What Is Next for Pharmacoeconomics and Outcomes Research in Asia?

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ABSTRACT

Objectives: Pharmacoeconomics and outcomes research have the potential for rapid adoption in the Asia Pacific region. Nevertheless, the region is characterized by great diversity in social and economic development, ethnicity, population size, health-care system, culture, language, and religion. Thus, the rate of adoption is also quite diverse across the region.

Methods: Among the countries reviewed in this article, governments take varying levels of interest in applying this research in health policy decisions. For example, some countries have already implemented systems that require pharmacoeconomic studies as one component of a new pharmaceutical product's approval for reimbursement, whereas others recommend such data but do not require it in policy and medical decision making. The literature in the countries reviewed is actually quite robust given the early stages of development of this field in most countries. The academic community has members trained in this field of research in all the countries reviewed and some universities have established departments whereas others have just introduced a few classes in the area.

Results: At the moment, pharmacoeconomics and outcomes research are being conducted mainly by academics. In addition, some pharmaceutical researchers are active and pharmaceutical companies are currently preparing to conduct more of this research as part of their strategy for Asian drug development.

Conclusions: Prospects for future growth and development in this field are quite good in Asia as rapid health-care inflation, increasing rates of chronic conditions and disabling conditions, changes in health-care technology, and increasing technology diffusion will underpin the need for greater awareness of the need to incorporate economic efficiency into the health-care systems.

Keywords: Asia, outcomes research, health care, pharmacoeconomics

Introduction

Between 1960 and 1990, Asia experienced rapid economic development, and despite the recent economic downturn, it remains important in the world marketplace, especially in health care and pharmaceutical consumption. For example, as a single country, Japan has the second largest pharmaceutical market second only to the United States. Nevertheless, many countries in the region now face financial difficulties that make paying for health-care services, including pharmaceutical products, challenging.

The concepts of pharmacoeconomics (PE) and outcomes research (OR) were introduced in western countries in the 1970s and formal PE guidelines were first established in Australia and Canada about a decade ago [1,2], in response to rapid health-care cost inflation. Asia too, though slightly later in time, now must respond to the typical factors that drive increasing health-care expenses such as an aging population, increased rates of chronic diseases and disabling conditions, changes in health-care technology, and increasing...
payments from third-party payers [3]. As such, PE and OR activities have become increasingly visible in Asia [4], yet one wonders how far these trends will proceed? Will PE as an evaluation tool for health-care decision making eventually be utilized in Asia to as great an extent as in western countries? To discuss this question, a Panel Discussion on Outcomes Research in Asia was organized (International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 7th Annual International Meeting, 2002), and this article expands on that session with a focus on the role of PE and OR in the current health-care systems in China, Hong Kong, Japan, Korea, Singapore, and Taiwan.

China

In China, PE and OR are not widely used in either the public or the private sectors because pharmaceutical policy and medical decision making are still dominated by traditional approaches focused on clinical efficacy, safety, and price considerations. Nevertheless, given the large population base, strong economic growth, and recent health policy reforms, one cannot underestimate the growing need for PE and OR. For example, PE or OR data may play an increasing role in recent important reforms, including expanded health insurance coverage, creation of a national drug formulary, the separation of drug dispensing from prescribing, a new drug pricing system, and China’s entry into the WTO.

Although most of rural China is still without health insurance, urban health-care programs are transitioning into community-based insurance systems aimed at increasing the insurance risk pooling covering an estimated 80 million urban employees in large cities, accounting for approximately one-third of the urban population nationwide [5–8]. It is expected that increasing public efforts will be made to extend the coverage for most of the employed sometime around 2003 to 2004 through the new insurance program.

In 2000, China’s national health-care expenditures were US$57.4 billion. Although this figure does not seem very high compared to that of many developed countries, the annual rate of growth has been well over 10%, far higher than the GDP growth rate in the 1990s [9]. This has led to a steady increase in the share of GDP on health-care expenditures, up from 3.5% in 1990 to 5.3% in 2000 [10], and this trend is anticipated to continue for the years ahead.

In 2001, sales of pharmaceutical products and services in China totaled US$33.3 billion, up 18.5% from 2000. This growth was higher than that of most other sectors in the economy. Demand for medication use in China is extremely high relative to the overall economy and total health-care spending [11]. This will likely continue owing to several factors. First, drug expenditures consume more than half of the total health-care budget in China. This is in sharp contrast with many other countries. For instance, in the United States, drug expenditures account for total health-care costs in the range of 8.7% in 1980 to 10.8% in 1999. During the same time period, the drug share of the total health-care budget in China ranged from 65% to 58% as shown in Fig. 1 [12].

Second, there is a strong income effect. During the 1990s, while annual economic growth rates ranged from −0.5% to 4.5% in the United States and 1.4% to 3.9% worldwide, China was among the few countries that maintained a much higher growth rate of 4.0% to 14.3% [10]. If such a trend continues in the future as is widely anticipated, this will entail a significant income effect on demand for health-care and medications [13].

