The Health Technology Assessment Environment in Mainland China, Japan, South Korea, and Taiwan—Implications for the Evaluation of Diabetes Mellitus Therapies

Tessa Kennedy-Martin, MSc1, Beth D. Mitchell, RN, BSN2,*, Kristina S. Boye, MS, MPH, PhD3, Wen Chen, PhD4, Bradley H. Curtis, DDS, MPH, PhD, FICD5, Jennifer A. Flynn, MSPH6, Shunya Ikeda, MD, DMSc7, Li Liu, PhD8, Yen Huei Tarn, PhD9, Bong-Min Yang, PhD10, Emmanuel Papadimitropoulos, PhD2

1Kennedy Martin Health Outcomes Ltd, Brighton, United Kingdom; 2Eli Lilly and Company, Indianapolis, IN, USA; 3School of Public Health, Fudan University, Shanghai, P.R. China; 4Eli Lilly Japan K.K., Kobe, Japan; 5School of Pharmacy, International University of Health and Welfare, Ohtawara-city, Tochigi, Japan; 6Lilly Suzhou Pharmaceutical Co., Ltd, P.R. China; 7School of Pharmacy, National Defense Medical Center, Taipei, Taiwan; 8Seoul National University, Seoul, South Korea

ABSTRACT

Background: Diabetes mellitus (DM) is associated with a significant global economic and humanistic burden. The condition presents a real challenge in Asia, which accounts for more than 60% of individuals with DM globally. Health technology assessment (HTA) is a field of scientific research used to inform policy and clinical decision making relating to the introduction and diffusion of health technologies. Objectives: This article, examines the present use and predicted evolution of HTA with respect to pricing and reimbursement of drugs in mainland China, Japan, South Korea, and Taiwan. It makes specific reference to important assessment considerations for DM therapies, which should assist key stakeholders in choosing which data to capture, and what approaches to use, to help quantify the value of treatment. Methods: The findings are informed by two Advisory Board discussions, a literature review, and the authors’ personal experience. Results: HTA already has a key role in South Korea and Taiwan, with current systems undergoing important changes. In contrast, in mainland China and Japan, HTA is not yet formally utilized, although this appears likely to change. Several elements are important for HTA to be meaningful and impactful for DM therapies, including a clear, transparent analytical framework for HTA that includes all relevant costs and outcomes; availability of local DM epidemiologic, economic, and quality-of-life data; acceptance of modeling as a core methodology; availability of real-life patient data; and recognition of specific evidence requirements associated with biosimilars. HTA has the potential to assist payors in making informed decisions about the coverage of DM medications. Keywords: Asia, diabetes mellitus, health technology assessment, pricing, reimbursement.

Introduction

Asia accounts for more than 60% of the global population of people with diabetes mellitus (DM) [1]. In the Western Pacific region, which includes mainland China, Japan, South Korea, and Taiwan, there are 131.9 million people (8.5% of the adult population) who have DM, and this region also has the highest number of deaths attributable to DM: 15% of all deaths in 2011 were related to DM [2]. The prevalence of type 2 DM (T2DM) is increasing; this is being driven by a number of factors, including economic development, dietary changes, and increasingly sedentary lifestyles [3,4]. Compared with people in other regions, people in Asia tend to develop diabetes with a lesser degree of obesity and at younger ages, suffer longer from its complications, and die earlier [5]. There is great diversity in social and economic development, population size, health care system, language, religion, and culture across Asia [6]. In this article, we focus specifically on mainland China, Japan, South Korea, and Taiwan, which, despite their differences, all commonly face the growing challenge of DM.

Despite the existing evidence on the importance of intensive glycemic management [7–9], DM control is suboptimal. Studies in mainland China, South Korea, and Taiwan report that the proportion of patients with DM achieving a glycated hemoglobin level of less than 7.0% ranges from 32% to 44%; in Japan, only 34% of the patients with DM have been reported to have a glycated hemoglobin level of less than 6.5% [10–13].

