Chapter 22. Priority-Setting Processes for Expensive Treatments in Cardiometabolic Diseases

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Abstract:

This chapter explores the difficulty of rationing health resources in low- and middle-income countries (LMICs), particularly for the treatment of cardiometabolic diseases. We discuss issues and dilemmas faced by policymakers in the allocation of scarce public resources for management of cardiometabolic diseases, explore how priority-setting policy instruments like national essential medicines lists can fail to influence patterns of use and spending around the world, and examine efforts to set priorities using more systematic processes in Thailand. We conclude with policy implications.

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Outline

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Introduction

Cardiometabolic diseases 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. The burden in LMICs accounts for 85 percent and 80 percent of global cardiometabolic DALYs and deaths, respectively (Institute for Health Metrics and Evaluation 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 transplants 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. The large and growing burden of cardiometabolic diseases 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, health benefit plans, and health technology assessment agencies. Yet, the processes to arrive at allocation decisions are rarely evidence-based, transparent, or participatory.

Further, 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 disease, 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 provides a framing of the topic of priority-setting in health. The second section explores a case study that shows how national essential medicines lists (NEMLs) largely fail to influence prescription shares of types of insulin without fully established marginal cost-effectiveness in several LMICs. The third section examines a second case study that shows the challenging nature of the priority-setting process in Thailand's decision to include dialysis in the benefits package of a national health insurance scheme.

Framing the Issues

A fundamental challenge for all health systems is to allocate 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 choices of what services to provide, how to provide them, at what quantity, to whom, at what time, and at whose expense. 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. Further, there are no universal answers to inevitable policy questions, such as the balance of support for preventive and therapeutic measures, or choices between disease control priorities. Insufficient institutional mechanisms to assess various proffered priorities, evaluate political and economic constraints, and gather input from citizens and stakeholders makes this problem particularly acute for LMIC policymakers.

The sheer size of the need for cardiometabolic treatments in LMICs forces the allocation of public resources to these conditions and ensures that these diseases will be an important concern for policy makers. Although noncommunicable disease has traditionally been perceived as a high-income health burden, LMICs are increasingly experiencing these problems. In 2010, 19 percent of total DALYs and 39 percent of total deaths in LMICs were attributable to cardiometabolic diseases, up from 16 percent of total DALYs (377.8 million) and 36 percent of total deaths (15.14 million), respectively, in 2000 (Institute for Health Metrics and Evaluation 2013). Additionally, complications that arise from diabetes affect societies more broadly (van Dieren, Beulens et al. 2010). As cardiometabolic disease 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 be costlier—although, ideally, more effective (Martins and Maisonneuve 2006). Making coverage decisions for an intervention requires analysis in terms 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 a low-cost, highly effective intervention that would benefit a large number of people and provide greater population health gains (Hutubessy, Baltussen et al. 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 be more inclusive of novel treatments.

For LMICs, the perspective of affordability is also needed. Although many health technologies may be cost-effective when assessed against a GDP per capita threshold, (Weinstein and Statson 1977, Johannesson and Weinstein 1993, Culyer, McCabe et al. 2007), 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. For chronic diseases, a treatment can be affordable at one stage of a disease but not another. For example, treatment at an

early stage may be cost-effective to the health system, but 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 a way that is evidence-based. Rights-based legal arguments, which have been used in some Latin American middle-income countries, have compelled the provision of expensive therapies without directly addressing how much should be spent, how the resources should be used, or trade-offs that might affect equity and health (Kinney and Clark 2004). However, it is important to recognize that many coverage decisions are taken 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

