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Article *in* Journal of Evidence-Based Medicine · May 2013

DOI: 10.1111/jebm.12030 · Source: PubMed

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JOURNAL OF EVIDENCE-BASED MEDICINE

Journal of Evidence-Based Medicine ISSN 1756-5391

BRICS

International experiences of promoting generics use and its implications to China

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Keywords
Generics; generics substitution; market competition; price; reimbursement.

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Received 10 January 2013; accepted for publication 15 January 2013.

doi: 10.1111/jebm.12030

Abstract

Objective: To summarize international experiences in promoting use of generics and to extract essence for China's reference.
Method: This is a commentary of two systematic reviews about policies to promote use of generics and its implications to China.
Result: Price, reimbursement, and generic substitution policies in European countries, and approaches in low and middle income countries in promoting market competition, appropriate intellectual property right protection strategy, and necessary demand side incentives, are all meaningful for China to contain soaring pharmaceutical expenditures, and to maintain the achievements and outcomes of the national health system reform.
Conclusion: Effective promotion of generics use must be practice based on the real situation. Tailor-made and comprehensive measures are needed to address both demand and supply sides barriers before achieving tangible cost containment effect without unexpected side effects.

Background

Growing health expenditure and uncertain global economic situation have been leading increasing financial pressure to the governments of many countries, particularly in countries which have higher coverage of publicly funded health care. Pharmaceutical expenditure is an important part of the health expenditure. Containing the growth of pharmaceutical expenditure is one of the important means to contain the growth of health expenditure, and to alleviate the financial pressure. Promoting use of generics can significantly save pharmaceutical costs.

A procurement program supported by the US President's Emergency Plan for AIDS Relief (PEPFAR) in 16 low and middle income countries (LMICs) reported that, the estimated yearly cost savings generated through generic antiretrovirals (ARVs) use were from USD 8.1 m to USD 214.6 m during 2005 to 2008 (1). In 2010, The World Health Organization (WHO) used the results of Health International Action (HAI) "Medicines Availability and Pricing Survey" and IMS data, and calculated the cost savings from replacing off-patent brand products with bio-equivalent generics of 18 commonly used medicines in 17 LMICs (2), which were up to 89% of the cost. In the public hospitals of China, replacing 4 of the above 18 medicines could save more than USD 86m (65% of the cost).

The 2009 report of the Southern Pharmaceutical and Economic Research Institute (3) showed that, among the top 10 market share anti-cancers, six were with over 50% market share captured by foreign firms and joint ventures, and four were fully supplied by foreign firms and joint ventures. Among the top 10 market share lipid-lowers, five were with over 95% market share captured by foreign firms and joint ventures, and two were fully supplied by foreign firms and joint ventures. The IMS report about 2009 version of the National Reimbursement Drug List (NRDL) showed that (4), during 2004 to 2009, the number of products listed by the Chinese basic health insurance programs and marketed by the top 10 multinational pharmaceutical companies increased 2 to 11, except one company whose marketed products

JEBM **6** (2013) 74–80

reduced two. In 2004, the market share of the products marketed by these top 10 multinational pharmaceutical companies and listed by the Chinese national basic health insurance programs had absolute advantages to the others, ranged between 73% and 91%. It all increased (2% to 23%) without an exception in 2009, reached 74% to 99%. The 2011 hospital medicines monthly consumption data (5) collected by the Guangdong Pharmacy Association showed that, among the top 55 month sales products, 29 were brand products supplied by foreign firms or joint ventures, and many expensive products were listed by Guangdong provincial basic health insurance program in recent years.

Like most of the other LMICs, China does not have a comprehensive national policy to promote use of generics, particularly not exist of pro-generics insurance reimbursement policies. There is no system design for promoting use of generics in the existing medicines use policies, and the research about this is almost a blank.

