Key components of increased drug expenditure in South Korea; implications for the future.

Hye-young Kwon Ph.D [1,2,*], Bongmin Yang Ph.D [1], Brian Godman Ph.D [3,4,5]

[1] Institute of Health and Environment, Seoul National University, Seoul, South Korea

[2] Harvard School of Public Health, Boston, MA, USA

[3] Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital Huddinge, Stockholm, Sweden

[4]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK

[5]Liverpool Health Economics Centre, Liverpool University, UK

(Accepted for publication Value in Health Regional Issues, 12/01/2015)

Abstract

Introduction: The cost of pharmaceuticals has increased rapidly in Korea in recent years. Expenditure is likely to grow further with the policy of expanding NHI coverage for four disease areas including cerebrovascular and cardiovascular disease, rare diseases and cancer. Consequently, there is a need to analyse the different components leading to this increased expenditure as a basis for suggesting future reforms in Korea.

Objective: Quantify the impact of new and established drugs on the growth of total drug spending in South Korea in recent years, specially focusing on the differentiated components of drug spending. These include treatment expansion and drug mix effects (switching from cheaper drugs to expensive ones and vice versa).

Materials and Method: A model was proposed and used to assess the impact of both new and existing drugs on changes in price, quantity, and drug mix over the 5-year period in Korea from 2006 to 2010. The database used was the National Health Insurance claims data, which covers about 97% of total population of Korea.

Results: Overall drug spending increased1.43 fold from 2006 to 2010. Drug-mix effect (ε_t=1.32) was the main contributing factor to increased drug spending, followed by increased drug utilization (Q_t=1.26). For existing drugs, treatment expansion (Q_I) and drug mix effect (ε_I) were measured at 1.28 and 1.24, respectively, while those of new drugs were 1.02(Q_N) and 1.03(ε_N). Therefore, existing drugs have a much greater effect on drug spending than new drugs.

According to the Anatomical Therapeutic Classifications, drug spending rose most significantly for the “sensory organs” class of drugs (E_t=1.78) followed by the “various” class (E_t=1.68). For existing drugs in the sensory organs class (S), drug mix effect (ε_I) was measured at 0.96. This implies that expensive drugs among existing drugs were replaced by cheaper ones. However, the quantity prescribed (Q_I) substantially increased by 1.88 fold. New drugs within this class that were more expensive than existing ones were also prescribed (ε_N=1.09) further increasing drug expenditure in Korea.

Conclusion: We found contrasting results from previous studies. The drug mix effect and existing drugs made the largest contribution to drug spending growth rather than new drugs. Policies targeting drug mix, such as promoting cost-effective prescription and rational use of drugs, including the use of cheaper cost generics without compromising care, should be primarily considered to help contain future drug expenditure.

Keywords : *Pharmaceutical expenditure, New drugs, Drug mix, Established drugs, Korea*

Key Points

• Over the last decade, pharmaceutical expenditure has steeply risen in South Korea. Early adoption of expensive new drugs and increased consumptions of drugs due to aging populations and the high prevalence of chronic diseases have been considered key drivers of cost increase in South Korea.

• A model was suggested and used to quantify the impact of new and established drugs on the differentiated components of drug spending including price, quantity and drug mix.

• The salient findings indicate that drug mix effect (switching cheaper to expensive drugs and vice versa) rather than quantity increase was the main factor for the growth of overall drug spending between 2006 and 2010. Furthermore, the effects of new drugs were minimal, compared to those of existing drugs although they positively affected on the growth of drug spending.

• Consequently, it is time to rethink pharmaceutical cost containment policy more focusing on rational use of drugs.