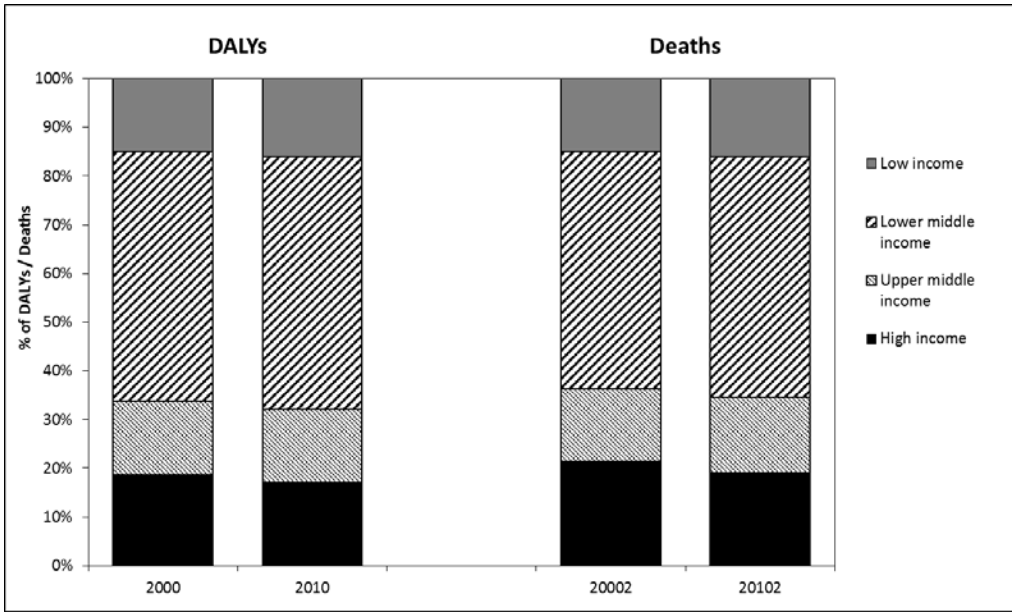
This case study examines how NEMLs often fail as an effective priority-setting mechanism to influence prescription shares of insulin analogs. First, it discusses the burden of disease, treatment, and guidelines. Second, it discusses NEMLs as a priority-setting mechanism. Then, it analyzes prescription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

Disease Burden and Context

As described in earlier chapters of this volume, diabetes mellitus (type 1 and type 2[1]) 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 sales of US$30.4 billion (Cohen and Carter 2010). Lower-middle-income countries carry 51.8 percent of the burden in terms of DALYs (24.2 million) and 49.3 percent of deaths (629 million) (Institute for Health Metrics and Evaluation 2013). Approximately 90 percent of total diabetes mellitus cases are type 2.

[1] People with type 1 diabetes have a total lack of insulin due to immune system response, while people with type 2 diabetes don't have enough insulin or are insulin resistant.

Figure __.1 Global Diabetes Mellitus DALYs and Deaths by Income Group, 2000-10



Source: IHME GBD 2010. (Institute for Health Metrics and Evaluation 2013)

Note: DALYs = disability-adjusted life year.

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 are new and have not yet established cost-effectiveness compared to conventional treatments, such as insulin analogs, agents with small changes to conventional human insulins, so that short-acting insulins work more rapidly and long-acting insulins deliver insulin more slowly (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 (Japan Pharmaceuticals and Medical Devices Agency 2013, Novo Nordisk 2013, European Medicines Agency 2014). Despite efforts to encourage the use of cost-effective medicines through such instruments as NEMLs and clinical practice guidelines, no insulin is continuously accessible in many LMICs (Beran and Yudkin 2010). The proportion of prescription volumes 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 (TZDs), glucagon-like peptide-1 agonists (GLP-1s), dipeptidyl peptidase-4

inhibitors (DPP-4s), and sodium-glucose linked transporters-2 (SGLT-2s), come later in the treatment paradigm or as substitutes for use in patients for whom the paradigm may need tailoring (Centre for Clinical Practice - National Institute for Health and Care Excellence 2009). However, these other agents, known as newer hypoglycemiants, are still being evaluated for safety and effectiveness (Pinelli, Cha et al. 2008, Karagiannis, Paschos et al. 2012, Qaseem, Humphrey et al. 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 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 NPH insulin injections in combination with oral glucose-lowering drugs.
- The person cannot use the device to inject NPH insulin (Centre for Clinical Practice - National Institute for Health and Care Excellence 2009).

Priority-Setting Mechanism: National Essential Medicines Lists

The essential medicines list (EML) is among the earliest efforts to inform explicit priority-setting in LMIC. Since 1977, the WHO publishes a model list with the intent to inform purchasing decisions by national health officials (van den Ham, Bero et al. 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" (page 2) (van den Ham, Bero et al. 2011). The model list—updated every two years based on applications—is published online. Countries often create their own versions of EML, with infrequent updating. As of 2011, 156 countries have 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% in public sector facilities and 64.2% in private sector facilities (Cameron and others 2009). The disconnect among the lists, availability, and actual use is likely to be related, at least in part, to the absence of attention and support for the analysis of affordability 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—while cost-effective—may be beyond the resources of the health system (Pan American Health Organization 2010).