In March and April 2012, the Generics and Bio-similars Initiative Journal of Belgian and German Health Policy published two systematic reviews in succession. One came from the Austrian Health Research Institute (WHO Collaborating Center for Medicines Price and Reimbursement), was about the impact of medicines price and reimbursement policies on generics use in 29 European countries (including all 27 European Union Members, Croatia and Norway). Another was jointly conducted by US Boston University, Harvard University, and Mexico National Institute of Public Health, was about the pro-generics policies in LMICs during 2000 to 2010. These two reviews systematically summarized different policies of promoting use of generics and its impact in developed and developing countries, respectively. They also analyzed the preconditions for implementation and policy environment, which are very meaningful for China to take a reference, in terms of developing policies to promote use of generics, containing pharmaceutical expenditure, and maintaining the achievements and outcomes of the national health system reform. International evidence indicated that, formulating and implementing proactive policies to promote generics use can make considerable cost savings. Such policies should also work in China, where health resource is scarce, basic health security level is low, and private health and pharmaceutical expenditures are high. It can help to relieve individual economic burden, save public funds for better insurance benefits and stronger health safety nets.

Evidence from European countries

Vogler's review (6) showed, two-thirds of the health care is publicly financed by the third party payers in the European Union. Under the dual pressure of growing pharmaceutical expenditure (increased during 2000 to 2009) and economic crisis, European countries usually contain medicines cost through direct price control, promote generics competition to indirectly lower the prices of generics and off-patent brand products, and promote generics use. Medicines price regulation and reimbursement policies are the key means for promoting generics use.

Medicines price and reimbursement policies

Major European countries only regulate the price of medicines listed by the insurance programs directly or indirectly. Regulations cover direct control by setting ex-factory price, and indirect control through setting the maximum wholesale price, fixing the distribution profit rate with regressive mark-up, and controlling the profit rate of manufacturers. There is no price control of medicines not listed by insurance programs.

Among the 29 European countries covered by this review, 22 countries implement medicines reference price system, that is, identical or similar products are clustered into a reference group, and each cluster has a maximum reimbursement amount. Many countries cluster medicines with the same active ingredient. External medicines reference price system is mainly used for setting prices of patent products. Internal medicines reference price system is used for setting prices of generics. Price of generics is a proportion of the price of off-patent brand products. Medicines reference price system has been widely used by European countries to promote generics use.

Generics substitution

Demand side measures are widely used in European countries, which include generics substitution policy (23 countries allow substitution, six compulsorily substitute), prescribing with generic names (24 countries require, five compulsorily require), advocacy of pro-generics policies, establishing and strengthening trust on generics by the public. In addition, a pilot project in Austria allowed patients of a small sickness fund to pay a lower prescription fee if they obtained a generic instead of a brand-name medication. As a result, the patients asked for the generics and the share of generics prescriptions rose (7). Most countries integrate several of the above policies. Twenty countries covered by this review formulate comprehensive policies which cover both generics substitution policy, prescribing with generic name policy, and medicines reference price system.

Evidence from Europe

Appropriate medicines pricing, reimbursement, and generics substitution policies promoted full competition, lowered medicines price, and promoted generics use, thus saved insurance funds. This has a significant implication to countries

toward the universal health insurance coverage, especially when several medicines have similar therapeutic characteristics. The medicines reference price system played a role in price cap: setting a fixed reimbursement amount, and leaving patients to pay or co-pay the price difference. A clear positive impact of medicines reference pricing system was also observed in developing countries (8). Following the introduction of the medicines reference pricing program, there was a downward price pressure due to that generics were trying to improve their positions.

Lessons for China

Following four-year national health system reform, China already claimed to achieve universal health insurance coverage. It is a time for China to take reference from these international experiences in promoting generics use. The following policy aspects need to be addressed and changed toward building a pro-generics policy environment in China:

Medicines price regulation focuses very much on retail price control. Cost-plus and mark-up method have been used for a long time as the main tools for price setting, which were abandoned by most developed countries. Medicines reference price system should be set up step by step.

There lacks a transparent price discount negotiation mechanism in process of medicines distribution. The ongoing "medicines zero mark-up policy" looks like an effective way to prevent public health facilities from making profits on medicines, but discards incentives of health facilities as the end-user to to gain the maximum discount through negotiation with suppliers.