Third, the population is rapidly aging. In the early 1980s when the 65 years and over cohort was about 6% of the total population worldwide, China’s elderly population was only 4.7%. In the year 2000, however, this figure in China reached almost the same level of the worldwide average at 7% (Fig. 2). Moreover, population census data suggest that over the next few decades China will face an even more rapid aging trend.
Pharmacoeconomic Studies in the Literature

Although pharmaceutical expenditures account for a major part of total health-care expenditures in China, little use has been made of PE in health policy and medical decision making until very recently when China launched several health-care system reforms. In the late 1990s, the concepts of PE and OR were increasingly introduced in China through many channels, mostly via training seminars, conferences, fellowships, and some actual studies. To better understand the current research capacity of pharmaceutical OR in China, we conducted an online search of China’s pharmaceutical literature database using the key words “pharmacoeconomics” and “outcomes research.” The preliminary statistics are as follows:

Without an in-depth review of each article, we found a total of 426 papers containing the key words, ranging from 117 in year 1999 and 106 in 2000 to 203 in 2001. In a recent review study, Liu [14] specifically analyzed the characteristics of 45 PE papers. Their data indicated that most of the studies were conducted by pharmacists (60%), followed by medical doctors (20%), college professors (9%), and all others (11%). Researchers in government agencies or industry did not seem to play much of a role in conducting these studies. Of the 45 papers, 18 were prospective studies, 12 were retrospective, and 15 were review studies. In terms of methodology, cost-effectiveness analysis is the most popular approach. This is consistent with our brief review of 39 papers published in the first half of 2002, in which 21 papers used cost-effectiveness methods, 3 used cost-minimization analyses, and none used cost-utility or cost-benefit analysis. The remaining papers were on theoretical discussions, policy debates or market analyses or were an introduction to international research in this field.

Prospects for the Future

The following major initiatives and developments are likely to drive the future use of PE and OR data in policy and medical decision making in China:

Urban Health Insurance Reform and Essential Drug Formulary (EDL) The Ministry of Labor and Social Security (MOLSS) administers the health insurance system and recently the drug formulary has been specifically targeted for cost savings. The drug formulary consists of two essential drug lists (EDL A and B). EDL A includes drugs defined as “clinically necessary, widely used, safe and efficacious; and price advantageous among its class” [15]. EDL A is a national list and cannot be modified by local governments. EDL B is defined similarly to EDL A except that prices are generally higher than similar drugs in EDL A. Local governments are allowed only to modify EDL B up to 15% of the total number of drugs included in the original list. Although cost-effectiveness was not part of the criteria for EDL selection, the recent revisions in the government EDL guidelines explicitly ask for the involvement of health economists in the determination of the EDL. Some foreign drug companies already are voluntarily submitting PE data along with their conventional submissions to MOLSS for EDL consideration.

Pharmaceutical Pricing In July 2002, The State Planning Commission issued a policy document titled “Reforming Pharmaceutical Pricing Management,” which established two mechanisms for pricing pharmaceuticals. One is a centralized government pricing of all drugs on the EDL based on drug production costs. This establishes a baseline price for each drug as a national reference. Capped at the baseline reference level, actual retail prices can vary downward, allowing retailers to make more competitive pricing. For drugs not on the EDL, in contrast, the pricing is primarily left to the determination of market demand and supply. From the government’s perspective, the current cost-driven pricing of EDL drugs is considered suboptimal, and it appears that cost-effectiveness will ultimately serve as the primary basis for pricing as a means of better allocating health-care resources.

WTO Entry and Its Impact The pharmaceutical industry, subject to many unique regulatory conditions, patent protections, and international trade constraints, will be greatly affected by China’s entry into the WTO. Following WTO agreements, China will allow foreign vendors to operate in a number of important goods and service markets, including...
drug distribution, pharmacy, and medical insurance. This, in addition to the reduction of trade barriers, will help the Chinese pharmaceutical market to become much more competitive, likely following international trends wherein PE data are utilized to assess the relative value of competing medical technologies. In the past, few foreign companies operating in China have taken major initiatives to lead the development of PE and OR; but this seems to be changing with some recent efforts of drug companies to support PE and OR research and training projects in collaboration with universities.

Other Government Initiatives In January 2001, MOLSS issued a new policy on the management and classification of prescription and nonprescription drugs [15]. This policy prohibits advertising for prescription drugs in any public news media. Because most EDL drugs are prescriptions, this policy challenges drug manufacturers to find alternative ways to demonstrate the value of their prescription drugs to the payers. Pharmaceutical OR may be such an alternative, especially for foreign drug makers with higher priced products. Other areas of potential use of PE data could include premarketing activities. These activities include early selection, research and development, and drug approval with the State Drug Administration (SDA). In fact, the SDA National Center for Drug Evaluation has recently suggested that PE assessments be considered in preparing phase IV clinical trails.

Hong Kong

Traditionally, the Hong Kong government, despite its low taxation rate, has been committed to providing health care to all its citizens. More than 95% of the total medical expenditures in Hong Kong have been shouldered by the government, which has maintained a health-care system comparable to that of western developed countries in many aspects. As a result of the rapid growth in the economy in the past decade, there has been a corresponding growth in demand for health-care services in Hong Kong. The aging population has also become a major factor underpinning an increase in the demand for intensive and long-term geriatric medical care. The economic downturn in recent years has, not unexpectedly, put severe restrictions on the government’s ability to maintain this model of health-care delivery. The Hong Kong government has a long-standing history of providing nearly free health care for all citizens, irrespective of financial status and of the government’s budget. The recurrent public health care expenditure has comprised approximately 15% of the government’s total public expenditure [16]. Though admirable, after many years of operation, the situation is slowly coming to a dead end.