Background

Pharmaceutical expenditure in South Korea is of particular interest to healthcare system

regulators. Over the last decade, pharmaceutical expenditure in Korea increased 3.05 fold, while total health expenditure increased 2.45 fold [1]. South Korea spent 21.6% of its total healthcare expenditure on pharmaceuticals in 2010 [1]. This compares to Organization for Economic Cooperation and Development (OECD) countries, which spent approximately 18-19% in 2009 [2]. However, in 2010 pharmaceutical expenditure actually fell in 2010 among some EU member states [3]. This may be due to a variety of reforms and initiatives including stricter regulations for granting premium prices for new drugs and managing their entry, compulsory price cuts for existing drugs as well as a range of demand-side measures to enhance the prescribing of low cost generics versus premium priced patented products in a class or related class [4-8]. Aging populations, the increased prevalence of chronic diseases, early adoption of expensive new drugs, and doctors' preference for prescribing high-cost drugs are often cited as explanations for the growth of pharmaceutical expenditure in Korea [9-10]. This is set to continue with the policy to expand National Health Insurance (NHI) coverage for four disease areas including cerebrovascular and cardiovascular disease, rare diseases and cancer, which has been initiated by new ruling government, drug expenditure [11].

Understanding which factors contribute to increased pharmaceutical expenditure is important to the Ministry of Health and Welfare (MOHW) and the National Health Insurance Service (NHIS), which are responsible for the financial management of national health insurance. A decomposition analysis is often used to identify factors that contribute to the increase in drug spending. Drug expenditure is usually broken down into price, quantity, and drug mix using an index method, such as Lasyperes, Paasches and Fisher’s Ideal [12-26]. However, this methodology has been criticized because it could not show the contribution of new drugs to the growth of drug spending on each component of drug spending [24-26]. New drugs are usually more expensive than incumbents (existing drugs) and are consequently considered one of key drivers of increases in pharmaceutical expenditure [4,26-27]. Switching from cheaper to more expensive drugs, the so-called “drug mix effect” is one of the effects induced by the introduction of new drugs. Unless demand-side measures are in place, new premium priced drugs could replace cheaper incumbents, increasing the cost of treatment. New drugs can also induce demand from those who could not be treated appropriately with existing drug therapies, also referred to as the “treatment expansion effect” [24,26-28].

In this study, we adopted a modified model of the decomposition analysis to assess the impact of new and the established drugs on the dynamics of drug cost, and to identify policy implications for drug cost containment. Our analytical approach followed on from the model of Gerdtham and colleagues [20-22] and Addis and Magrini [23], but we aim to quantify drug mix effect and treatment expansion effect of both new and existing drugs, respectively. The remainder of this article is organized as follows: an overview of the Korean pharmaceutical market and the

introduction of new drugs; limitations of the decomposition analysis that has been applied in previous studies; details of our approach applied in this study; and ending with conclusions drawn from our analysis.

The Korean pharmaceutical market and the introduction of new drugs

Drug expenditure in Korea has grown steeply following the implementation of the Separation of Drug Dispensing and Prescribing (SDP) policy in 2000 [Figure 1]. The market size for pharmaceuticals in 2011 was 16,402 trillion Korean Won (KRW) (USD 14.325 billion) and pharmaceutical expenditure by National Health Insurance (NHI) amounted to 81.9% of the total market [29]. Most medicines available on the market were consumed under the NHI scheme, although the number of reimbursable drugs accounted for only 36.8% of all drugs approved by Ministry of Food and Drug Safety (MFDS)[Figure 1].

[Insert Figure 1]

Most new chemical entities (NCEs) were supplied by multinational companies. Approximately 270 local companies supplied generic drugs. Few local companies have the potential to develop NCEs, and to date only 18 NCEs have been developed by local companies [29].

The entry of new drugs is regulated by the Positive List System (PLS) and through price negotiations with National Health Insurance Service (NHIS), the single payer. A list of reimbursable drugs has been established in accordance with the introduction of the PLS in 2007. Subsequently, manufacturers have had to submit new drugs to the MFDS for marketing approval, and then to the MOHW to have a drug covered by the NHI. The Drug Reimbursement Examination Committee (DREC), part of the Health Insurance Review and Assessment Service (HIRA), then makes a final decision. The criteria used to determine reimbursement eligibility for new drugs include: clinical usefulness, cost-effectiveness, budget impact, current status of reimbursement, and price in other countries [9, 26, 30-32]. Once a drug has been assessed as reimbursable, the manufacturer must enter into price negotiations with NHIS before the drug can be listed in the formulary. Since 2007, the average number of newly introduced NCEs per year has dropped significantly to 27.6, as compared to 36.8 introduced between 2003 and 2006[34].

