Health Technology Assessment and Its Use in Drug Policies in China

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A B S T R A C T

Objective: To review drug policies, health technology assessment (HTA), and HTA’s use in drug policies in China, to further improve the quality and efficiency of drugs. Methods: This study draws on multiple methods. A systematic review of the literature, review of Chinese government documents and statistical handbooks, and authors’ experiences in drug policies and HTA in China were combined to achieve the objective. Results: Of 571 studies identified in the initial search, 14 eligible articles (6 English, 8 Chinese) were finally included. On the Web site of the National Health and Family Planning Commission, the National Development and Reform Commission, and the Ministry of Human Resources and Social Security, we found that HTA or pharmacoeconomics evaluation is mentioned in recent years and its frequency has been increasing; however, there was not one hit about HTA or PE on the Web site of China Food and Drug Administration. Conclusions: The decision makers have realized the importance and value of HTA and have tried to integrate HTA into drug policies and regulations. However, the application of HTA findings to drug policymaking is not yet widespread and there are a number of challenges in using HTA in China. Therefore, it is necessary to establish a national HTA commission and develop pharmacoeconomics guidelines to support the use of HTA in decision making. Moreover, the most important steps are to encourage technology innovation, groom more HTA experts, and build reliable databases in China. Keywords: China, drug policies, health technology assessment, pharmacoeconomics, regulation.

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Introduction

Drug policy is a crucial component of health care system in any country, especially in China, in which drug expenditure was responsible for the largest share of the total health expenditure [1,2], and grew at an average annual rate of 9.6% during 2012 and 2015 [3]. China is one of the largest drug markets in the world; however, this condition depends on the size of its population, because the market is not yet mature [4,5].

Chinese drug sales soared to ¥332.7 billion in 2016, propelled by an average annual rate of 8.86% during 2011 and 2016 [6]. However, there is lack of a market concentration and nationally developed patent drugs [7]. Most drug companies are small-scale with scattered geographical layout and duplicated production processing, and many larger companies are government-owned with overproduction and constant operating losses [7]. By 2014, there were 7108 drug manufacturers, most of which produce generics. Generic sales were ¥614.8 billion in 2015, accounting for 85% and 80% of total drug sales and prescription sales, respectively [5]. However, the drug distribution network, too, is fragmented, complex, and inefficient. There were more than 13,000 drug wholesalers by 2009 and the top 3 had only a 22% market share in 2010 [8]. It often takes six to nine intermediaries in the distribution from factories to patients, which creates strong financial incentives for drug prescription, form a major part of Chinese hospitals’ income, and lead to significantly higher drug costs for patients [9,10].

Three key aspects of drug policies are market authorization, which is an application submitted by a drug manufacturer seeking permission to bring a newly developed drug to the market; reimbursement, which relates to how and to what extent insurers compensate someone for an out-of-pocket expense for drugs; and pricing, which describes how to price drugs. Market authorization, reimbursement, and pricing in China not only affect drug safety and quality but also are linked to drug affordability and access. In 2009, reforms had been carried out in the Chinese health care system with the aim to establish a health care system in which all people have access to quality health services without facing undue economic burden [1,11–15], and drug policy is one of the five key reforms. Also, this reform strongly accords with the basic concept of universal health coverage defined by the World Health Organization [16,17]. New Rural Cooperative Medical System, basic medical insurance for urban residents, and basic medical insurance for employed residents, as three main insurance schemes in China, had covered more than 95% of its population by 2015 [13]. In addition,
the share of health care financing from out-of-pocket expenses dropped down from 59.97% in 2001 to 29.27% in 2015 [13].

Despite major reform efforts, there are still many issues in the current system. Drug policies are more and more comprehensive and detailed. Therefore, health technology assessment (HTA) is required to give priority. HTA is the systematic evaluation of properties, effects, and/or impacts of health care technology, which involves the direct, indirect, intended, and unintended consequences of technologies [18]. HTA is a way of assessing the additional value of a drug in view of both clinical benefits and cost effectiveness. In general, HTA policy reports or suggestions are provided after a series of recommendations, revision, review, and feedback. The whole process can determine whether drugs or policies should be continued, expanded for widespread use, or canceled. Because China is still a developing country with limited health resources and high drug expenditures, the government has expressed interest and paid attention to HTA, but there is still a long way to go.