Over the past decade or so, spending on health care in Hong Kong has been around 5% of GDP [17]. Nevertheless, the estimated annual budget as percentage of GDP is only 2.5% and, hence, there has been a consistent overspending. Major factors contributing to overspending include:

1. Heavy subsidization of inpatient and outpatient services;
2. Abuse of accident and emergency services that are free for all local citizens; and
3. Increased share of inpatients compared with the private sector.

There have been numerous debates as to what the future direction of the government’s role should be. Yet the single most urgent question is, “How long can this system be sustained?” Therefore, although often praised by overseas counterparts as one of the most admirable and generous providers of health-care services, the Hong Kong Hospital Authority (HA), which is a solely government-funded organization, assumes the role both of the provider and of the payer of health-care services. At the moment, decision makers in Hong Kong, as in some western countries as well, decide on choices of medications or procedures with considerations given mainly to safety, efficacy, and their unit costs rather than their long-term cost-effectiveness, and only a few senior doctors with little scientific and clinical evidence often carry out therapeutic substitutions empirically.

To address more specifically the future health needs of Hong Kong, a Health Care Reform Consultation Document was prepared and released by the Hong Kong government in December 2000. Among the proposals, it was suggested that medical technological progress should be effectively exploited to the optimum advantage of the community [16]. All of these issues have led to an important landmark in the health-care history of Hong Kong: an upcoming overall health-care reform in which our finite resources will have to be spent in a targeted and cost-effective manner.

Globally, PE data are the most effective tools in decision making during the process of selection of formulary choices or procedures. At the moment, local officials tend to focus on addressing the acute crisis rather than the long-term effects of health-related problems. Conceptually, the word “cost-effective” is often used, either consciously or subconsciously, to describe a drug or procedure that
would cost less, yet the true long-term value of it in comparison to the existing alternative often remains unclear. Hence, the unit prices of drugs often take precedence over their long-term cost-effectiveness in decision making.

At the moment, formulary decisions for the public sector are the primary responsibility of the Drug Advisory Committee under the Hong Kong Hospital Authority. Among the information required in new drug applications are data in relation to PE analysis, yet there is no requirement as to where the data should be generated. Nevertheless, it is generally recognized that declined applications are usually not due to lack of relevant PE data or their quality. Hence, the proper utilization of PE data in the government hierarchy in Hong Kong remains to be further enhanced.

Despite this, many activities pertaining to PE have been introduced in recent years; the driving force has been mainly from the pharmaceutical industry and academics. PE and OR studies started to emerge around 1999. So far, more than 20 projects have been completed with at least 8 of them published in top international peer-reviewed medical journals. An additional 20 or so abstracts have been presented at international meetings. Among the completed projects, quite a large proportion of them are in the gastrointestinal area [18–20]. As a result, the subject of PE has begun to receive attention from many different directions including the government, the medical profession, the economists, and the media. Nonetheless, public awareness in this area still needs to be substantially increased.

**The Perspective from Academia**

Despite this lack of encouragement and clear recognition from the government, local academics and some health-care practitioners have been extremely active in PE and OR activities. Apart from initiating PE and OR studies of their own, academics in Hong Kong have been participating, and in a few cases acting, as the major driving force in international multicenter PE studies.

In December 2000, a few of these active members, with the support of five multinational pharmaceutical companies, established the Chinese Chapter of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) in Hong Kong, the first regional chapter of the Society in the Asia Pacific area.

Since its establishment, close links have been maintained with the local authority as well as officials in Mainland China. The Chapter has published regularly in the *Chinese Medicine Economic News*, which is one of the most widely circulated health-care periodicals in China. Because the subject is still in its developing stage, only a few institutions have the expertise and infrastructure to perform studies of their own. With the rapid development of the discipline worldwide and the dedication of the local academics, it is anticipated that it will only be a matter of time before PE and OR studies will gain their recognition and status in the health-care system. Academics should therefore take a proactive role in advocating the use of PE and OR data and their value in assisting the decision-making process both at the university and at the government levels.

**Japan**

At present, PE is still at an early stage of evolution within the health-care scene in Japan. This is in part due to institutional factors related to how health-care policy is formulated in Japan and also to the incentives, or lack thereof, for delivering cost-effective medical care. Historically speaking, Japan has not put much emphasis on analytical assessments in the formation of health-care policy. Policy making has instead been more a process of consensus building among all the key stakeholders [21,22]. Having said that, there has been a recent show of interest by the government in improving the health services research infrastructure in Japan. For example, in health economics, several formal programs in academic and quasi-governmental institutes have been established to collect analytical health economics or PE data. The Institute for Health Economics and Policy, originally funded by the Ministry of Health (MHLW) in 1993, was established “to survey and research health economics and to collect and supply information on the subject in order to contribute to the development of medical services and health policy in Japan” [23]. Also, the University of Tokyo established in 2000 the first Division of Pharmacoeconomics in Japan [24].

Health-care decision makers do not regularly require PE data because in Japan’s fee-for-service (FFS) system of MHLW-established medical care reimbursement rates [25] few economic incentives exist at the provider level to promote cost-effective delivery of health care. This may explain the historically high average hospital length of stay in Japan, which in 1996 was 40.8 days [26,27].