DM imposes substantial demands on health care resources: it is estimated that the total global health care expenditure on DM in 2010 was at least US $376 billion, and this figure is expected to increase to US $490 billion by 2030 [4]. The International Diabetes Federation has
estimated country-by-country expenditures on adults with DM aged 20 to 79 years, expressed in US $ and in international dollars—a US dollar that is adjusted to account for differences in purchasing power [4]. National-level cost data for mainland China, Japan, and South Korea are presented in Table 1. A separate study reported that the total cost of DM to society in Taiwan is approximately US $2.96 billion, equivalent to approximately 0.8% of the gross domestic product [54].

The economic burden of DM is driven primarily by the cost of complications [15]. In a Japanese study, the medical costs for patients with DM with nephropathy were 2.1-fold higher than for those without nephropathy, while evidence of retinopathy and neuropathy was associated with 2.6-fold and 3.3-fold higher costs, respectively [16]. A Korean study reported that annual direct medical costs for a patient with only microvascular, only macrovascular, or both macrovascular and microvascular complications were 1.5, 2.7, and 2.0 times higher than the medical costs for patients without these complications [17].

Health technology assessment (HTA), as defined by the International Network of Agencies for Health Technology Assessment, is a multidisciplinary field of policy analysis, studying the medical, economic, social, and ethical implications of development, diffusion, and use of health technology [18]. It is accepted that through benefit-harm assessment and economic evaluation, a major use of HTA is to inform pricing, access, and reimbursement decisions. The main focus of our article, therefore, is to report whether, and if so how, HTA is presently used as part of the decision-making process to inform coverage and funding decisions of DM medications in mainland China, Japan, South Korea, and Taiwan, and to discuss how this could evolve in the future. The general themes included in this article were informed by discussions at Advisory Boards held in Hong Kong (October 2011) and Tokyo (October 2011) and were further refined through review of the published literature and the personal experience of the authors. We provide a brief overview of evidence-based assessment systems in mainland China, Japan, South Korea, and Taiwan, and discuss the implications of these systems on the pricing and reimbursement of DM medications. We anticipate that this overview will help to ensure that relevant outcomes and perspectives are included in future HTA analyses of DM treatment strategies and medications and that it will also assist manufacturers in choosing which data to capture to help quantify the value of their therapies for future evidence-based assessment and HTA analyses.

**Overview of the Role of HTA in Pricing and Reimbursement of Drugs**

Table 2 summarizes the current process for pricing and reimbursement for drugs, the role that HTA has in the current health care systems, and how this is expected to change in the future in mainland China, Japan, South Korea, and Taiwan. HTA already has a key role in the assessment of medications in South Korea and Taiwan. In contrast, HTA is not yet formally utilized in reimbursement and price decision making in mainland China or Japan, although this may change in the future.

In South Korea, economic evidence is required for a drug to be included in the Positive List Scheme (PLS). There is no benchmark for the incremental cost-effectiveness ratio because the Health Insurance Review Agency (HIRA) makes flexible judgments alongside other criteria such as disease severity and innovation. Nevertheless, a benchmark of approximately one times the gross domestic product per capita (US $26k, 2007) has evolved as a general reference value [19]. An assessment of 47 evaluations that were approved by HIRA after the introduction of the PLS found that, on average, 14 of the 20 items on the HIRA checklist for quality assessment of pharmacoeconomic evaluations submitted for coverage decisions were fulfilled. Where cost-utility analysis was undertaken, the incremental cost-effectiveness ratios from a societal perspective ranged from dominant to US $28k per quality-adjusted life-year for “recommended” submissions (n = 6), US $8k to US $20k per quality-adjusted life-year for “recommended with restricted use” submissions (n = 4), and US $13k to US $59k per quality-adjusted life-year for “not recommended” submissions (n = 3) [19]. Bae and Lee [20] reported that by the time of their published analysis in 2009, only 10 of these 47 drugs were actually priced and listed by the National Health Insurance Corporation [20]. The separation of the reimbursement recommendation by HIRA and the price/volume negotiation between the technology manufacturer and the National Health Insurance Corporation has led to claims that there is administrative duplication. In addition, the “listing lag” has generated skepticism from the industry [21]. Significant changes are currently ongoing in Taiwan since the second generation of the National Health Insurance system was implemented in 2013. The drug manufacturer submits the dossier according to the structure specified by the National Health Insurance Administration (NHIA) (see Table 2). The NHIA sends the dossier to the National Institute of HTA (previously the HTA group within the Center for Drug Evaluation), which conducts an independent assessment using comparative effectiveness and economic evidence, as well as undertaking its own budget impact analysis. The assessment report is then sent to the NHIA, where an expert consultation group conducts the initial appraisal. The new system introduced in 2013 involves a Pharmaceutical Benefit and Price Schedule Stakeholders’ meeting between the NHIA and public and medical professional representatives, who will make the final value judgment on the recommendations put forward by the expert consultation group. The judgment arising from the Stakeholders’ meeting is sent to the NHIA for a final decision. The price is initially recommended by the expert consultation group, and further approval is given at the Stakeholders’ meeting before the recommendation is sent to the NHIA. Similar to the previous system, the stronger the evidence for the drug, the higher the support for inclusion in the PLS. In addition, there are incentives offered for the use of local economic data, whereby a price premium of up to 10% is available if data from a local pharmacoeconomic study are submitted in the dossier.