In this study, three methods, a systematic review, a review of Chinese government documents and statistical handbooks, and authors’ experiences in drug policies and HTA, have been used to present an overview of drug policies, HTA, and HTA’s use in drug policies in China, to further improve the quality and efficiency of drugs.

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**Background to Drug Policies**

**Market Authorization**

Drugs must first receive market authorization before being used by patients. China Food and Drug Administration (CFDA) has the primary authority to approve all marketed drugs. This approval procedure is complex and may take years to navigate because a drug is very different from other consumer goods [19]. Efficacy, safety, and quality are the three standards that a drug must meet to be approved by CFDA [20]. The Drug Registration Regulation came into effect in 2007 and was then amended in 2016 to make the procedures more formal and strict [20]. Randomized clinical trials with efficacious and high-quality clinical data are required to indicate which drugs were truly clinically superior compared with those currently available. However, there is a special approval requirement of CFDA that a drug marketer must also be a drug manufacturer, which is different from that in other countries. In other words, the drug marketers can apply to the CFDA for drug licenses only when they become drug manufacturers [5]. This requirement brings some challenges, because more and more traditional manufacturers lack innovativeness, whereas many innovative drug marketers lack productivity [21].

**Reimbursement and Pricing**

After receiving approval and market authorization from CFDA, drugs can be included in one of the two major reimbursement lists: the Essential Drug List (EDL) or the National Reimbursement Drug List (NRDL). The former has not been updated since 2012 and the latter was updated in 2009 and in 2017, which means that most essential drugs are not easily accessible and most new drugs must be paid for by patients [22,23]. To take care of the financial burden caused by major diseases, China has introduced catastrophic health insurance catastrophic diseases reimbursement drug list, which covers expensive and new drugs [24]. Reimbursement caps have the potential to narrow the gap in price between off-patent and generic drugs, to minimize out-of-pocket payments, and to further improve equity. Tending for off-patent drugs and direct negotiation for on-patent drugs are two major drug pricing mechanisms. Tending really is the strongest and most effective pricing policy, but it is more heavily weighted toward pricing rather than quality. Negotiations between manufacturers and hospitals or pharmacies can involve multiple distributors, and each may charge a markup. For primary care institutions, provinces will directly procure from tendering winners, and pharmacies can bypass the tender process and directly negotiate with manufacturers. However, hospitals, as the largest market, engage with tendering winners in a secondary negotiation process. In this process, hospitals usually secure a price lower than the tendering price and before 2009 hospitals could charge a 15% markup if they sold the drugs directly to patients [24].

**New drugs**

To ensure the affordability and access of new drugs, reimbursement is the first choice. However, new drugs must comply with the rigid requirement of “over 2 years of clinical use” before being introduced into the reimbursement list. NRDL pointed out that drugs can be updated every 3 years. In other words, new drugs have only one opportunity to enter NRDL every 3 years. However, NRDL is not updated in time. This reimbursement lag means that many new drugs are not timely obtained by more people [25]. The National Development and Reform Commission (NDRC) is responsible for setting pricing for new drugs, which are usually given a higher price to encourage innovation. However, there is a phenomenon in China that an old and cheap drug disappears and is replaced by a so-called new drug with a higher price, but with only a small change in dosage, route of administration, usage, or packaging [1].

**Generics**

The generic market is fast growing as the result of a competitive market, driven by the demand for cost-effective drugs and availability of high-value drugs [26]. Compared with patent drugs, generic drugs are more likely to be purchased by patients with low incomes, and they are easily affected by government pricing controls and reimbursement. In general, the price of equivalent generic drugs is 80% lower than that of patent drugs. However, the pricing of generic drugs in China faces a problem. Reimbursement needs to set a pricing based on China Approved Drug Names, but not entirely based on it. Because of this, it is difficult to guarantee consistency in quality and efficacy between generic drugs and patent drugs [27]. Therefore, China began to promote the quality and efficacy consistency evaluation of generic drugs in 2016 to achieve drugs’ mutual substitution clinically. Some provinces even promised that generic drugs offered for consistency evaluation will be given priority in reimbursement [28].