Recent health-care policy initiatives indicate, however, a greater interest in promoting cost-effective delivery of health care as a means of con-
Pharmacoeconomic Studies in the Literature
A review of the published literature on PE was recently conducted and a total of 68 publications were found for the period 1980 to 2001 [30]. In this review, Doherty and Sato [30] found that the existing PE literature is quite broad in its application of numerous methodologies: 54 of the 68 were cost-effectiveness studies, 16 were cost-consequence studies, and 11 were cost-benefit analyses. The authors also concluded that clinical trials, observational databases, patient medical charts, patient bills, expert opinion, and other such data sources are all available in Japan; however, some of these sources are in limited supply. Furthermore, with regard to medical care cost data in Japan, the authors point out that the MHLW-determined system of reimbursement fees can readily be used in PE analyses to indicate the cost of various medical treatment alternatives to the MHLW's health insurance system. Keeping in mind that drug pricing decisions also take place within the MHLW, an economic analysis using these MHLW fee data would seem particularly useful in the drug pricing process [30].

Prospects for the Future
Upcoming health-care reforms may have a direct impact on the demand for PE data. For example, introduction of a nationwide diagnosis-related group (DRG) system could abruptly increase the demand for PE data. In fact, recently, a DRG-type payment system was implemented at all National University medical hospitals called the Diagnosis Procedure Combination system (July 2003). Additionally, nationwide DRG demonstration studies involving around 300 hospitals are at present under way and are scheduled to conclude in 2003.

In Japanese universities, two other major movements are afoot that should impact PE research: 1) an administrative readjustment of National Universities and 2) an awareness of evidence-based medicine among medical professionals. All national universities are readjusting their administrations into a new quasi-public system designed to have the flexibility of a private university. During such transitions opportunities exists for policy makers to break through existing barriers to introduce a greater awareness of the importance of medical care efficiency.

Although this initial burst of activity seemed quite promising, the academic activities in PE have not developed as quickly as had been expected. One reason has been the conservative environment of the leading universities, most of which are national universities, which lack the flexibility needed to adjust quickly to such new challenges and opportunities. Another impediment has been the traditional dominance of the medical community, in all aspects of medical research, to the exclusion of public health researchers, pharmaceutical department researchers, and pharmaceutical company scientists. Finally, a lack of an interdisciplinary environment in Japanese universities is another factor that slowed the development of PE studies since this field is typically taught in Schools of Public Health, which by their nature offer an interdisciplinary environment that is rare in Japan. In addition, Japan's academic outcomes researchers have been discouraged by the poor capability of university-affiliated information systems, which are insufficient to conduct reliable outcomes studies.

Despite these impediments, researchers are actively preparing for a new era of PE and OR in Japan. In fact, ISPOR, a leading international OR organization with strong academic ties, held an Asia Pacific meeting in Kobe, Japan, in September 2003.
accelerated by the recognition of the usefulness of evidence-based medicine (EBM). It is in this context that some of the leading national universities, such as the University of Tokyo, Kyoto University, and Kobe University, have been developing the various graduate training programs related to PE. This awareness of EBM is expected to grow in the coming decade.

Drug pricing reform is another important topic in Japan. The new Drug Pricing Organization (DPO) established in 2000 reiterated its willingness to accept PE data as one element to be considered in their pricing decision, and one board member is an economist. It is important to note that PE research that establishes the relative value of a new drug compared to existing treatments may be used to justify a premium prices for new drugs at the DPO. According to a recent survey of the conditions of PE studies at pharmaceutical companies in Japan, 47% of surveyed companies use PE data in their drug pricing negotiation process, and 77% actually acknowledged the value of this data. Nevertheless, these same respondents were not certain just how influential these data are at the MHLW at present [31]. If the Japanese government would disclose the process of how it uses or plans to use the PE data in pricing or reimbursement decisions, then this would give some needed guidance to companies and researchers. Overall, the field of PE in Japan has great potential for growth and as the need for these data continues to increase so too will the demand for better sources of underlying raw data and more academic programs in the field.

Korea

The Korean health-care system is a market-oriented, private-sector-dominated, FFS payment system. The role of the government has been limited primarily to the public health area with little regulation or monitoring of the ever-growing number of private providers.

The system is market-oriented in the sense that health care is viewed as an economic good, but not as a social good. With high levels of copayment and special charges, the amount and level of care one receives depends largely on income level. For example, there are designated treatment charges (DTCs). When patients prefer to be treated by regular staff physicians, or board specialists, in a general hospital, they are supposed to pay DTCs on top of the scheduled fees. If they cannot afford the DTCs, interns or residents are automatically assigned to them.

FFS has been the dominant method of payment for physicians, clinical services, and pharmacists. Case-based payment (called DRGs) experiments began in early 1997. Already, a DRG system is being used for some inpatient cases, but only on a voluntary basis. Physicians at hospitals are paid salaries, and occasionally they are paid performance-based bonuses.

Health Insurance

Started in 1989, the Korean National Health Insurance (NHI) program covers all citizens on a compulsory basis. The National Health Insurance Corporation [32], a single payer, collects premiums through employment payroll deductions for the employed and through a means test for the self-employed to finance the NHI.

Providers are paid by FFS in return for providing services that are covered by insurance. Total expenses are reimbursed, in part, by the insurance funds. The remaining cost is paid through patients’ out-of-pocket payments. Two types of cost-sharing features are found. The first feature is a deductible, applied to each unit of service. On top of the deductible, a patient pays coinsurance rates of 30% for clinic outpatient services, 50% for hospital outpatient services, and 55% for general hospital outpatient services. The coinsurance rate for inpatient services is 20% across all types of providers. Under the NHI, for insurance-covered services, providers (hospitals and clinics) are reimbursed according to a set of fee schedules. The government plays a major role in setting the fee schedules, although stakeholders negotiate the level of fees at the national level.