The type 2 antidiabetic medicines on the 18th WHO essential medicines list (updated March 2013) are the following: metformin, NPH insulin, zinc suspension insulin, neutral insulin, glibenclamide, and gliclazide (World Health Organization 2013). Table __.1 compares the agents on the WHO 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. The countries are selected based on the availability of IMS MIDAS[2] medical data. Although Turkey has IMS MIDAS medical data available, it does not have an NEML. [3]

A comparison of antidiabetic medicines on the WHO model list and those on NEMLs showed that in most sampled countries, NEMLs conform closely to WHO recommendations. In terms of human insulins, few countries include other types on their NEML. Indonesia, the Philippines, South Africa, Thailand, and República Bolivariana de Venezuela include pre-mix (biphasic) insulin on their NEMLs. Only Argentina and Colombia includes any insulin analog. Argentina's NEML includes insulin aspart (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 __.2 shows the proportion of each type of treatment out of total insulin retail prescriptions, which includes human insulins and insulin analogs (ATC4 code A10C) for June 2013 from the IMS MIDAS medical database.

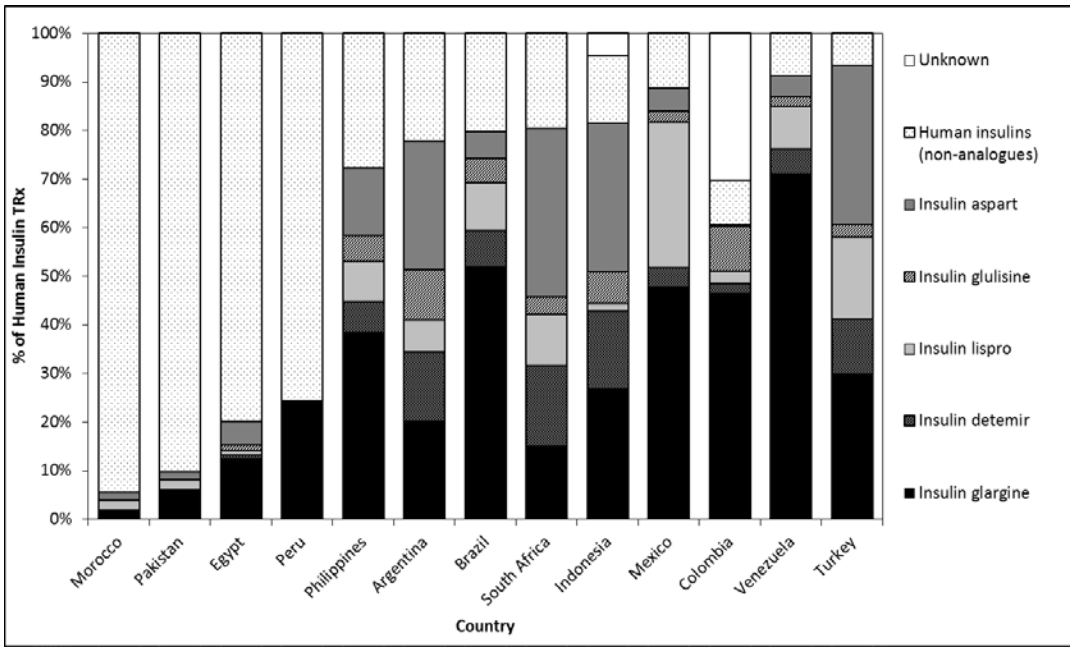
Prescription data however shows a high use of insulin analogues in many countries, despite NEML guidance. In several countries, non-analogous human insulins make up the vast majority of retail prescriptions, as in Morocco (94.5 percent), Pakistan (90.5 percent), the Arab Republic of Egypt (79.9 percent),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

However, in other countries, insulin analogues make up the majority of the retail prescription market share, even though only Argentina and Colombia included insulin analogues on their respective NEMLs. Long-acting insulin analogues—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).

Figure __.2. Percentage of Total Human Insulin Retail Prescriptions by Treatment by Country, 2013

[2] IMS MIDAS medical data shows 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 sometime supersede essential medicines lists, which become defunct and disappear.