Limitations of previous decomposition studies

Several studies have analyzed drug expenditure by separating it into constituent elements, including price and quantity [12-26]. Gerdtham and colleagues [20-22] examined total drug expenditure in Sweden, emphasized the importance of residual (in other words, “drug mix”). Without changing price and quantity, drug costs can increase as a result of switching from a

cheaper drug to an expensive one in a class or related class; this is the so-called “drug mix” effect. They pointed out that standard price indices do not reflect price changes resulting from changes in drug consumption, especially changes resulting from the introduction of new drugs. Several studies have examined drug mix effect and identified it as major factor in drug spending growth [20-24]. Dubois and colleagues [25] tried to quantify the impact of new drugs by calculating price and volume factors including changes in average price per day, the number of prescriptions per person, and the number of days per prescription. Their results indicate that prescribed days, prescriptions, and the number of patients were significant factors in expenditure growth.

According to Gerdtham and colleagues’ model [20-22], drug mix (residual) and treatment expansion effect (quantity increase) were measured. These effects were attributable to both new and existing drugs. However, previous studies didn’t distinguish these effects according to types of drugs. In this study, we tried to quantify the impact of new drugs on the components of drug cost. To do so, we proposed a modified formula to segregate drug mix and treatment expansion effects by types of drugs: new and existing drugs. We then applied this formula to investigate the factors contributing to increased drug expenditure in the period from 2006 to 2010 in South Korea, and quantified the effects of new and existing drugs on changes in each component of drug cost. Finally, we have made some suggestions for the authorities to consider when deliberating future reforms. These are based on activities successfully undertaken by European health authorities and health insurance agencies.

Materials and Method

Data collection

The data used in this study were obtained from the National Health Insurance Service (NHIS), which covers about 97% of Korean population. Total pharmaceutical expenditure data from NHIS claims for the years from 2006 to 2010 were used. Over 12,000 reimbursable products (about 4,000 ingredients) were included for analysis. Each ingredient identified in the NHIS data was matched to the Anatomical Therapeutic Classification (ATC) code [33]. The data were compiled based on ingredients. Medicines that incurred no charges in 2006, but appeared in the data in 2010 were regarded as new drugs. All other listed drugs were considered incumbents. Quantity data was collected as the minimum unit for each drug and delivery system, e.g. ampoules, tablets, patches, inhalers and capsules, as it proved impossible to calculate all utilisation in terms of defined daily doses.

Study methodology

The equation (Equation 1), first proposed by Gerdtham and colleagues [20-22] shows changes in

price (P), quantity (Q) and drug mix (ε). The price change (P) is calculated by Laspeyres index. According to this index, the price of new drugs is not detected because their prices are not available at the base period. Thus, Laspeyres index (P) reflects only the price of incumbents only. The quantity ratio (Q) shows changes in the quantities of prescribed drugs including both new and incumbent drugs. Drug mix (ε) indicates changes in the weighted average cost of drugs attributable to both new and existing ones. Thus, quantity change and drug mix are attributable to both new and existing drugs. Consequently, we can measure drug mix and treatment expansion effects due to new drugs and existing drugs, separately.

$$E = \frac{\sum P_1 Q_1}{\sum P_0 Q_0} = P_t \, X \, Q_t \, X \, \varepsilon_t = \frac{\sum P_1 Q_1}{\sum P_0 Q_0} \; X \; \frac{\sum Q_1}{\sum Q_0} \, x \, \frac{(\sum P_1 Q_1 / \sum Q_1)}{(\sum P_1 Q_0 / \sum Q_0)} \qquad (1)$$

NB: Q_0: quantity of drugs in 2006; Q_1: quantity of drugs in 2010; P_0: price of drug in 2006; P_1: price of drug in 2010, Pt : Change in Price, Qt : Change in Quantity, εt : Drug mix effect