Drugs account for a relatively high percentage of health insurance expenses, for example, 33% in 1997. Historically, the prescription and dispensation of drugs were both handled by providers. Nevertheless, as part of a pharmaceutical reform and cost control effort, the Korean government launched a new system that as of July 1, 2000, separated prescribing and dispensing medication. In addition, to curb escalating drug costs, a new reimbursement system of drug prices, actual transaction pricing (ATP) system, was introduced in November 1999. ATPs are the real drug prices that are transacted between pharmaceutical manufacturers and health-care providers, mostly clinics and hospitals, upon purchase of drugs. Formerly, the prices of drugs reimbursed to physicians and pharmacists were government-approved ceiling prices. Under the ATP system, from November 1999, health insurance reimburses the lower of the two: government ceiling prices or ATPs. By regulation, hospitals
are required to report ATPs periodically to the health authority. Since September 1, 2002, submission of economic data has been required by the health insurance authority to determine reimbursement prices for new drugs. Before this regulation, to have a better position in pricing decisions, some pharmaceutical companies voluntarily prepared economic data for their key products and submitted them to the health authority upon suggestion. Nevertheless, it is not known how much impact the economic data played in the determination of reimbursement prices of new drugs, and there is little publicized evidence available in this regard.

Pharmacoeconomic Studies in the Literature

Results from several PE studies have been publicized to date. They are classified into two types: cost analysis and cost-effectiveness analysis (CEA). A study by Yang et al. [33] on hepatitis B is of the first type and examined the direct and indirect costs of diseases related to hepatitis B in Korea. Another cost analysis investigated the direct and indirect societal costs of diseases related to osteoporosis [34]. One can find several other PE studies within the framework of CEA [35–40].

Most PE studies rely on the following data sources. For clinical probabilities and epidemiology, Korean studies and population statistics are used, when available. If not available, statistics from foreign studies are used as references. In this case, meta-analysis and/or expert opinion are also employed in modifying the foreign probabilities and epidemiology data.

Cost Data in Korea

For cost data, the NHI database contains information regarding claims for reimbursed medical services, by diagnosis. The data are on a per-person basis. Patients with a certain disease often make copayments for medical services and buy additional services that are not reimbursed by the NHI (e.g., magnetic resonance imaging, ultrasound, herbal medicines, medicines bought over the counter from pharmacies, dietary supplements, and auxiliary nursing care). Patient charts are used to assess the level of copayments for medical services that are not covered by health insurance. Patient questionnaires are often used to capture costs of nonwestern medical services and of nonprescribed medicines.

In summary, the NHI database:

- Captures the total number of outpatient visits and inpatient days in each disease category;
- Captures insurance reimbursements and patient copayments in each category;
- Does not show other out-of-pocket payments and patient charts;
- Does not capture noncovered services and costs incurred in hospitals/clinics; or
- Does not capture all other payments for treatment, including spending on oriental medicine.

The Government’s Perspective

Rising health costs are now viewed as a serious problem in Korea. From 1975 through 1995, the health-care share of the total economy (GDP) has grown from 2.8% (1975) to 5.4% (1995), with an annual rate of increase of around 28%. Between 1975 and 1995, the Korean economy recorded unprecedented high growth rates. The increasing share of health costs as a proportion of GDP therefore signifies how fast the health sector expanded during this period [41]. The continuing increases in treatment costs in health insurance have reduced accumulated surpluses. Finally, the health insurance fund fell into deficit in 2001.

The Korean government thus strove to find ways to contain health care costs. Both macro and micro reforms are now being considered. One micro measure targets the growing pharmaceutical expenditure. As part of this effort, a new rule to determine maximum reimbursement prices for new pharmaceuticals was recently proposed in June 2002 by the Ministry of Health and Welfare. In September 2002, after a public hearing process, a new regulation was fixed and is now being enforced. This regulation requires that economic data be submitted along with the clinical data for drugs that are newly manufactured by Korean companies as well as drugs that are used overseas but waiting to be approved into the Korean market. This is a rather big change for pharmaceutical companies who are about to introduce a new product into the Korean market. A guideline for PE studies to be used in new drug pricing is currently under preparation by the Health Insurance Review Agency (HIRA), using foreign guidelines as reference and a special committee was formed to determine new drug prices, using published PE guidelines.

A concern arises with regard to the new regulation. There is an apparent lack of research capacity for PE or OR on the part of universities, government agencies, research institutions, and pharmaceutical companies. Therefore, a balanced approach by the health authority in terms of law enforcement
and research capacity building is highly desirable at this moment.

Proscets for the Future

Even with the positive results from consolidation of insurance funds and adoption of a drug dispensing separation policy, experts argue that several basic problems remain unsolved in the Korean health-care system. Two major problems are limited insurance coverage, especially in cases of major risks, and cost increases that precipitate financial insolvency in the health insurance system. Both macro and micro reforms are essential for a sustainable health insurance system, controlling expenditures and increasing efficiency, by a strengthened role of payers, increased accountability of purchasers, and better purchasing agents. Placing budgetary caps on expenditures is one option being considered as a long-term strategy.

Whether future health reform is in the form of DRGs, global budgeting, capitation, or any other type, as long as it is targeted to gains in efficiency in health financing, the number of PE studies used for health policy in Korea will increase. Because this is highly likely, concerted preparation by all parties involved is indispensable.