In both mainland China and Japan, there are indications that HTA will have a future role in access to medicines (Table 2). The structure that this will take within the overall process of pricing, reimbursement, and access environment, however, is still under discussion.

**The Assessment of DM Medications within an HTA System**

A set of 15 best practice principles has been proposed that can be used to assess existing HTA programs. These are organized into four categories: structure of HTA programs, methods of HTA, processes for conducting an HTA, and use of HTAs in decision making [22]. It is not our aim to apply these principles to the geographies of interest, but rather to focus on some key features of an assessment framework that would have specific relevance to the appraisal of DM therapies. The list is not meant to be exhaustive and is intended to

<table>
<thead>
<tr>
<th>Region</th>
<th>National-level cost estimate (x1,000)</th>
<th>US $</th>
<th>ID</th>
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<tbody>
<tr>
<td>Mainland China</td>
<td>4,968,697</td>
<td>19,322,712</td>
<td></td>
</tr>
<tr>
<td>Japan</td>
<td>22,150,915</td>
<td>18,846,385</td>
<td></td>
</tr>
<tr>
<td>South Korea</td>
<td>4,130,467</td>
<td>5,361,541</td>
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</table>

DM, diabetes mellitus; ID, international dollars.
There are strong indications that HTA will be used in future listing, pricing, and reimbursement of pharmaceuticals. The 2009 NRDL revision plan states that costs and benefits of products in each base subcategory will be compared using pharmacoeconomic principles (insulin, e.g., is a base subcategory of “insulin and other blood sugar-influencing drugs”) [42].

In the 2013/2014 NRDL review, and in the future negotiation process for the Provincial Reimbursement Drug List (PRDL), pharmaceutical companies may be allowed to submit HTA data for premium-priced innovative drugs.

In addition, the NDRC in the “Guideline for Reform of Drug and Medical Service Pricing” [43] has expressed that pricing for substitute and innovative drugs should gradually adopt pharmacoeconomic evaluation.
Usefulness I premium, and 68 (16.8%) achieving a Usefulness II premium [45]. If there is no similar drug for comparison, the base price is calculated according to actual costing data (costs of research and development as well as costs of production and distribution), as supplied by the company [44].

After the base price for the new drug is determined, a foreign price adjustment is undertaken to minimize the price differential between Japan and other countries [44].

Every 2 years after listing, there is a repricing analysis based on market activity. There is currently little to no opportunity for a manufacturer to submit new evidence in defense of the price—this can be performed only during market expansion repricing, which is a separate activity with different triggers.

South Korea

The Korean National Health Insurance (KNHI) system funds drugs that are on the PLS. The PLS was introduced by the Government of South Korea as part of a Drug Expenditure Rationalization Plan [39].

Reimbursement and price decisions for new drugs are separated. The Health Insurance Review and Assessment Service (HIRA) is responsible for reimbursement assessment, and the NHIC negotiates the price with the pharmaceutical company [48].

When the new PLS was implemented in 2007, South Korea became the first Asian economy to require economic evidence for drug reimbursement [20].