Source: IMS Health, IMS MIDAS Medical Data, June 2013.

(IMS Health 2013)

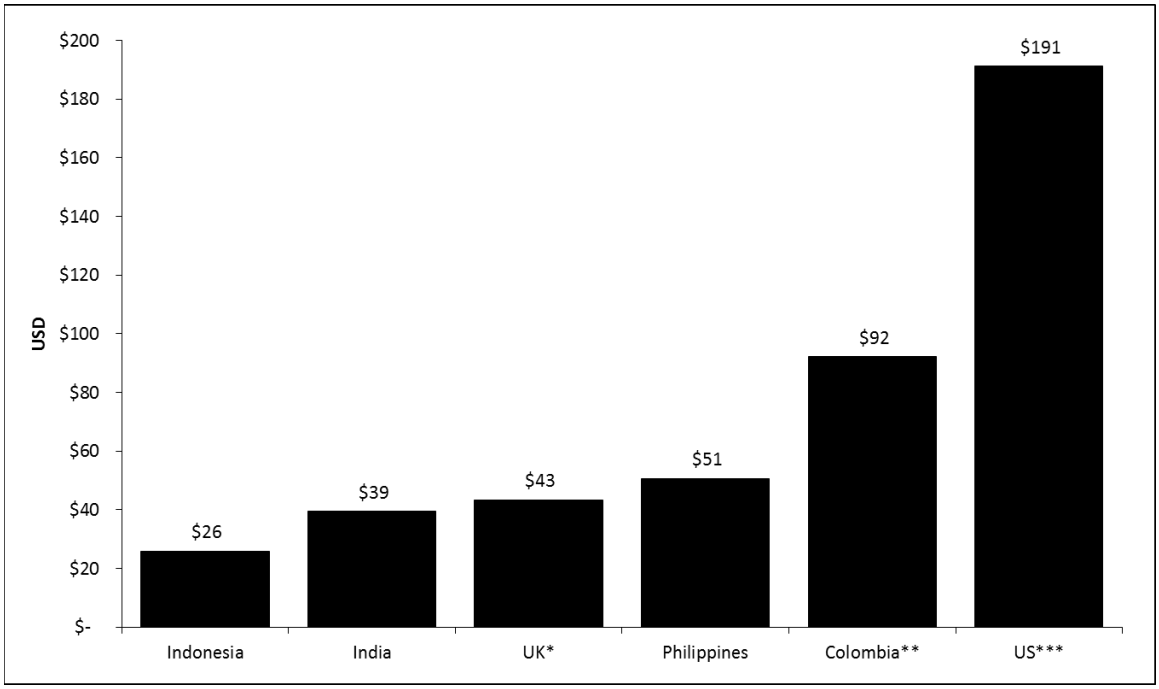
There are several limitations to our analysis. First, the retail prescription market does not capture the full market and thus does not show the whole picture. However, the results are indicative of extensive use in insulin analogues in a number of countries. Second, not all type 2 diabetes patients undergo insulin therapy, so we capture only part of the patient population. Examining other classes of antidiabetics would be interesting for further research. Third, the data captures only the moving average target of June 2013.[4] Extending the time period may provide a different composition of prescriptions and reveal broader trends in adoption and prescription of insulin analogues. Nevertheless, our current analysis gives a snapshot of the insulin market in LMIC that was not previously available in literature and provides a starting point for follow-on work.

Box __.1 Analogous 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 of the United Kingdom and several middle-income countries (figure B__.1). In 2013, the Colombian government announced that it would regulate several hundred drugs 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 ml unit. The regulated price is closer to the price of the United Kingdom, although it is still higher than that of other countries.

[4] Average of May, June, and July 2013.

Figure B__.1 Price Per Package (10 Ml) Of Lantus (Insulin Glargine) (US$), 2014



Countries selected based on availability of price information.

*2011; **Regulated price; ***Wholesale Acquisition Cost (WAC).