Singapore

Singapore is an island republic with a population of approximately 4 million [42]. The population is aging rapidly and the percentage of elderly is projected to increase to 27% by the year 2030. Given the trend of aging population, the health status indicators (Table 1), and the leading causes of morbidity and mortality, mainly noncommunicable diseases including cancer, cardiovascular disease, stroke, diabetes, and injuries (with cancer and cardiovascular disease accounting for about 62% mortality), the problems in health-care delivery in Singapore are similar to those in developed economies [43].

The total health-care expenditure in 1999 was S$4.3 billion or 3% of GDP, with the government subsidy on public-health-care services being S$1089 million, or 0.8% of GDP (1998) and S$919 million or 0.6% of GDP (1999) [44]. In Singapore, health-care delivery and management is under the purview of three ministries, namely, Ministry of Health (MOH), Ministry of Environment (ENV), and Ministry of Manpower (MOM) (Table 2), with the Ministry of Health as the ministry responsible for provision of preventive, curative, and rehabilitation services; formulation of national health policies; coordination of the development and planning of the public and private health sectors; and regulation of health standards (Table 2).

In addition to the provision of funding to the public hospitals, the Ministry of Health in Singapore has maintained a Standard Drug List (SDL) since 1979. The SDL is essentially a national formulary for the public-health-care institutions in Singapore. It lists all drugs that will be subsidized by the government for its citizens and permanent residents. It is modeled after the WHO Essential Drug List (EDL) with modification to suit local disease patterns.

According to the definition used by the MOH, a standard drug is defined as a drug that is necessary for the treatment of a common ailment. Standard drugs are usually essential first-line drugs in a specific therapeutic class. At present, there are two categories of standard drugs in Singapore:

**Standard Drug List I (SDL I)**

These drugs are considered as essential and cost-effective first-line drugs required by many patients.

**Standard Drug List II (SDL II)**

In 1992, the Ministry introduced this new category of drugs into the SDL. The aim initially was to make

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<tr>
<th>Table 1</th>
<th>Health status indicators in South Korea (1999)</th>
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<tr>
<td>Infant mortality rate per 1000 live births</td>
<td>3.2</td>
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<tr>
<td>Life expectancy</td>
<td>77.6 (women), 71.9 (men)</td>
</tr>
<tr>
<td>Fertility rate (number of live births per woman)</td>
<td>1.75</td>
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<tr>
<td>Hospitalization rate per 1000 population</td>
<td>96</td>
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<tr>
<td>Average length of stay in acute hospital (days)</td>
<td>5.1</td>
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<tr>
<td>Doctors-to-population ratio</td>
<td>1:730</td>
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<tr>
<td>Hospital beds-to-population ratio</td>
<td>1:330</td>
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<th>Table 2</th>
<th>Ministries managing health-care delivery in South Korea</th>
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<tr>
<td>Authority</td>
<td>Health-care and public-health-related functions</td>
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<tr>
<td>Ministry of Health (MOH)</td>
<td>Provides preventive, curative, and rehabilitation services</td>
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<td></td>
<td>Formulates national health policies</td>
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<td></td>
<td>Coordinates development and planning of public and private health sectors</td>
</tr>
<tr>
<td></td>
<td>Regulates health standards</td>
</tr>
<tr>
<td>Ministry of Manpower (MOM)</td>
<td>Responsible for industrial and occupational health of workers</td>
</tr>
<tr>
<td>Ministry of Environment (ENV)</td>
<td>Responsible for environmental health services</td>
</tr>
</tbody>
</table>
some expensive first-line cytotoxic drugs partially subsidized by government, because cancer is one of the top causes of mortality in Singapore. In recent years, other expensive noncytotoxic drugs have been included, e.g., angiotensin-converting enzyme (ACE) inhibitors and long-acting calcium channel blockers, which have been proven to be effective first-line treatment for hypertension. The current number of drugs, exclusive of different strengths and dosage forms, the in SDL stands at 455, including 372 as SDL I and 83 as SDL II.

In addition, the MOH also publishes various treatment guidelines based on an evidence-based approach using the hierarchy of evidence as suggested by the Cochrane Center. To date, 20 clinical practice guidelines have been published, including treatment guidelines for asthma, diabetes, osteoporosis, and hypertension [45–49].

Pharmacoeconomic Studies in the Literature

The major types of PE studies being carried out in Singapore are cost-effectiveness studies and the cost-of-illness studies. The clinical probabilities are mainly those obtained from the literature supplemented by local data whenever available. Other OR includes publications on the validation of several health-related quality-of-life instruments [50–52].

In performing PE studies, cost information has been obtained from the MOH based on DRGs for inpatients, which are updated at regular intervals, and charges for outpatient attendance, which are established nationally by the MOH.

The Government’s Perspective

As mentioned in the previous section, the MOH in Singapore maintains an SDL. At present, there are no formal PE requirements for inclusion into the SDL; hence, there are no formal guidelines for the conduct of PE studies. Nevertheless, attempts have been made to include financial data and some rudimentary PE evaluation in the decision-making process.

The Perspective from Academia

In Singapore, academic training for PE is being conducted mainly at the Department of Pharmacy at the National University of Singapore. Pharmacy students are given a brief introduction to the concept of PE at the undergraduate level during their final year of their 4-year course of study. The students attend approximately 10 hours of didactic instruction. The Department of Pharmacy also offers a PE module at the graduate level that runs for a whole semester.