**Essential drugs**

The reimbursement ratios of essential drugs are higher than those of nonessential drugs. The National Health and Family Planning Commission (NHFPC) stated that all primary health care institutions in both urban and rural areas must use essential drugs and other health care institutions have to give priority to essential drugs [7]. Although a drug being in the EDL is an advantage for patients, it also means higher scrutiny on drug price, given that the government shoulders part of the cost burden. For the pricing of essential drugs, NDRC first sets a guiding pricing, and then the provinces generate a purchasing pricing through bidding. This process not only simplifies the distribution links, improves the purchasing efficiency, and reduces the pricing of essential drugs [3] but also ensures the availability of essential, high-quality, and low-cost drugs nationwide.
Background to HTA: Current Status

The development of HTA in China is relatively new. Lots of studies, especially related to drugs, are not always named as ‘HTA’ but named as pharmacoeconomics (PE) [2]. HTA or PE organizations in China are mainly concentrated in universities, medical institutions, and government. The Medical Technology Assessment & Research Center was established at the former Shanghai Medical University in 1994, was approved as Key Lab of Health Technology Assessment in 2004, and was designated as a World Health Organization Collaborating Center for Health Technology Assessment and Management in 2007. A multidisciplinary center for PE evaluation and research was established at Fudan University in 2002. The Biomedical Engineering Technology Evaluation Center and the Medical Ethics Evaluation Center were established in the Zhejiang University in 1994 and the Guangzhou Medical University in 1999, respectively. In addition, medical institutions are actively involved in HTA. An evidence-based medicine center was established in the West China Hospital in 1997, and was designated as the Chinese Clinical Trial Register of World Health Organization International Clinical Trials Registry Platform in 2007. These above organizations have carried out both research and education in HTA. They offer courses, organize meetings, conduct research, and introduce international experiences related to HTA. In 2008, the Chinese Pharmaceutical Association started to draft Chinese PE guidelines, which were officially released and posted on the Web site of the International Society for Pharmacoeconomics and Outcomes Research in 2011 [29]. However, some studies found that the overall quality of PE studies was average [30], and the methods of literature evaluation did not accord with PE guidelines [31]. To our knowledge, PE guidelines are recommended by experts rather than being made mandatory by the Chinese government. Thus, the guidelines have encountered many difficulties and challenges, and have not played their due roles yet [29].

With the HTA development, government has also begun to pay attention to HTA and provide some support. In 2016, the China Health Policy and Technology Assessment Network was established by NHFPC, which is also trying to establish a technology licensure mechanism, a national HTA committee, and HTA experts’ database [2]. CFDA, NDRC, and the Ministry of Human Resources and Social Security (MHRSS) are also responsible for HTA works, especially in drugs policies or regulations [32]. In addition, international and national drug companies have begun to be involved in HTA [32]. Compared with international drug companies, it is difficult for national drug companies to provide evidence and data to support drug effectiveness and safety, and they lack professionals and technology to conduct PE analysis.

Methods

A multifaceted method was used for this study. It included a systematic review, a review of Chinese government documents and statistical handbooks, and authors’ experiences in drug policies and HTA.

We performed a systematic search to identify studies focusing on HTA and its use in drug policies published up to December 21, 2017. The following databases were searched: Web of Knowledge (including Web of Science, MEDLINE, BIOSIS Citation Index, Derwent Innovations Index, and Chinese Science Citation Database) and PubMed for English-language studies; and China National Knowledge Infrastructure, Wanfang Data, and Chongqing VIP for Chinese-language studies. The following search terms were applied to all published studies: (health technology assessment, health technology evaluation, pharmacoeconomic assessment, pharmacoeconomic evaluation, or HTA) and (policy, regulation, decision making, or rule) and (drug, medicine, or pharmaceutical) and (China or Chinese) (specific search strategies are listed in Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2018.01.010). We also searched for additional English and Chinese studies in the reference lists of the studies. Two researchers independently reviewed and screened the search results, and then independently extracted the relevant data. Any disagreements between the researchers were resolved by discussion. Finally, data were extracted regarding the characteristics of each identified study, including first author, publication year, language, study design, and main opinions on HTA and its use in drug policies (Table 1).

