbers-based evidence provided by economic analysis by including evidence that involves equity, ethical, social, and legal implications.

Including Input from All Key Stakeholders

The case study shows that the priority-setting process affects many different parties—including policy makers in the Ministry of Public Health, academics, providers in hospitals and health clinics, community health workers, professional associations, and patients. In Thailand, the HTA through HITAP in theory provides an avenue for all stakeholders to play a role in policy change, and this was true for decisions around dialysis.

Through accountability mechanisms such as the appointment of an independent, multidisciplinary committee or establishing an appeals process, the public can take ownership of policy decisions. A transparent priority-setting process via information sharing can limit conflicts between interests (Tantivess and others 2013). For example, physicians recommended coverage of hemodialysis rather than PD based on favorable medical evidence. However, through information sharing—especially of the cost-effectiveness data—and an inclusive process, providers were convinced to accept the decision for PD as first-line therapy.

Incorporating Disease Prevention Measures in the Priority-Setting Process

The burden of noncommunicable disease—specifically cardiovascular, respiratory, and related chronic disorders—will continue to increase in the absence of serious efforts to control risk factors. And because interventions for noncommunicable disease can be expensive and perhaps required for a lifetime, publicly financing these treatments can place a serious burden on a country's economy.

An important component of the UCS is health promotion, and the Thai government continues to invest in such programs. For the early detection and prevention of diabetes and hypertension, the Ministry of Public Health in 2011 launched a US\$76 million program of screening measures in 5,500 communities. Still, some in the NHSO consider the health promotion funds to be insufficient and hope to increase efforts to promote healthier lifestyles and prevent noncommunicable diseases overall, not only kidney disease (Treerutkuarkul 2010).

Interventions that target disease prevention cannot be left out of the priority-setting process. When policy makers invest in an expensive curative intervention, it is

also important to consider the opportunity cost of investing in preventive interventions. In some cases, treatment alone can be cost-effective but not when coupled with screening.

Using Priority-Setting to Strengthen Overall Health System Capacity

Including an intervention in the benefits package is not just about gathering the evidence and making a decision. For the government to be able to deliver on promises, other parts of the health system must adjust to accommodate new policies. In Thailand, the NHSO encouraged the establishment of clinics that could provide PD in public facilities, particularly first-level hospitals, and partnered with private facilities when it realized that the capacity of public facilities was insufficient (Tantivess and others 2013).

Since 2008, the infrastructure and human resources to accommodate the inclusion of dialysis in the UCS benefits package have been developed. The number of PD clinics increased from 23 to 160 between 2008 and 2012, and the number of nurses trained to care for dialysis patients increased from 56 to 423 during that same period (Tantivess and others 2013). Finding the resources to build the capacity for the provision of dialysis has enabled many to benefit from dialysis coverage under the UCS.

It is not yet clear whether the inclusion of dialysis has had a population health impact, such as improved life expectancy, on the UCS population. As in the previous case study, the Thai dialysis example shows that review of current interventions included in a benefits package, not just new technologies, is crucial in the priority-setting process.

CONCLUSIONS

This chapter brings to light the challenges facing evidence-based resource allocation for health, especially to meet the increasing demand for the treatment of cardiovascular, respiratory, and related chronic disorders. Policy makers in LMICs must weigh prevention, affordability, and ethical considerations in addition to cost-effectiveness when deciding on whom and for what the government will spend. Interventions, both preventive and curative, can be cost-effective, depending on the context, such as disease progression. The priority-setting process can be greatly influenced by political considerations.

The first case study examines prescribing data for human insulin for type 2 diabetes, and reports that, despite being available, an NEML may not have an impact on what treatments physicians actually prescribe

and patients actually use. The second case study examines Thailand's decision to include dialysis in the UCS benefits package. Thailand has a sophisticated, explicit priority-setting mechanism—HITAP, its HTA agency—yet, the NHSO still has to make difficult coverage decisions.

Both examples show that countries can benefit from reviewing available interventions in addition to new ones. Crucially, the examples show the importance of institutional capacity in carrying out the process of explicit priority setting to guide technology adoption decisions. Explicit priority setting uses a transparent, deliberative process led by an independent, multidisciplinary committee that considers evidence—as well as other factors, such as inclusiveness—to drive decisions.

A better priority-setting system can provide a fair and transparent mechanism for managing the politics of resource allocation, connect evidence-based decisions to budgets, and create permanent institutional channels for considering resource allocation choices over time.

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NOTES

World Bank Income Classifications as of July 2014 are as follows, based on estimates of gross national income (GNI) per capita for 2013:

- Low-income countries (LICs) = US\$1,045 or less
- Middle-income countries (MICs) are subdivided:
 - (a) lower-middle-income = US\$1,046–US\$4,125
 - (b) upper-middle-income (UMICs) = US\$4,126–US\$12,745
- High-income countries (HICs) = US\$12,746 or more.

1. People with type 1 diabetes have a total lack of insulin due to immune system response, while people with type 2 diabetes do not have enough insulin or are insulin resistant.
2. IMS MIDAS medical data show exactly what is being prescribed for a disease or therapy area and is standardized internationally.
3. Many countries, including Turkey, are moving to health insurance formularies that sometimes coexist with and sometimes supersede EMLs, which become defunct and disappear.
4. Average of May, June, and July 2013.
5. Hemodialysis uses an artificial kidney outside the body to filter blood; peritoneal dialysis uses the lining of the abdominal cavity to filter blood.

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