The Pharmaceutical Society of Singapore also organizes workshops on how to apply the principles of PE in the practice of pharmacy in an ad hoc manner by inviting academics from the university to conduct the workshops. At present, the lack of a critical mass of researchers in the area, full appreciation of the potential importance and application of PE studies, and relatively poor technical skill of the health-care professionals, especially among the pharmacists, are the main barriers to advancing the field at a more rapid pace [53].

The academic community has not at this juncture been involved in development of guidelines for conducting PE studies. Nevertheless, as mentioned in the previous section, the Center for Pharmaceutical Administration has set up the Pharmacoeconomics and Drug Utilization Unit and has planned to apply PE principles in assisting in the decision of drug inclusion into the SDL. It is likely that at least an informal guideline will be developed in the process.

In view of the relative lack of available PE expertise in the public sector in Singapore, it is envisaged that in the near future, the academic community will be involved in the development of guidelines for PE evaluation as the MOH is moving toward the direction of applying PE principles in evaluating applications for inclusion into the SDL. Nevertheless, the extent of involvement of the academic community in the evaluation of PE studies is still evolving.

Prospects for the Future

During the past few years, the Singaporean government has introduced several measures to reform health-care delivery in Singapore. These include the introduction of DRG funding for inpatient treatment in October 1999 and the regrouping of the public hospitals into two major clusters, National Healthcare Group (NHG) and Singapore Health Services (SHS) to improve efficiency through economy of scale in March 2000. Recently in March 2001, the MOH formed a task force to review the drug prices in Singapore. One of the recommendations of the task force was to review the role of the SDL in health-care delivery.

As mentioned previously, the concept of cost-effectiveness has been considered in the decision-making process of drug inclusion into the SDL, although no formal PE studies have yet been required for the decision process in granting subsidies. The government is reviewing the funding and financing of the SDL and it is likely that the MOH will adopt PE principles in the decision-making process for drug inclusion in the SDL. This is shown
by the fact that at the national level, the Center for Pharmaceutical Administration (CPA) has recently set up a Pharmacoeconomic and Drug Utilization Unit in 2001. At the local level, the western cluster of public hospitals, National Healthcare Group, is planning to implement formal PE studies for drugs that are applying for inclusion in their formulary. Therefore, it is likely that PE data will become more important in deciding drug inclusion for the SDL and the formulary of the hospital clusters.

Taiwan

Before the inception of NHI, the Republic of China’s (ROC) social insurance was divided into three major sectors: labor insurance, government employee insurance, and farmer health insurance. In 1994, the Bureau of National Health Insurance Organizational Statute was passed, and the Bureau of National Health Insurance (BNHI) was formally established on January 1, 1995, as the statutory insurer in charge of NHI operations. The NHI program officially started on March 1, 1995, in Taiwan.

The NHI program targets all ROC citizens as beneficiaries. At the end of the year 2000, 21.4 million people were enrolled in the NHI plan, accounting for 96.2% of the target population. The reimbursement of medical resources utilization was initially by FFS on both inpatient and outpatient services. Starting in 1998, a case mix payment methodology was introduced for 50 procedures and surgeries. Dental care was reimbursed by a global budget system in 1998. Then, a global budget methodology was later implemented for Chinese medicines (2000), primary care (2001), and then finally hospital care (2002). Renal dialysis and respiratory care by ventilator are still reimbursed by a per-diem method.

Table 3 presents medical resources used in outpatient care, both by primary care and by outpatient clinics affiliated with hospitals [54]. Drug expenditures were 33.0% to 34.6% of the total outpatient care in these 4 years. Dispensing fees increased significantly from 1997 to 1999 owing to the increase in the number of prescriptions. Drugs used in inpatient care accounted for approximately 15.5% of the total inpatient care costs, and approximately 25% of health-care expenditures were spent on nontraditional Chinese medicine in Taiwan during this period.

Currently in Taiwan, there are at least three methods used to determine the price of to-be-listed new pharmaceutical products: the international

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Outpatient care expenditures using western medicine in Taiwan (in New Taiwan dollars [NT$])</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1997</td>
</tr>
<tr>
<td><strong>Expenditures</strong></td>
<td><strong>%</strong></td>
</tr>
<tr>
<td>Diagnosis fees</td>
<td>48,438,161,904</td>
</tr>
<tr>
<td>Treatments and medical supply</td>
<td>45,322,860,492</td>
</tr>
<tr>
<td>Drug fees</td>
<td>48,375,623,320</td>
</tr>
<tr>
<td>Dispensing fees</td>
<td>16,924,104,280</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>146,837,348,954</td>
</tr>
</tbody>
</table>

*% change from last year.*
median price of 10 countries, the international price ratio using comparator(s), and the treatment course or daily cost using comparator. The 10 countries used to assess the international median price are the United States, Canada, the United Kingdom, Germany, Sweden, Belgium, Switzerland, France, Australia, and Japan. Advantages or disadvantages of the new product on efficacy, dosage form, or pharmacokinetic profile are considered for additions or deductions to the price. In a few circumstances, the lowest price from among the 10 comparison countries or a price-volume negotiation strategy is used by the government. The estimated time needed from submission to public announcement of the reimbursement price is from 3 to 6 months. Upon receiving the notice from the BNHI concerning the price approval, pharmaceutical companies must reply to the BNHI as to whether the price is accepted or not within 7 days. The reimbursement price is guaranteed for 1 year. During that year, the only mechanism of price cut is through a price-volume survey. Nothing else can change the price once it has been established in this first year.