In the process of listing a new drug, the manufacturer makes an application that is reviewed by HIRA, which also sources additional data and expert opinion. HIRA has published guidelines for submission that are publicly available (but not translated into English). HIRA evaluates the evidence and communicates the review results to the Drug Reimbursement Evaluation Committee (DREC) within HIRA, which then makes a recommendation on listing (positive recommendation, rejection, or restriction by indication). This decision is informed by cost-effectiveness data, clinical usefulness, the availability of alternatives, the severity of the condition to be treated, the budgetary impact, assessments from other countries, and the uncertainty of the evidence presented [20].

Based on HIRA’s assessment and international price referencing, the NHIC negotiates with the company on price. If the negotiation fails, the drug will not be placed on the PLS.

The HTA framework in Korea has not had any major changes since its inception in 2007. However, there have been some recent refinements in the methods outlined in the Pharmacoeconomic Submission Guidelines. For example, there are new guidelines for indirect comparison methodology, intended to help researchers use proper methods to assess clinical benefits. This is important because, historically, there was an excessive dependence on expert opinion to estimate the clinical benefits of new medical technologies. In addition, transparency of the review process is increasing with the availability of a preconsultation with HIRA reviewers. This interaction should help those submitting a dossier to identify data requirements early in the data preparation stage.

A number of future changes are anticipated in the Korean HTA framework. More flexible use of ICER thresholds may allow for slightly higher thresholds for selected technologies that manage severe diseases. In addition, the use of risk-sharing modules in reimbursement decisions for selected new technologies is now under consideration by the NHIC reimbursement authority, although the ultimate role of these modules would be expected to evolve over time within the Korean HTA system.

Taiwan

The reimbursement of drugs is determined by the National Health Insurance Administration (NHIA), which sits within the Ministry of Health and Welfare (MHW).

In Taiwan, HTA is undertaken for all new drugs for which reimbursement is sought through the NHIA program. A number of new developments were implemented when the second-generation NHIA law was passed in 2013.

Patient involvement as part of the HTA process is written into the new mechanism but a process for implementation is currently lacking. The NHIA is preparing a template that could be used for patient...
Following a positive appraisal by the NHIA, the drug is added to the National Health Insurance (NHI) formulary, after which it can be prescribed in any health care facility in Taiwan. A co-payment is required; this is determined by the price of the drug and is usually 20% of the drug price. If the drug is not listed, the patients can self-pay if they wish. The drug price is set by the NHIA according to the formula prepared by the NHIA staff and is determined in the appraisal meeting by the committee members. A new HTA process and a new committee for drugs, medical services, and medical devices was formed in April 2013. The reimbursement process (which now includes devices) involves three stages: 1) an HTA review by the NHIA, undertaken through the National Institute of HTA; 2) scientific judgment by an expert appraisal group; and 3) a recommendation on drug listing for the NHIA following the PBPS Stakeholders’ meeting, which consists of various agencies, experts/scholars, the insured, employers, and health care providers. The HTA process involves analysis of comparative effectiveness, pharmacoeconomics, and budget impact, as well as consideration of the social, legal, and social aspects of treatment. The National Institute of HTA gathers evidence from other HTA bodies, such as NICE, the Australian Pharmaceutical Benefits Advisory Committee (PBAC), and the Canadian Agency for Drugs and Technologies in Health (CADTH). The group searches the published literature for clinical and economic data on the drug. Using this evidence, and expert input if required, the group prepares a review within 42 d that includes an assessment of comparative effectiveness, pharmacoeconomics, and a budget impact model (BIM). This is based on evidence from the manufacturer’s submission, existing HTA reports, and the published literature rather than a stand-alone analysis (as is the case for the BIM). This report is sent to two reviewers on the Drug Expert Group who develop their own short (1–2 page) report, which is used by the PBPS committee to make listing, coverage, and pricing recommendations. Price incentives are offered, including the use of data from a local pharmacoeconomic study (up to 10%), improved efficacy (up to 15%), better safety (up to 15%), and greater convenience (up to 15%).