The second part of the review involved a search of Chinese-language documents and statistical handbook related to drug policies on government Web sites, including NHFPC, CFDA, NDRC, and MHRSS, using their own search engine. Search terms included health technology assessment, health technology evaluation, pharmacoeconomic assessment, or pharmacoeconomic evaluation in combination with each of the following terms: drug, medicine, or pharmaceutical.

This study also draws on opinions from authors’ experiences in drug policies and HTA. They have carried a few health policy and HTA projects in Zhejiang province, which provide some examples or cases in this study.

Results and Discussion

Information Identified

Systematic literature identified

A total of 571 studies were identified through the original database search, including 392 English-language studies and 179 Chinese-language studies. Two additional studies were identified through other sources. After duplicates were removed, 483 studies were retrieved on the basis of title and abstract. The initial screening resulted in 51 studies for detailed assessment. After reading full-text articles, 14 eligible studies were finally included in the systematic review (Fig. 1).

Of the 14 eligible studies included in our review, 6 were in English and 8 were in Chinese. All studies were literature review or policy analysis, and some studies combined with interview or survey methods. All studies described the overall HTA development in drug policies, 12 studies were for the current status of HTA application in drug policies, and 10 studies were for the future HTA development in drug policies (Table 1).

Government Web site identified

On the Web site of NHFPC, NDRC, and MHRSS, we found that HTA or PE evaluation is mentioned in recent years and its frequency has been increasing, which demonstrates that the decision makers have begun to have a good understanding of HTA or PE, and they have started using it in their routine management. The needs of HTA or PE were clearly put forward in many drug policies and regulations, including EDL, NRDL, New Rural Cooperative Medical reimbursement drug list, drug pricing, and drug purchasing by centralized bidding. Unfortunately, there was not one hit about HTA or PE on the Web site of CFDA; however, we found that many regulations by CFDA are required for review and discussion by professional groups to reach a consensus before a preliminary formulary, which are the portent of HTA use (Table 2).
<table>
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<tr>
<th>Study</th>
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<th>Language</th>
<th>Study design</th>
<th>Main opinions</th>
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<tr>
<td>Hu and Mossialos [24]</td>
<td>2016</td>
<td>Eng</td>
<td>A review of the academic and gray</td>
<td>1) The 2009 reforms called for increased use of health economic data when drug companies seek new drug approvals. A memorandum of understanding was also signed between China’s National Health Development Research Center and UK’s National Institute of Health and Care Excellence in 2010, although much of the work has focused on clinical pathways and guidelines. The National Health and Family Planning Commission is currently developing national HTA guidelines that could be institutionalized. Provincially, Zhejiang’s Health and Family Planning Commission has recently created a PE evaluation committee to help contribute to the pricing process of tenders. 2) HTA and CER are relatively new in China. In general, although HTA has been researched and piloted, it is yet to be incorporated broadly into policy. CER looks at differences in clinical effectiveness between therapies without economic consideration. Although it is less methodologically challenging than HTA, CER is also not used extensively when making pricing or reimbursement decisions. 3) HTA and CER should be encouraged at multiple levels in the health care system. From a regulatory perspective, it can guide which drugs should receive priority approval. From a supply-side perspective, HTA and CER can be used in guiding price negotiations. From a demand-side perspective, using HTA or CER to inform value-based reimbursement can help rationalize prescribing.</td>
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<tr>
<td>Guan et al. [39]</td>
<td>2017</td>
<td>Chi</td>
<td>Review</td>
<td>1) In the selection of reimbursement drug list, similar drugs are compared according to PE; in the purchase of drugs, new drugs may be evaluated according to PE and evidence-based medicine to meet the needs of disease prevention and treatment; in the selection and adjustment of essential drugs, it is necessary to evaluate according to PE and evidence-based medicine. 2) A lot of drug policies and documents clearly state that it is necessary to provide PE evidence for drugs; however, PE and decision making have not really been linked. 3) On the basis of experiences from other countries and practices in China, we recommended that PE guideline should be mandatory. It is recommended to set up a national PE institution, and update or supplement the guidelines regularly.</td>