Pharmaceutical companies provide evidence to be evaluated by experts invited by the BNHI and the Pharmacy Benefit Committee. Results from randomized controlled clinical trials are required, with a preference for published head-to-head comparisons of efficacy and safety. PE evidence is encouraged.

PE Studies in the Literature

Until July 2002, only one new drug product, donepezil, had completed the evaluation process for the BNHI with local PE evidence attached. According to the BNHI, if the estimated market of a new product exceeds NT$100 million/year (New Taiwan dollars or US$3 million/year), then a price-volume negotiation strategy can be considered. The BNHI will negotiate the price of the new product with the pharmaceutical company for 3 years and, at the end of the third year, a PE study would be completed and used to determine a new price. The study would need to include cost and outcomes data for the Taiwanese population. If a new product is first introduced to the Taiwan market, a PE study is recommended by the BNHI. Owing to the lack of experience by local physicians, the PE data can be referenced from overseas literature. Nevertheless, local cost data are required in the modeling study.

Currently, several PE studies are ongoing within a number of international pharmaceutical companies in Taiwan. Hepatitis prevalence and its treatment, for example, are major issues in Taiwan. Approximately 20% of Taiwanese population have hepatitis B, and 2.9% to 5.4% have hepatitis C [55,56]. Both hepatitis B and C have new drug products on the market, and they are expensive. Therefore, the BNHI needs to decide whether or not to reimburse the new drug products. Also, owing to the global budget system, and the forthcoming implementation of a DRG reimbursement system, as well as the trend toward disease management, cost-effective treatments are generating an increasing amount of interested at the BNHI and among hospital managers and medical practitioners. Thus, it is believed that economic evaluations will be an important issue for academia, industry, and healthcare decision makers in the next decade.

The Government’s Perspective

The development of a standardized mechanism for economic evaluation is still at the beginning stages in Taiwan. Guidelines published from Canada and Australia were reviewed; however, standardization is still in progress. Experts in this field are uncommon and few scholars from academia have been organized by the BNHI to develop the evaluation procedures. Nevertheless, the BNHI has expressed strong support of the mechanism of economic evaluation. From the Canadian experience, the BNHI is trying to develop a Taiwan Coordinating Office for Health Technology Assessment (TCO-HTA). A written document outlining this effort and highlighting the strong commitment of BNHI regarding PE evaluation is under development. The organization of several academic groups to help in evaluation process is under way. Initially, two groups will be formed a therapeutic evaluation group and an economic evaluation group at the first stage.

At this time, only one school of pharmacy has PE courses taught at the graduate level. This program is new, established just 2 years ago. Five professors in the public health arena have training in health economics and are interested in exploring the field. Additionally, one new association named the Taiwan Society for Pharmacoeconomics and Outcomes Research (TASPOR) was organized. Members have been recruited since the government approval of this organization on August 9, 2002. The healthcare system in Taiwan is facing the need of economic evaluation on medical device, procedures, and drug treatments. The planning of organizational structure, the academic research groups, the research manpower training, the Association, and the pharmaceutical industry are all aware and became more accepting.
Owing to the global budget system, and the forthcoming implementation of a DRG reimbursement system, as well as the trend toward disease management, cost-effective treatments are generating an increasing amount of interest at the BNHI and among hospital managers and medical practitioners. Thus, it is believed that economic evaluations will be an important issue for academia, industry, and health-care decision makers in the next decade.

**Discussion**

Asia is known for its diversity in terms of social and economic development, ethnicity, population size, health-care system, culture, language, and religion. The speed of adoption of PE is highly sensitive to local situations and, as this article illustrates, the rate of adoption has been quite variable across Asia. There are some countries that are progressing quite quickly along the path of development of governmental requirements for PE data in the approval process for new pharmaceuticals. Academic circles are being newly established in most countries and are expanding in size with a growing number of PE courses being taught and in some cases full PE departments being established.

A few pharmaceutical companies have established departments of OR in the region or are assigning global headquarters staff to liaison positions for Asia. The number of PE publications is quite large in some countries and not that far from some European countries in terms of annual publications. Still there appear to be a number of challenges being faced across Asia.

One challenge that may be more relevant to Asia in general is data availability. As was indicated in many of these country reports, local data sources for things such as medical efficacy of the new technologies and epidemiologic databases are in short supply.

Another challenge, which is perhaps particularly acute for international pharmaceutical companies, is how to incorporate PE elements into the clinical trials being conducted in Asian countries. Whereas the medical component of a clinical trial may be repeatable across countries, there is no one-size-fits-all approach for PE components, because the diversity among these countries particularly the data sources will most likely require country-specific study designs.

A third challenge relates to the interpretation of PE results. This challenge is twofold: 1) when there are no local data, how do researchers bridge results from other countries to the local situation? 2) When the data are generated from the local Asian region, how can the results be generalized to other Asian countries? This is perhaps particularly acute in Asia because it is often not among the first regions chosen for initial drug development/registration.

In summary, there are challenges but none too large to block the progress of the use of PE in Asia. Learning the lessons that other countries have gone through will be an advantage that all Asian countries can benefit from as they continue to adapt the concepts of PE and OR. Certainly the driving forces that have ushered PE into the mainstream in western countries such as rapid health-care inflation and an aging population are also present in Asia, and these will likely form the underpinnings for the continued development and growth of PE research in Asia as well.

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