**Table 2 – continued.**

<table>
<thead>
<tr>
<th>Geographic area</th>
<th>Current drug pricing and reimbursement system</th>
<th>Role of HTA in health care system</th>
<th>Expected changes relating to the use of HTA in drug pricing and reimbursement</th>
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<tr>
<td></td>
<td></td>
<td>A new HTA process and a new committee for drugs, medical services, and medical devices was formed in April 2013. The reimbursement process (which now includes devices) involves three stages: 1) an HTA review by the NHIA, undertaken through the National Institute of HTA; 2) scientific judgment by an expert appraisal group; and 3) a recommendation on drug listing for the NHIA following the PBPS Stakeholders’ meeting, which consists of various agencies, experts/scholars, the insured, employers, and health care providers. The HTA process involves analysis of comparative effectiveness, pharmacoeconomics, and budget impact, as well as consideration of the social, legal, and social aspects of treatment. The National Institute of HTA gathers evidence from other HTA bodies, such as NICE, the Australian Pharmaceutical Benefits Advisory Committee (PBAC), and the Canadian Agency for Drugs and Technologies in Health (CADTH). The group searches the published literature for clinical and economic data on the drug. Using this evidence, and expert input if required, the group prepares a review within 42 d that includes an assessment of comparative effectiveness, pharmacoeconomics, and a budget impact model (BIM). This is based on evidence from the manufacturer’s submission, existing HTA reports, and the published literature rather than a stand-alone analysis (as is the case for the BIM). This report is sent to two reviewers on the Drug Expert Group who develop their own short (1–2 page) report, which is used by the PBPS committee to make listing, coverage, and pricing recommendations. Price incentives are offered, including the use of data from a local pharmacoeconomic study (up to 10%), improved efficacy (up to 15%), better safety (up to 15%), and greater convenience (up to 15%).</td>
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HTA, health technology assessment; ICER, incremental cost-effectiveness ratio; PBPS, Pharmaceutical Price and Benefit Schedule.
It is important that a transparent analytic framework for HTA is incorporated appropriate methods for assessing costs and benefits.

We suggest that the following five elements are important for HTA to be meaningful and impactful for DM therapies now and in the future Table 3.

1. **A clear, transparent analytic framework for HTA that incorporates appropriate methods for assessing costs and benefits**

It is important that a transparent analytic framework for HTA is in place and that the methods are clearly specified and, ideally, have been developed through a process of consultation with the various stakeholders (health care providers, patients and patient advocates, government agencies, pharmaceutical industry).

There are some challenges with the current systems in which HTA influences access to medicines, and these have implications for the assessment of DM drugs. In South Korea, a key issue has been the choice of the comparator, with different alternatives proposed by the company and HIRA, and attempts are being made to resolve this by initiating a prior consultation system [20].

The definition of clinical value or utility will be a key area for future discussion, not just in Asia but also across the world. One example comes from England, where the National Institute for Health and Care Excellence will have a central role in the future value-based pricing system for the National Health Service. This pricing system is expected to include an assessment of criteria such as severity of illness, the extent of unmet need, and the wider societal impact—including the effect on caregivers and the quantification of health gain [23]. Therefore, for DM medications it will likely be important to consider not only clinical effects (e.g., glycemic control, systolic blood pressure, and total cholesterol) and side effects (e.g., hypoglycemic events and weight gain) of treatment but also other aspects of value such as process-related elements (e.g., improved patient convenience), societal benefits (e.g., reduced impact on family members), and level of innovation.

It is also important to consider how the value of patient benefits could be recognized within the HTA framework. In DM, this could relate to an improved patient experience through the use of a better delivery device or regimen. In Taiwan, for new drugs approved as category 2 (moderate improvement or similar therapeutic value), and where the Dosage Regimen Ratio method is used to determine the drug price, there can be a price premium of up to 15% if the drug is more convenient or has other advantages (e.g., better route of administration and longer dosing interval).

2. **Availability of local epidemiologic, cost, and quality-of-life data**

It is highly preferable that local economic evaluations attempt to capture the epidemiologic profile of the relevant population and that they also include local cost data; country-specific utility data should be included if a cost-utility approach is being taken.