The following equation is proposed (Equation 2) to identify how new and incumbent drugs affect the dynamics of drug cost. The growth of total drug expenditure (E_t) is attributed to new drugs (E_N) and incumbents (E_I).

$$\mathrm{E} = \frac{\sum P_1 Q_1}{\sum P_0 Q_0} = E_N \times E_I = \sum P_1^N Q_1^N \times \frac{\sum P_1^I Q_1^I}{\sum P_0^I Q_0^I} \qquad (2)$$

NB: E_N: growth of drug spending on new drugs; E_I :growth of drug expenditure on existing drugs;Q_1^N: quantity of new drugs in 2010; P_1^N: price of new drugs in 2010;Q_0^I: quantity of existing drugs in 2006;Q_1^I: quantity of existing drugs in 2010;P_0^I:price of existing drugs in 2006;P_0^I:price of existing drugs in 2010.

Equation 2 can then be rewritten as Equation 3 and 4:

$$\mathrm{E} = \frac{\sum P_1 Q_1}{\sum P_0 Q_0} = P_t \times Q_t \times \varepsilon_t = E_N \times (P_I \times Q_I \times \varepsilon_I) \qquad (3)$$

$$E_N = Q_N \times \varepsilon_N = \frac{Q_t}{Q_I} \times \frac{\varepsilon_t}{\varepsilon_I} \qquad (4)$$

NB: P_t: price index between 2006 and 2010; P_I : price index of existing drugs; P_N : Price index of new drugs; Q_t : quantity change between 2006 and 2010; Q_I: quantity change of existing drugs; Q_N: quantity change of new drugs; ε_t: drug mix index between 2006 and 2010; ε_I:Drug mix index of existing drugs; ε_N:Drug mix index of new drugs.

E_N is constituted with Q_N and ε_N because P_t is equal to P_I. If E_N> 1, new drugs positively contribute to the increase in drug spending. If E_N=1, no impact from new drugs is observed, signifying there has been no introduction or penetration of new drugs. Q_N indicates the treatment expansion effect of new drugs, and ε_N indicates a shift in prescriptive patterns to expensive new drugs. If one of these indices is greater than 1, new drugs positively contributed to the growth of drug spending, either by creating demands for new drugs, or by a shift in prescriptive patterns to expensive new drugs. This modified equation (Equation 3) can also detect the impact of existing drugs on the component of drug cost through P_I, Q_I and ε_I.

Results

Table 1 presents the quantified impact of new and incumbent drugs on overall drug spending from 2006 to 2010. Overall pharmaceutical expenditure increased by 43%. Drug mix (ε_t=1.32) was the main contributing factor for increased drug spending, followed by quantity increase (Q_t=1.26). The price index (P_t)was 0.86, indicating that prices of existing drugs decreased by 14% in 2010, as compared to 2006. Existing drugs (E_I=1.36) rather than new drugs (E_N=1.05) substantially affected the increase in total drug spending. Approximately 83% of the increase in drug expenditure was attributable to existing drugs. Quantity (Q_I) and drug mix (ε_I) for existing drugs increased by 1.24 and 1.28 fold, respectively. This indicates that manufacturers of existing drugs have continued to expand their market, and that more expensive drugs have been used rather than cheaper alternatives.

Table 1. Decomposition analysis for total, incumbent and new drug expenditures

Category	E	P	Q	ε
Total	1.43	0.86	1.26	1.32
Incumbents	1.36	0.86	1.24	1.28
New drugs	1.05	1	1.02	1.03

New drugs have positively contributed to increased drug spending, although minimally compared with established drugs. In this regard, 17% of the increase in drug expenditure from 2006 to 2010 resulted from the use of new drugs. P_N was set at 1 because the prices of new drugs were not available in 2006. Consequently, price changes for new drugs could not be identified within our equation. However, the drug-mix effect (ε_N) induced by new drugs measured 1.03, which indicates a switch from incumbents to marginally more expensive new drugs. The impact of new drugs on quantity increase (ε_N) was 1.02, which is not significant. Notably, it was found that the treatment expansion and drug mix effects were much larger for existing drugs than for new drugs. This is different to the general belief that new drugs are generally regarded as a key driver of increased drug expenditure.