Sources: Indonesia, India, and the Philippines: MIMS, MIMS Drug Information, 2014); United Kingdom: British Medical Association and the Royal Pharmaceutical Society of Great Britain, British National Formulary 61, 2011; United States: Truven Health Analytics, Red Book Online, 2014

(British Medical Association and the Royal Pharmaceutical Society of Great Britain 2011, MIMS 2014, Truven Health Analytics 2014)

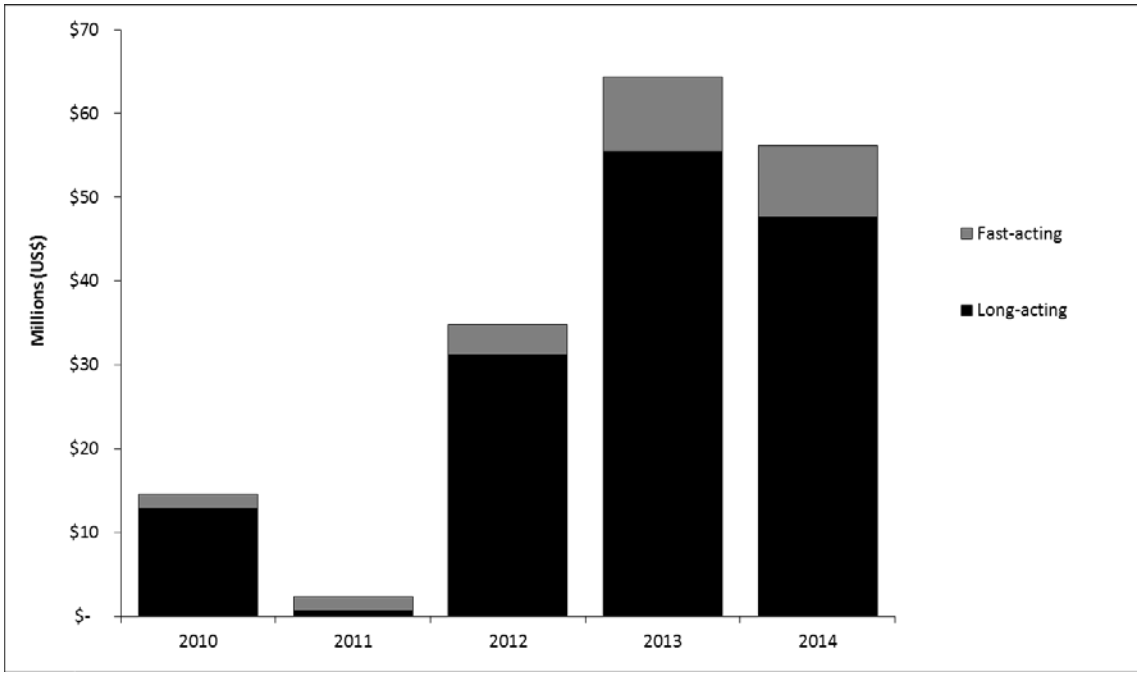
In 2011, several insulin analogues were included in Colombia's publicly-funded health benefits plan, which uses a national NEML as a reference to define the medicines included. Since then, government spending on insulin analogues has accelerated. All insulin analogues except insulin degulec are included in Colombia's NEML.

Industry and wholesaler reported data from a mandatory Ministry of Health system indicates sales to the public sector. This data shows rapidly increasing sales of insulin analogues from 2010 to 2013 and a slight decrease in 2014 due to changes in regulation to change the reimbursable price for insulin analogues (figure B__.2). Total sales of fast- and long-acting insulin analogues increased by 102% and 143%, respectively, before (2010) and after (2012) the updated benefits plan. In dollar terms, long-lasting insulin analogues had sales of US$48 million in 2013, over five times the sales of fast-acting insulin analogues. In the past several years, insulin glargine—a long-

acting insulin analogue—has had the biggest sales among insulin analogues, with US$48 million in 2013, an increase from US$13 million in 2010.

Note: [a]Using average 2013 exchange rate, 1 COL$ = US$0.0005.

Figure B__.2 Analogous insulin sales to the institutional chain (US$), 2010-14



Source: Ministerio de Salud y Protección Social Colombia, Sistema de Información de Medicamentos, 2014. (Ministerio de Salud y Protección Social Colombia 2014)

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

The drugs on the NEML and NHI formulary should be synchronized for available agents as well as for new products. The insulin analog case study is one example that shows that countries will 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, found that 57 percent of Kyrgyzstan's insulin expenditure goes to insulin analogs. Based on their analysis, switching from an insulin analog to a human insulin can release enough resources to treat twice as many people (Abdraimova and Beran 2009).