There are currently gaps in the cost data. For example, there are limited cost data on the economic burden of DM in mainland China, although recent initiatives, such as the study by Le et al. [24], which quantified the direct, indirect, and intangible costs in the rural Yunnan province of China, are attempting to bridge this gap. Further information is needed, not only on the overall economic burden of DM but also on the cost of managing DM and associated complications, so that these can be incorporated in economic analyses. It is important to recognize that some costs of DM fall on social care or community budgets and that these also need to be considered within the perspective of the analysis.

Regarding the availability of utility data, there are a number of studies in which the EuroQol five-dimensional questionnaire has been used in patients with DM, for example, in Korea [25], Japan [26], mainland China [27], and Taiwan [14]. Five-level EuroQol five-dimensional questionnaires are available in Chinese (traditional and simplified), Korean, and Japanese. In Korea, data from the Korea National Health and Nutrition Examination Survey IV (2007–2009) were used to quantify the relationship between DM and utility [28]. A recent study involving 2257 patients with T2DM from mainland China, Korea, Malaysia, Thailand, and Taiwan reported that mean EuroQol five-dimensional questionnaire scores were significantly lower for patients who had

<table>
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<tr>
<th>Type of premium</th>
<th>Level of premium</th>
<th>Criteria</th>
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<tbody>
<tr>
<td>Innovativeness</td>
<td>70%-120%</td>
<td>Applied to new products in the NHI price lists meeting all the following requirements:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. The newly entered drug has a clinically meaningful new mechanism of action.</td>
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<tr>
<td></td>
<td></td>
<td>2. The newly entered drug has been shown objectively to have greater efficacy and safety than existing (comparator) drugs in the same class.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. The newly entered drug has been shown objectively to improve the treatment of the indicated disease or trauma.</td>
</tr>
<tr>
<td>Usefulness I</td>
<td>35%-60%</td>
<td>Applied to new product drugs in the NHI price lists that meet two of the three requirements listed above</td>
</tr>
<tr>
<td>Usefulness II</td>
<td>5%-30%</td>
<td>Applied to new products in the NHI price lists that meet one of the following requirements (excluding products already covered by Innovativeness or Usefulness I premium):</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1. The newly entered drug has a clinically meaningful new mechanism of action.</td>
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<td></td>
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<td>2. The newly entered drug has been shown objectively to have greater efficacy and safety than existing (comparator) drugs in the same class.</td>
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<tr>
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<td>3. The newly entered drug has been shown objectively to offer, as a result of formulation improvement, greater than therapeutic usefulness than other drugs in the same class.</td>
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<tr>
<td></td>
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<td>4. The newly entered drug has been shown objectively to improve the treatment of the indicated disease or trauma.</td>
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NHI, National Health Insurance.
hypoglycemic symptoms versus those who did not (0.88 vs. 0.90, P < 0.0001) [29]. It is important to assess whether utility values exist for all key DM health states.

Where appropriate, it is necessary that studies be undertaken to address evidence gaps so that future analyses can more accurately cover the costs and benefits of a treatment in that specific health care environment. The development of local data should be encouraged and rewarded, as is the case in Taiwan where a maximum premium of 10% can be added to the price of a therapy if a local pharmaco-economic study has been undertaken as part of the evidence-generation package.

3. Acceptance of modeling as a core methodology to project long-term outcomes and comparative effectiveness, and to provide insight on economic impact including cost-offset and budget impact

In a chronic condition such as DM, mathematical models are often used to estimate the impact on lifetime health outcomes [30]. The need for such an approach was recently acknowledged in the American Diabetes Association Consensus Panel Guidelines for Computer Modelling of Diabetes and its Complications [31]. The use of such models has been accepted by groups such as the National Institute for Health and Care Excellence in their assessment of DM technologies. There are examples of economic models being used to extrapolate long-term outcomes and costs in Asia. For example, Pollock et al. [32] developed a discrete event-simulation model to estimate long-term clinical and cost outcomes in Japanese patients with DM treated with a rapid-acting insulin analog compared with regular human insulin; rapid-acting insulin significantly reduced cardiovascular complications over 5 and 10 years, resulting in increased quality of life and decreased costs.