Hospital pharmacy is the main channel for access to medicines. Hospital medicines procurement policies in many areas prefer off-patent brand products due to quality considerations. Doctors and consumers also generally prefer off-patent brand products. There is a clear rule requires prescribing with generic names, but enforcement has always been a problem. Many prescriptions are prescribed with both brand and generic names. Even if only generic name is prescribed, once strength and package are indicated, it implies a specific brand product. This is because that, regulation on strength and package in process of marker authorization is not stringent, too many strength and packages are marketed in China. Sometimes each company has its own unique strength and package.

Fee-for-service is the most commonly used payment method of health insurance programs. There are no incentives to doctors and pharmacists to prescribe and dispense generics. No matter brand products or generics are used, and how large the price gap is (sometimes the price gap between brand product and generics could be 35 times (9), and health insurance programs pay a fixed reimbursement rate to the full actual expenditure. Some insurance programs exclude brand products through listing brand names, and restrict reimbursement of brand products, which is not in line with the market competition rules for fair competition. Majority of health insurance programs do not formulate incentives for doctors and pharmacists to prescribe and dispense generics through appropriate payment method.

Summary

In the case of satisfying the pre-requisites of promoting use of generics (strengthening medicines regulation, securing quality of generics, and fully inform the general public), following pro-generics policies should be adopted in China: setting medicines reference price system, fixing the reimbursement amount for one product or even one category of products, adopting mixed prospective payment method (capitation, case based, and global budget), allowing generics substitution, fully enforcing prescriptions with generic names, etc. These policies can help to create incentives for manufacturers, health facilities, doctors, pharmacists, and patients to use generics.

Evidence from LMICs

Warren's systematic review (10) showed that, among the international literatures about generics use published during 2000 to 2010, majority of them were published by the USA (32%) and Europe, only 25% were from LMICs, among which, India and Brazil were the key representatives (7%). Thirty-two percent of the studies in LMICs, especially in Brazil and India, focused very much on trade and intellectual property right policy. Studies in this area conducted by high income countries (HICs) were only 3%. More than half of the studies took care of medicines price, prescription behavior, and market competition. Studies about medicines regulation in HICs were two times of that in LMICs. Comparing with HICs, LMICs have been subjected to many restrictions in terms of technical skills, economic development, and policy formulation and implementation capacity. Medicines regulatory authority is not functioning, medicines policies are with low efficiency. Limited studies were conducted about medicines regulation and health insurance reimbursement in LMICs. Research about generics use promotion policies for consumer is very few. Only 17.7% of the studies conducted in LMICs were supported by the governments including Brazil, South Africa, Zimbabwe, and Thailand. There was a lack of policy impact assessment on generics use in LMICs. Only quite a few of them adopted appropriate methodologies to do the assessment, which produced evidence for intervention impact on increasing use of generics.

Market competition

Evidence form LMICs

Competition helped lowering medicines prices. Promoting competition was a strong policy tool for promoting use of generics in LMICs, which included competition between generics and brand products, and among generics. If prices of generics were set too low by the government, it will not generate incentives for generics market entry.

Lessons for China

Chinese pharmaceutical industry is a generics-based industry, its R&D (research and development) capacity has been generally weak, and generics competition has been very intensive. Multinational pharmaceutical companies had ever enjoyed super national benefits in China (preferential taxation, pricing and procurement policies for both patented and off-patent brand products, etc), which brought them advantages in monopolizing the market. Added the non-pro-generics characters of the health insurance programs, there has been no competition strong enough in some categories of medicines between its off-patent product and generic versions. On the contrary, some expensive off-patent products always have better market share than the cheaper generics (9).

Price control authority has been repeatedly and significantly cut the medicines price off. Generics have always been the first ones being affected. Some products were forced to leave the market. Manufacturers replaced these products with new brands with different strengths and packages but same attending functions, which enabled them risk-averse. Although the government has been trying to reduce the huge price gaps between off-patent brand products and generics, the process has been hard and slow due to very strong lobby capacities of the multinational pharmaceutical companies.