Review of already 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 represent efficient resource allocation (Elshaug, Hiller et al. 2007). Interest in disinvestment is growing due to budget constraints in countries across all levels of development status.

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 (National Institute for Health and Care Excellence 2012). The database includes several recommendations for type 2 diabetes.

From guidance TA203:	Liraglutide (GLP-1 agonist) 1.8 mg daily is not recommended for the treatment of type 2 diabetes.
From guidance CG66:	Exenatide (GLP-1 agonist) is not recommended for routine use in type 2 diabetes.
From guidance TA288:	Dapagliflozin (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 the efforts to promote disinvestment, it is difficult to know the extent to which "do not do" lists are implemented, as 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 and the necessary, indication-specific precision (Garner and Littlejohns 2011). Drug utilization studies are critical. In addition, independent information interventions directed to 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 of disinvestment.

Case Study Insights

Despite the attempt of policy makers 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 outlier. 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 NEMLs of many countries differ from the model list. In Morocco, the NEML does not include non-analogous 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 failing 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 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 the retail markets showed vastly different compositions across countries, at least of those captured in the IMS MIDAS database. Non-analogous insulins make up over 90 percent of human insulin prescriptions in Morocco and less 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 qualities such as region, development status, burden of disease, or health system. In addition to the WHO model list, the NEMLs and processes of other countries could be a good benchmark when selecting treatments to include on an NEML or in a health benefits package. Data on actual use are helpful in learning about how prescribing levels of various treatments differ in similar countries. NEMLs are easy to obtain online, but getting data on actual use is more difficult. It may be costly to obtain use data from a third party; to compare data captured by governments internally requires a large amount of coordination among countries. These data need to be more readily available, so countries are able to compare their own priority-setting mechanisms and processes with similar countries.

Staying Up To Date on the Market Authorization Process

The case study showed that across countries, the composition of human insulin treatment prescriptions is vastly different. Since discrepancies occur between NEMLs and actual prescribing, the prescribing differences among 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 adopt for public subsidy increases.

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

Communicating Priority-Setting Processes and Decisions

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

Awareness of the decision-making process and dissemination of the supporting evidence allow a payer/listing entity or the drug regulation entity to remain accountable for its decisions. Accountability mechanisms, such as the appointment of an independent, multidisciplinary committee or the establishment of an appeals process, are discussed in the following section. (World Health Organization 2011). These mechanisms reduce the ability of marketing pressures to heavily influence a priority-setting decision; even if such pressures do have an impact, the mechanisms allow regulators to subsequently manage and minimize risk of poor prescribing decisions.

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

In most countries, there is no explicit decision making mechanism of any kind, but there is progress. LMIC policymakers are increasingly adopting policy instruments that explicitly define, limit, control, or guarantee particular health technologies, interventions, and benefits to be funded and sometimes provided by the government. For example, one approach to explicit priority-setting has been to establish health technology assessment entities to assess new and current medical technologies.

Case Study 2: Dialysis in Thailand

This case study explores the country's decision to include dialysis in the benefits package of a national health insurance scheme. First, it discusses the burden of disease, treatment, and health coverage. Second, it discusses health technology assessment agencies as a priority-setting mechanism. Then, it examines Thailand's decision to include dialysis under a "peritoneal dialysis (PD) first" policy in the Universal Coverage Scheme's 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 (CKD) increased by 55 percent between 1990 and 2010 (11.0 to 17.1 million); the number of deaths has increased by 87 percent in the same period (0.29 to 0.54 million) (Institute for Health Metrics and Evaluation 2013). The increasing trend is worth noting, although the actual burden of disease values, as recognized earlier in this volume, for acute kidney injury (AKI), CKD, and end-stage renal disease (ESRD) are understudied.

In Thailand, the burden has increased at an accelerated pace—the incidence of ESRD was 122 per million population (about 8,000 cases) in 2004 and 160 per million population (over 100,000 cases) in 2007 (Tantivess, Werayingyong et al. 2013).

Patients with chronic kidney disease require lifetime renal replacement therapy through peritoneal dialysis 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 (QALY) threshold for cost-effectiveness set by the National Health Security Office (NHSO) (Treerutkuarkul 2010). Peritoneal dialysis costs US$7,300 per year. Instead of receiving treatment as 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, Werayingyong et al. 2013).