4. Availability of real-life patient data in DM to capture costs and benefits in clinical practice

We should also recognize that the assessment of technologies will not be restricted to launch and that there will be increasing emphasis on the need for ongoing demonstration of value through evidence generation. DM disease registries and databases are available in some geographies. The Japan Diabetes Clinical Data Management Study Group initiative involves the collection of clinical data from 60 to 70 specialists covering up to 35,000 patients and a range of DM indicators. A recent study reported on the time and costs of newly registered outpatients with T2DM [33], while another study assessed the efficacy and safety of switching Japanese patients with T2DM from neutral protamine Hagedorn insulin to an insulin analog [34]. In Taiwan, the National Health Insurance Research Database, which was launched in 1995, contains registration files and original claim data for reimbursement. Large databases derived from this system are accessed by scientists in Taiwan for research purposes. Access to real-life effectiveness data can help to inform both the evidence-based management of patients with DM and ongoing funding decisions, but in some geographies, access to observational patient data can be limited.

5. Assessment of the specific evidence requirements of biosimilars

An area in which HTA and the DM therapeutic disease state are of particular interest is follow-on biologics or biosimilars. Specifically, several DM manufacturers are currently developing biosimilar insulins, and it is anticipated that these will be on the market in the near future. It is acknowledged that there are challenges around the HTA evidence requirements for biosimilars [35]. In Korea, there is a government pricing policy for biosimilars: for a small-molecule drug, the price is 53% of the innovative product price, and for the larger-molecule drug, it is 70%; clinical evidence of purity, quality, efficacy, and tolerability is required, and safety should be similar to the original product. The assessment of biosimilars is a key area for consideration beyond the region. For example, a recent (October 2013) consultation exercise was undertaken by the Canadian Agency for Drugs and Technologies in Health on the establishment of a Common Drug Review procedure and process for reviewing subsequent entry biologics [36]. In addition, the Association of the British Pharmaceutical Industry released a position paper on biosimilar medications in February 2013, which argued that they should be subject to HTA [37].

Implications for the Future

HTA has the potential to assist payors in making informed decisions about the coverage of DM medications. It is possible, however, that a poorly designed or managed HTA process runs the risk of denying patients appropriate access to medical technologies, inefficiently allocating resources, constraining clinical freedom, and sending distorted signals to medical technology providers [38]. It is important that the key HTA principles, as defined by The International Group for HTA Advancement [22], are followed and that the system is designed to capture the full value of medication. In DM, the analysis should include all relevant costs and benefits over the long term. It is also imperative that the impact on the patient of both DM and the medication is considered. It should be emphasized that the aim of this article was to provide a forward-looking perspective on specific considerations for the assessment of DM medications within evolving HTA systems. We are not aware of any published articles that have documented the recent HTA experience of DM therapies in these geographies, but we recognize that an appraisal of specific examples would be a valuable addition to our understanding.

A second round of evidence-based evaluation of drugs after the regulatory hurdle can delay or impair patient access to medications. In South Korea, following the introduction of the PLS, there was a delay in the time to market entry, and these effects were greater for new chemical entities than for incrementally modified drugs [39]. There are some concerns that the new three-stage system in Taiwan, which requires consensus at both the consultant meeting and the Pharmaceutical Benefit and Price Schedule Stakeholders’ meeting and includes the possibility of re-review, could delay patient access to new medications. It will be important for this situation to be closely monitored, and ways of streamlining the process explored. If HTA is to have a formal future role in mainland China and Japan, there needs to be agreement on how the findings of the assessment would influence health care decision making, and how this could be implemented without compromising patient access or other important principles such as equity. Furthermore, building and maintaining an HTA system is a highly resource-intensive activity, and endeavors should be made to ensure that the system has adequate capacity.

Conclusions

In summary, to ensure that HTA is an effective mechanism, it is necessary to develop systems that adequately capture the costs and benefits of treatments that are important to patients, physicians, and payors. International alliances and examples of best practice will provide important insights; however, individual governments need to develop approaches and systems that meet local needs and expectations. This is especially pertinent in DM,
for which the human and economic burden is great and growing, and for which new effective therapies provide wide-ranging benefits to patients and to society as a whole.

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REFERENCES