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<td>Rong et al. [42]</td>
<td>2017</td>
<td>Chi</td>
<td>Literature review and key person</td>
<td>2) HTA is still in its infancy because of the shortage of researchers and the unavailability of data. 3) The international advanced methods, such as reference pricing and pharmaceutical economic evaluation should be applied to improve the affordability of patent medicines. Third-party independent PE evaluation organizations will be gradually established.</td>
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<tr>
<td>Koh et al. [43]</td>
<td>2016</td>
<td>Eng</td>
<td>Literature review and authors’ experience</td>
<td>1) HTA is used in many markets to control rising health care costs and to help decide the allocation of health care resources. As health care costs in China increase, the government has expressed an interest in this. 2) HTA is currently not implemented at a national scale in China to evaluate pricing and access to drugs despite the fact that China’s PE guidelines have been published, with the most recent update in 2011. 3) Experience from Australia shows that HTA should not be viewed as a budget control tool and should be balanced with overall population health needs to achieve health outcomes goals.</td>
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<tr>
<td>Liu et al. [44]</td>
<td>2014</td>
<td>Chi</td>
<td>Document review, key personnel interviews, and official Web site</td>
<td>1) It is necessary to conduct cost-effectiveness, cost-utility, and cost-benefit analysis in new drugs clinical trials; high-risk, high-cost, and low-efﬁciency drugs in the National Reimbursement Drug List can be replaced according to the results of PE evaluation; PE evaluation is required for new or patent drugs before pricing. 2) Compared with other countries, PE evaluation in China is still in an initial stage, because the methods and results have not really been introduced to decision making. 3) The PE system can be constructed; the process of PE in decision making can be clarified; experts’ database can be set up; evaluation methods can be perfected.</td>
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<td>Liu et al. [33]</td>
<td>2014</td>
<td>Chi</td>
<td>Literature review, expert consultation, questionnaire survey, and semi-structured key informant interview</td>
<td>1) The “ladder-like” characteristic of knowledge translation was illustrated by the results of questionnaire survey of HTA researchers. Namely, some primary stages of knowledge translation were relatively easier to complete than some advanced stages. For instance, about 40% of HTA researchers reported that they often published HTA results in academic journals or submitted HTA results to policymakers, whereas only 15% of HTA researchers have research evidence adopted in decision making or applied on a wider scope. The results of qualitative interview also showed that a large part of HTA researchers have only a handful of HTA results applied as references or evidence for policy document. 2) Although some HTA research had been conducted and some HTA results have played important roles in decision making, the overall level of HTA knowledge translation is still low and the impact of HTA research still needs to be expanded. 3) To improve the HTA knowledge translation and further promote scientiﬁc and evidence-based decision making, some improvements need to be made at the institutional level and the individual level of research and decision making, as well as in the design of macro mechanism.</td>
</tr>
<tr>
<td>2012</td>
<td>Eng</td>
<td>documentary reviews, experiences of policymakers</td>
<td>1) Guideline development and PE evaluation agency establishment. PE evaluation plays important roles in the efficiency of drug...</td>
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and reimbursement decision making. Pharmacoeconomists not only compare the drugs under PE views and methods but also analyze the impact of these drugs on the funds of medical insurance, work injury insurance, and maternity insurance. Only those with PE advantages and optimal impact on the funds are selected. All information is reviewed and discussed by professional groups to reach a consensus before a preliminary formulary is formed. 2) However, China needs to overcome some barriers to strengthen PE, including the number of pharmacoeconomists, comprehensive and valid database of drug price information, safety, professional agencies, and training. 3) It is recommended that pharmaceutical companies provide the relevant data and participate in the negotiation process. Independent review experts will be in charge of submitting review proposals, checking data, and also conducting PE.