Procurement policies in some areas made the matters worse, which left no space for fair generics competition. The "one product two strengths" procurement policy originally expected to contain vicious competitions among multi-suppliers for one product, but evolved into a common practice of "one generic and one off-patent brand product." This has been in fact equivalent to a formal market capture guarantee to the off-patent brand products. A market without strong generics competition will definitely lead to long-time monopoly by off-patent products. A wishful rigid administrative provision did not play its expected positive function, but brought unexpected negative impact. Accompanied by these policy deficiencies, the pooled medicines procurement system did not fully achieve its desired cost containment effect, although provincial level negotiations might strengthen the positions of buyers.

Summary

In the case of satisfying the pre-requisites of promoting generics use (strengthening medicines regulation, securing quality of generics, and fully informing the general public), following positive choices to promote generics competition should be formulated in China: abandoning rigid administrative regulations, creating market rules-respected competition mechanisms, and securing fair pricing and procurement competition policies to generics.

Trade and intellectual property right

Evidence form LMICs

Effective approaches for LMICs to access to affordable life-saving medicines were: fostering self-production capacity of generics, setting up medicines intellectual property right protection strategy with public health perspective, fully using the flexibilities of Trade Related Intellectual Property Rights (TRIPS) agreement, challenging medicines patent which was granted not in line with the public health principles, negotiating with medicines patent holders for lower prices or voluntary license, and even issuing compulsory license.

Experiences of Brazil and Thailand were that, price negotiation with patent holders was not sufficient enough to develop optimal ARV prices. Brazil had to pay four times of the international price for the 2nd line ARVs. It lately successfully lowered the prices of ARVs through self-production of 1st line generic ARVs and issuing compulsory license to patented ARVs (11).

The US-Thai Free Trade Agreement extended 10 years of patent protection to medicines in Thailand, postponed generics entry, medicines prices thus increased 32% (12), medicines expenditures increased at least USD 0.8064 to 5.2 billion (13). Following promulgated the *Patent Laws* in 1992, the market share of off-patent brand products in Thailand increased 1% to 6% annually, and reached to the peak in 1997, when the market share of generics and off-patent brand products were 33% and 67%, respectively. Since 2006, the Thai government issued compulsory licenses to patented ARVs, cardiovascular medicines, and anti-cancers in succession. The Thai Government Pharmaceutical Organization (GPO) was large scaly granted with compulsory licenses, and imported generic ARVs from India under the same grant. The procurement cost was reduced 67% to 98% (14).

Lessons for China

Most new anti-cancers, ARVs, and medicines for rare diseases are under patent protection in China. Even if there is a self-production capacity, the national free treatment program for HIV/AIDS has to pay much higher price for the patented ARVs (15). The basic health insurance programs

have to spend considerable public resources on patent and off-patent brand products. For those medicines which were yet covered by the basic insurance programs, families went into bankruptcy or slipped into poverty because of extremely high out-of-pocket expenditure for those patent or off-patent brand products, some were compelled to give up treatment due to unaffordable prices (16).

Summary

Government use oriented compulsory license has been one of the most important tools for many countries to secure access to affordable life-saving medicines either for its own people, or for people in less developed countries. Among countries who had ever granted compulsory licenses, we saw both developing and developed nations such as the USA, Canada, and Italy. Compulsory license granted to the critical medicines which are meaningful for the national economy and livelihood, and balanced intellectual property right legislative system, should be one of the important topics for China's national medicines policy research under the new global situation.

Demand side measures

Evidence form LMICs

Demand side measures to promote generics use in LMICs were weak. This was because that, implementation of demand side measures generally required higher comprehensive coordination capacity. However, policy formulation and implementation in LMICs were restricted by unsound health systems. LMICs had less experience in demand side measures such as encouraging doctors to prescribe, pharmacists to dispense, and consumers to use generics. Training has always been used as the most common tool for demand side measure. However, one South African control study to evaluate the impact of education and training on generics use found that (17), education was quite time consuming and labor intensive, and its medium/long-term impact and cost was unclear.