BOX __.2 Health coverage in Thailand

In Thailand, nearly all citizens have health insurance coverage through three main schemes: the Social Security Scheme (SSS), the Civil Servant Medical Benefit Scheme (CSMBS), and the Universal Coverage Scheme (UCS). SSS and CSMBS cover private and public employees; UCS—launched in 2001 through a reform of 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 contracted hospitals and referrals to second- or third-level hospitals in urban areas.

UCS makes available a comprehensive benefits package 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.

Priority-Setting Mechanism: Health Technology Assessment Agencies

Health technology assessment (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 developed nations have long used HTA to inform public reimbursement or coverage decisions. Almost all countries have national HTA agencies that prepare evidence dossiers, including cost-effectiveness analysis, as part of applications for including new medicines for public reimbursement. Since 2005, HTA agencies or units have been established in upper middle-income or newly high-income countries, including Brazil, Chile, Colombia, Croatia, Estonia, the Republic of Korea, Malaysia, Poland, Thailand, and Uruguay—and are increasingly influential in informing 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 front-runner in its use of evidence to inform explicit priority-setting decisions. A highlight of Thailand's health system is that decisions for

[5] Hemodialysis uses an artificial kidney outside of the body to filter blood, while peritoneal dialysis uses the lining of the abdominal cavity to filter blood.

inclusion and exclusion in the UCS health benefits package are made through an ongoing, explicit priority-setting process by a 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 health technology assessment; 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 SSS. However, the benefits packages of SSS and CSMBS have included peritoneal dialysis and hemodialysis since 1985 and 1990, respectively, while UCS does 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 equity and financial protection, goals of UCS (Treerutkuarkul 2010, Tantivess, Werayingyong et al. 2013). At the time, patient groups were not well known in the health technology assessment process, but for dialysis, an organization called the Thai Kidney Club received support from the HIV and cancer patient networks, as well as the Thai Nephrologists Association (Treerutkuarkul 2010, Tantivess, Werayingyong et al. 2013). 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 can 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 peritoneal dialysis nor hemodialysis was cost-effective relative to Thailand's threshold. However, providing peritoneal dialysis would be a relatively cost-effective option, compared to hemodialysis. Based on the study's estimates, peritoneal dialysis would cost 466,000-497,000 Baht (US$15,000) per life year saved or 667,000-700,000 Baht (US$21,400) per QALY gained, depending on the patient's age (Teerawattananon, Mugford et al. 2007). The infrastructure and human resources needed to treat patients with hemodialysis were concentrated in urban centers, making it inaccessible to rural populations, while peritoneal dialysis had a home treatment option (Tantivess, Werayingyong et al. 2013). Based on the results of the study, the NHSO decided in 2007 to offer peritoneal dialysis as a first-line therapy in the UCS benefits package—the PD-first policy.

In order 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 was accompanied by knowledge strengthening and training to provide information throughout the continuum of care (Tantivess, Werayingyong et al. 2013).

Despite the measures taken to reduce the burden of kidney disease, the sustainability of this policy is in question. Over the course of two years, annual hemodialysis incidence increased by 8

percent (Tantivess, Werayingyong et al. 2013); peritoneal dialysis incidence increased by 150 percent (Praditpornsilpa, Lekhyananda et al. 2011). Since 2008, many more patients receive peritoneal dialysis—the number of patients grew from less than 1,000 to nearly 8,000 per quarter in 2011 (Tantivess, Werayingyong et al. 2013). By 2012, the number of units had increased from 23 to 160 and plateaued at this level, with each unit taking on an increasing number of patients (Tantivess, Werayingyong et al. 2013). Budget allocations for dialysis started out at US$5 million (160 million Baht), or 0.2 percent of the total NHSO budget in 2008, but it grew to US$115 million (3.9 billion Baht), or 3.4 percent of the total budget in 2012 (Tantivess, Werayingyong et al. 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 fully scaled (Treerutkuarkul 2010).

Box __.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 receive dialysis. The rest of the patients relies on public health insurance coverage under a system that has to save money for other health priorities.

A dialysis selection committee of each hospital decides which patients receive coverage for dialysis treatment; there is no explicit decision-making system. Even though apartheid ended in South Africa in 1994, a study found that white patients were nearly four times more likely to be accepted for dialysis treatment than non-whites 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.

The South Africans are working on making the priority-setting process more equitable and transparent. Until 2010, medical staff made decisions based on what may have economic benefits 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 transport to a renal unit.