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<th>Language</th>
<th>Methodology</th>
<th>Highlights</th>
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<tr>
<td>Chen and Gao [37]</td>
<td>2012</td>
<td>Chi</td>
<td>Policy analysis</td>
<td>1) The role of PE is clearly put forward in many policies and regulations of new health reform. 2) It is necessary to strengthen the popularization and education of PE, and further to develop it in the application process. 3) PE evaluation can be used to guide drug pricing, select essential drugs, submit an expense account to medical insurance, and ensure rational drug use in the clinic.</td>
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<td>Oortwijn et al. [32]</td>
<td>2010</td>
<td>Eng</td>
<td>Document review, and Web-based survey among professionals working in public and private health insurance, industry, regulatory authorities, ministries of health, academic units, or HTA</td>
<td>1) Organization mainly involved in HTA: Department of Science and Education. Role of HTA: The new health reform proposal (October 2008) mentioned that health economic studies will be gradually requested when drug companies apply for new drug approval. The increasing number of PE and pharmaceutical outcome research studies has had some impact on decision making. 2) In China, HTA is not yet used in the Chinese State Food and Drug Administration.</td>
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<tr>
<td>Lu et al. [46]</td>
<td>2010</td>
<td>Chi</td>
<td>Review</td>
<td>2) PE development is relatively late in China. There is a lack of effective technical standards, so it is difficult to integrate the results into decision making. 3) Introducing PE into pricing is not only to learn from international experiences but also to innovate pricing methods and to construct the demand of drug value.</td>
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<td>Chen et al. [2]</td>
<td>2009</td>
<td>Eng</td>
<td>Literature review, and Web site searching</td>
<td>1) A technology licensure mechanism based on HTA, including technology permission for use, institution licensure, and workforce licensure, is being gradually carried out by the Ministry of Health in China. 2) However, compared with the international HTA community, HTA in China is still in the development stage. HTA is not widely applied. Policymakers might have some awareness of HTA, but they do not use HTA in routine decisions. 3) Moreover, HTA can play an important role in technology market entry, insurance benefit coverage, formulary, clinical pathway, reimbursement, etc.</td>
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<tr>
<td>Li et al. [47]</td>
<td>2009</td>
<td>Chi</td>
<td>Document review</td>
<td>2) Insufficient experts engaged in PE research; the influence of PE is limited; absence of PE guidelines. 3) We should strengthen the</td>
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<tr>
<td>Yu [48]</td>
<td>2007</td>
<td>Chi</td>
<td>Literature review</td>
<td>1) The government began to organize relevant experts to develop PE guidelines, which can be applied to new drugs, reimbursement, pricing, and the formulation of clinical diagnosis and treatment norms. 2) PE is a newly developed discipline. It has been given much attention by the Chinese government and many sectors, such as health, labor and social security, drug administration, pricing departments, and drug enterprises.</td>
</tr>
<tr>
<td>Doherty et al. [36]</td>
<td>2004</td>
<td>Eng</td>
<td>Literature review</td>
<td>2) The 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 the Ministry of Human Resources and Social Security for EDL consideration. However, in China, PE and outcome research are not widely used in either the public sector or the private sector because pharmaceutical policy and medical decision making are still dominated by traditional approaches focused on clinical efficacy, safety, and price considerations. 3) PE and outcome research 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. Cost-effectiveness will ultimately serve as the primary basis for pricing as a means of better allocating health care resources.</td>
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Note: 1) Text appearing in point 1) indicate the current status of HTA application in drug policies. 2) Text appearing in point 2) indicate the overall HTA development in drug policies. 3) Text appearing in point 3) indicate the future HTA development in drug policies.

CER, comparative effectiveness research; Chi, Chinese; EDL, Essential Drug List; Eng, English; HTA, health technology assessment; PE, pharmacoeconomics; WTO, World Trade Organization.
Use of HTA in Decision Making

Regulations
To support drug policies, government in China has already published some regulations [15], some of which mentioned HTA or PE application, such as market authorization, reimbursement, and pricing. After the 2009 reforms, drug companies are encouraged to provide PE data when they seek approvals for new drugs [24]. Some regulations highlighted the significance of drug evaluation but did not refer to the use of HTA [20]. These drug regulations, except drug quality, reimbursement, and pricing, usually were promulgated before 2007. Although the decision makers made efforts to merge HTA into drug policies or regulations in recent years, it is still difficult for us to trace HTA in early drug regulations [33].