Lessons for China

There have been perverse economic incentives in Chinese health systems due to historical reasons (medical service price was far below the real costs, low salary for medical professionals, allowing fixed proportion mark-up on medicines to compensate diminishing government budget in public health facilities, out-of-control informal deals on medicines, etc). Such perverse incentives led to a popular preference with high price off-patent medicines by prescribers and pharmacists.

There has been an absence of national policy on generics use promotion. The main reasons of this included, the national medicines regulatory authority and the quality of generics produced by local companies yet gained full trust of the general public, and qualified with internationally recognized stringent standard. Medical professionals and consumers have traditional perceptions of "poor quality local generics." Official information about generics and its quality were disclosed and published insufficiently. All these led to a situation that off-patent brand products were the first choice of doctors, pharmacists, and patients. Consumers were forced to spend more money for much expensive off-patent brand product, in order to achieve psychological satisfaction to quality medicines. Health insurance programs payment and reimbursement policies yet created incentives for prescribing, dispensing, and using generics. The much expensive the medicines were consumed, the more the insurance programs paid. Demand side mechanisms were blank.

Summary

In the case of satisfying the pre-requisites of promoting generics use (strengthening medicines regulation, securing quality of generics and fully informing the general public, and removing perverse incentives in the health systems), the following pro-generics use policies should be developed in China: creating medicines information disclosure mechanism with public credibility, reversing the traditional perceptions of the health professionals and the consumers, and integrating these with the above pricing, reimbursement, and procurement policies. These were necessary measures to build effective pro-generics use policies and demand side adjustment mechanisms.

Out-of-pocket expenditure on health accounted 35.29% of the total health expenditures in China. Pharmaceutical expenditure was 40.25% of the total health expenditure (18). Medicines financial burdens on individuals were quite heavy. Proactive demand side measurements will help to resolve the affordability problem, which is one of the top two questions of the national health system reform.

Conclusion

Based on the evidence from both European countries and LMICs, if China is willing to develop effective interventions on generics use, the following barriers will need to be overcome:

Supply side barriers

Intellectual property right protection and market authorization

TRIPS flexibility and intellectual property right protection strategy with public health perspectives have been used by many developing and developed countries. However, these

are yet comprehensively studied under the support of the government in China, and there lacks a strong political willingness to really practice them, although no legislative barriers exist. Majority of the ongoing studies are supported and conducted by nongovernmental organizations, and are in exploratory stage. There are also systematic problems like data protection and patent linkage in process of generics market authorization.

Economic incentives

Generic substitution policy is yet implemented in China. The medicines supply and distribution systems are not transparent enough to allow public oversight. Perverse incentives exist in health systems, which inappropriately induced high volume consumption of expensive medicines. The medicines pricing, procurement, and insurance reimbursement policies are not in favor of full competition between generics and off-patent brand products.

Management and institutionalization

The Chinese medicines regulatory system is still in a process of making development and improvement. More stringent quality assurance system is to be fostered to secure bio-equivalence, and to enforce effectively at all levels. A credible medicines information disclosure mechanism with public trust is to be established. The public advocacy of using generics is not strong enough. The prospective feasibility study and retrospective impact analysis of generics use policies are very limited, and almost a blank.

Demand side barriers

Information asymmetry and public perception

Chinese health professionals and consumers always have a traditional perception of "poor quality local generics," due to medicines information asymmetry among manufacturers, distributors, health professionals, and consumers. To change such a negative public perception, both medicines regulatory authorities and manufacturers need to take concrete actions, strengthening regulations toward internationally recognized stringent criteria, securing quality of generics, and timely offering quality assurance information of marketed generics to the general public.

Economic incentives

Effective economic incentives for prescribers, pharmacists, and consumers to use generics need comprehensive design and considerations of multiple approaches from the perspective of pricing, procurement, and health insurance reimbursement policies. Prepolicy situation analysis, in-process regular monitoring, and postpolicy impact analysis are three necessary steps for timely situation understanding, problem identification, and problem-solving with adjusted policy.

Effective promotion of generics use must be practiced based on the real situation. Tailor-made and comprehensive measures are needed to address each of the above barriers before achieving tangible cost containment effect without unexpected side effects.

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