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

Source: (Fink 2010, Renal Services Task Team 2010)

Case Study Insights

Thailand is a leader in the universal health coverage movement through 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 health technology assessment agency that sets priorities through an explicit and evidence-driven process. This case study explored the process of including dialysis in the UCS benefits package and some of the considerations involved. 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 include in or exclude from a benefits package. The decision to include PD in the UCS benefits package was deliberate, taking 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 UCS and the other two schemes, since all are supported by public funds. In addition, UCS aims to reduce catastrophic 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 UCS did not deliver on its promise of financial protection. This case study shows that health technology assessment goes beyond the numbers-based evidence provided by economic analysis—it includes 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 health technology assessment through HITAP in theory provides an avenue for all stakeholders to play a role in policy change, and this was true in the case of the 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 in policy decisions. A transparent priority-setting process, via information sharing, can limit conflicts between interest (Tantivess, Werayingyong et al. 2013). For example, physicians recommended coverage of hemodialysis over peritoneal dialysis 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 peritoneal dialysis as first-line therapy.

Incorporating Disease Prevention Measures in the Priority-Setting Process

The burden of noncommunicable disease—and specifically cardiometabolic diseases—will continue to increase without serious efforts to control risk factors. Since interventions for noncommunicable disease also can be either more expensive and/or required for a lifetime, publicly financing these treatments can place a serious burden on a country's economy.

An important component of 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 covering screening measures in 5,500 communities. Still, some in the NHSO consider the health promotion funds insufficient and hope to increase efforts to promote healthier lifestyles and prevent noncommunicable diseases overall, not only dialysis (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 peritoneal dialysis in public facilities, particularly first-level hospitals, and partnered with private facilities when it realized that the capacity of public facilities was insufficient (Tantivess, Werayingyong et al. 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 peritoneal dialysis 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, Werayingyong et al. 2013). Finding the resources to build the capacity for the provision of dialysis has enabled many to benefit from dialysis coverage under 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 the review of current interventions included in a benefits package, not only new technologies, are 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 cardiometabolic diseases. Policy makers in LMICs must weigh prevention, affordability, and ethical considerations on top of 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 politics.

The first case study, which examines prescribing data of human insulin for type 2 diabetes, illustrates that despite the availability of an NEML, it may not have an impact on what treatments physicians actually prescribe and patients 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 health technology assessment 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 those that are new. Most important, they show the importance of an explicit priority-setting mechanism to inform technology adoption decisions. Explicit priority-setting employs a transparent, deliberative process led by an independent, multidisciplinary committee, which uses evidence to guide decisions while promoting inclusiveness.

A better priority-setting system—whether global or national—can increase the rigor and relevance of evidence considered, provide a fair and transparent mechanism to manage the politics of resource allocation, connect evidence-based decisions to budget, and create permanent institutional channels to consider resource allocation choices over time.

Note

<<unnumbered>>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 to US$4,125
  b) upper-middle-income (UMICs) = US$4,126 to US$12,745
- High-income countries (HICs) = US$12,746 or more.

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Table 1. Antidiabetic treatments on WHO and national essential medicines lists

	WHO (2013)	Argentina (2005)	Brazil (2010)	Colombia* (2015)	Egypt** (2006)	Indonesia (2008)	Mexico (2010)	Morocco (2008)	Pakistan (2007)	Peru (2010)	Philippines (2008)	South Africa (2008)	Turkey (No NEML)	Venezuela (2004)
Human insulins and analogues														
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, Pre-mix (biphasic)				X		X					X	X		X
Insulin aspart				X										
Insulin detemir				X										
Insulin glargine				X										
Insulin glulisine				X										
Insulin lispro		X		X										
Sulfonylureas														
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			
Biguanides														
Metformin	X	X	X	X	X	X	X	X	X	X	X	X		X
Alpha-glucosidase inhibitors														
Acarbose		X		X				X			X			

*Colombia included insulin analogues in 2011, all others (NPH, neutral, zinc) were included in 2006 (Source: Authors); **For Egypt, insulins are listed as “Human Insulins Short Acting,” “Human Insulin Intermediate Acting,” “Human Insulin Long Acting.”

Source: Country-specific NEMLs available at http://www.who.int/selection_medicines/country_lists/en/, accessed October 22, 2013.