Reimbursement and pricing
HTA or PE is very useful for the drug reimbursement process to promote the use of effective and cost-efficient drugs [34]. NHFPC and MHRSS highlighted HTA use or PE analysis in the reimbursement drug list. It was pointed out that PE analysis needs to be conducted to determine whether to include effective but expensive drugs in national, industrial injury, and maternity reimbursement drug lists. International HTA was groundbreaking in that it introduced the adjustment of NRDL in 2017, in which drug companies are encouraged to calculate the expected payment standard for drugs in NRDL and to make a quantitative prediction on the basis of increase in sales volume [29]. In addition, drug companies, research institutions, and other institutions are encouraged to carry out PE analysis in the selection and adjustment of essential drugs. Even the decision makers are trying to set up a mechanism, and establish the experts' database of HTA or PE for EDL. Some drugs in EDL can be replaced by better risk-benefit ratio or cost-benefit ratio drugs according to the results of HTA or PE [13,35]. Therefore, some international drug companies are already voluntarily submitting PE evidence along with their conventional submissions in order to be included in EDL consideration [36]. In Zhejiang province, drug companies are encouraged by MHRSS to provide PE report in the negotiation in order to enter 2018 catastrophic diseases reimbursement drug list.

In addition, HTA or PE can be used to guide scientific and reasonable drug pricing, which is the key to solve the problem of "virtual-high drug pricing." It was clearly put forward in 2009 that the PE evaluation system of prepricing was gradually to be applied to new and patent drugs, and further demonstrated in 2010 that drug companies need to submit the PE report for completely alternative but expensive drugs [37]. For drugs on the market, drug companies need to set a reasonable pricing according to the comparative PE results between these drugs and competitive drugs [37]. HTA is playing an important role in the purchase of drugs by centralized bidding, in which the drugs being purchased and other similar drugs need to be compared for economy, safety, effectiveness, rationality, affordability, and compliance to be included in the centralized purchasing drug list [13,37–39]. NHFPC in Zhejiang province in 2014 set up a PE committee in the centralized bidding process [25], but the later issued mechanism of centralized bidding in public hospitals in 2015 did not mention the PE application [40].

Challenges
Overall, the scope of HTA or PE application in drug policies is very narrow and there are a number of challenges in using HTA or PE in China. Most drugs apply for approval as so-called new drugs with a high cost, but often there is only a small change in dosage, route of administration, usage, or packaging [2]. Reimbursement may stimulate a higher demand for drugs, and virtual-high drug pricing negatively influences the availability of drugs. Thus, it is urgent to introduce HTA to address the above problems in the future.
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<th>How to use HTA in drug policies or regulations</th>
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<tr>
<td>NHFPC</td>
<td>Standard for nosocomial infection management</td>
<td>Please pay attention to PE, and reduce the cost of anti-infective drugs for patients</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a></td>
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<tr>
<td>NHFPC</td>
<td>Regulations on pharmaceutical management in medical institutions</td>
<td>Using the theory and method of PE to make a comprehensive evaluation and research on drug resource utilization</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a></td>
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<td>NHFPC, NDRC</td>
<td>Management on the national EDL</td>
<td>1) The expert group of the national EDL is mainly composed of experts in medicine, pharmacy, PE, medical insurance management, health management, and pricing management. 2) The expert group technically evaluated for the selected drugs, put forward opinions, and formed an alternative list according to evidence-based medicine and PE. 3) The national EDL should be adjusted every 3 y in principle; two adjustment reasons are related to PE: evidence-based medicine and PE evaluation for marketed drugs and it can be replaced by a better high-benefit or cost-benefit ratio drug according to PE evaluation. 4) We should establish standard and mechanism of evidence-based medicine and PE, to scientifically and rationally formulate the national EDL. 5) Research institutions, drug companies, and social organizations are encouraged to carry out the evidence-based medicine and PE evaluation for drugs in the national EDL</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a>, <a href="http://www.ndrc.gov.cn/">http://www.ndrc.gov.cn/</a></td>
</tr>
<tr>
<td>NHFPC, MHRSS</td>
<td>RDL for the New Rural Cooperative Medical System</td>
<td>The drugs that do not meet the PE evaluation shall be transferred out of the national EDL in time</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a>, <a href="http://www.mohrss.gov.cn/">http://www.mohrss.gov.cn/</a></td>
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<tr>
<td>NHFPC</td>
<td>Notifications on centralized procurement drugs</td>
<td>We compared the cost between negotiating drugs and other similar drugs from drug safety, effectiveness, rationality, affordability, and compliance on the basis of evidence-based medicine and PE, to guide the purchase of patent and generic drugs</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a></td>
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<tr>
<td>NHFPC, NDRC</td>
<td>Notifications on deepening the reform of health care system in the 13th Five-Year Plan</td>
<td>1) Drug approval, patent application, and PE are regarded as the important content of drug pricing negotiation. 2) To explore evidence-based medicine and PE application in essential drugs selection and adjustment</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a>, <a href="http://www.mohrss.gov.cn/">http://www.mohrss.gov.cn/</a></td>
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<tr>
<td>NHFPC, MHRSS</td>
<td>National RDL</td>
<td>The innovative drugs that meet the needs of medical insurance are included in the national RDL</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a>, <a href="http://www.mohrss.gov.cn/">http://www.mohrss.gov.cn/</a></td>
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<tr>
<td>NHFPC</td>
<td>The implementation of the ‘‘two ticket system’’ in the drug procurement in public hospitals</td>
<td>It is necessary to establish PE evaluation system to determine the drug pricing</td>
<td><a href="http://www.nhfpc.gov.cn/">http://www.nhfpc.gov.cn/</a></td>
</tr>
<tr>
<td>NDRC</td>
<td>Notifications on the 13th Five-Year Plan for health service development</td>
<td>To establish a suitable health technology extension mechanism in primary health care institutions; to improve the HTA and ethical review system; to actively carry out medical science popularization work</td>
<td><a href="http://www.ndrc.gov.cn/">http://www.ndrc.gov.cn/</a></td>
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<tr>
<td>MHRSS</td>
<td>Adjustment for national RDL in 2017</td>
<td>This adjustment groundbreaking introduced HTA. Drug companies are encouraged to calculate the expected payment standard by using cost-utility methods for drugs in the national RDL and to make a quantitative prediction based on the increase in sales volume</td>
<td><a href="http://www.mohrss.gov.cn/">http://www.mohrss.gov.cn/</a></td>
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<tr>
<td>MHRSS</td>
<td>Adjustment of national, industrial injury, and maternity RDL</td>
<td>For effective but expensive drugs, we will introduce PE and comparative effectiveness methods, and the evaluation results and experts' opinions can determine whether to include those drugs in the RDL</td>
<td><a href="http://www.mohrss.gov.cn/">http://www.mohrss.gov.cn/</a></td>
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EDL, Essential Drug List; HTA, health technology assessment; MHRSS, Ministry of Human Resources and Social Security; NDRC, National Development and Reform Commission; NHFPC, National Health and Family Planning Commission; PE, pharmacoeconomics; RDL, Reimbursement Drug List.
Besides, most national drug companies are small generic drug manufacturers without databases, professionals, and technology, and have not yet realized the full value of HTA. HTA in China is still in the development stage, and is yet to be incorporated broadly into drug policies. The decision makers may have some awareness of HTA, but it is difficult to use HTA in original drug policies and regulations. In addition, because HTA is not mandatory but only recommended in drug policies, gaps may have existed between HTA evidence and decision making. There is no national HTA commission in China to coordinate HTA activities at the different institutions [41] and the Chinese PE guidelines have not played their due roles yet, too.

Conclusions

When we review the history of HTA and its use in drug policies, we find that the decision makers have realized the importance and value of HTA in China. Although the decision makers usually do not use the terms HTA or PE in their routine decisions, they have started paying attention to drug evaluation, cost, effective, benefit, and so forth. There is some evidence to demonstrate that HTA has been integrated into drug market authorization, reimbursement, and pricing, and such applications have some positive impacts. Conducting HTA and using HTA findings to influence decision making are two things. Compared with the international HTA, HTA in China is still in an initial stage. The application of HTA findings to drug policies is not yet widespread, and the integration of HTA in decision making is in its infancy.

Therefore, it is necessary to set up a national HTA commission to support the use of HTA in decision making. Moreover, the most important steps are to encourage technology innovation, groom more HTA experts, and build reliable databases, and further to conduct studies according to Chinese PE guidelines. It is hoped that once decision makers insist on the use of HTA, it will provide a strong message to ensure drug quality as well as reasonable pricing from drug companies, to reduce irrational prescription from hospitals and doctors.

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Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2018.01.010.

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