Table 2 presents the results according to ATC codes. Drug spending has risen most significantly in the “sensory organs” class of drugs (E_t=1.78), followed by the “various” class (E_t=1.68). Increases in expenditure for the various class (V), sensory organs(S), anti-neoplastics & immune modulating agents (L), blood and blood forming organs(B), cardiovascular system(C), nervous system(N) and respiratory system(R) were greater than the average growth rate (1.42). Growth of expenditure for all groups was mainly attributed to incumbent drugs. New drugs influenced expenditure most greatly for the “sensory organs” class (E_N=1.13). No new drugs were launched during the observation period for class P (anti-parasitics, insecticides, and repellents). Although drug spending for class C drugs increased by 1.53 fold, they represented the greatest percentage of total drug spending.

Table 2. Growth of drug expenditures for ATC groups

Anatomical therapeutic class	*Overall*	*Incumbents*	*New drugs*	*Percentage of TPE[a]*
(A) Alimentary tract and metabolism	1.37	1.29	1.06	16.3%
(B) Blood & blood forming organs	1.59	1.54	1.04	9.0%
(C) Cardiovascular system	1.53	1.44	1.06	19.7%
(D) Dermatologicals	1.16	1.11	1.05	1.2%
(G) Genitourinary system and sex hormones	1.39	1.25	1.11	2.4%
(H) System hormonal preparations	1.36	1.34	1.02	0.8%
(J) Antiinfective for systemic use	1.25	1.20	1.04	15.1%
(L) Antineoplastic & immune modulating agents	1.60	1.52	1.05	7.3%
(M) Musculoskeletal system	1.22	1.17	1.05	7.1%
(N) Nervous system	1.49	1.41	1.06	9.2%
(P) Antiparasitics, insecticides & repellents	1.03	1.03	1.00	0.1%
(R) Respiratory system	1.49	1.42	1.05	5.7%
(S) Sensory organs	1.78	1.58	1.13	2.6%
(V) Various	1.68	1.64	1.02	3.5%

a: Percentage of total pharmaceutical expenditures (TPE) in 2010.

A breakdown of drug expenditure factors for each ATC group, and each type of drug, is presented in Table 3. Price indices for all classes are less than 1, indicating a decrease in the prices of existing drugs. A major factor in total drug expenditure growth was increased quantities for all classes except ATC classes A, J, M, N and R, for which the drug mix effect was a more significant factor. Drug mix for all classes increased (ε_t>1) except for class P (ε_t=0.86). The effects of new drugs equalled 1 for ATC class P. This indicates that cheaper drugs in ATC class P were used instead of expensive ones, without the introduction of new drugs. For ATC class S, cheaper existing drugs replaced more expensive ones (ε_I =0.96), but the quantity (Q_I) increased substantially (1.88 times). New drugs within this class, which were more expensive than incumbents, were introduced and prescribed (ε_N =1.09), which led to the increase in overall drug expenditure. Cheaper anti-parasitic drugs were increasingly used (ε_t =0.86) without the introduction of new drugs. For ATC class S, drug quantities substantially increased (Q_I=1.88) and cheaper existing drugs were frequently used (ε_t=0.96). In addition, expensive new drugs were introduced (Q_N=1.03 and ε_N=1.02). Overall, these factors contributed to an increase in drug spending.

Table 3 Growth of drug expenditures for ATC groups

Anatomical therapeutic class	***Total***			***Incumbents***			***New drugs***	
	P	**Q**	**ε**	**P**	**Q**	**ε**	**Q**	**ε**
(A) Alimentary tract and metabolism	0.88	1.16	1.34	0.88	1.15	1.28	1.01	1.05
(B) Blood & blood forming organs	0.88	1.50	1.20	0.88	1.43	1.22	1.05	0.98
(C) Cardiovascular system	0.84	1.50	1.22	0.84	1.44	1.19	1.04	1.02
(D) Dermatologicals	0.86	1.26	1.07	0.86	1.24	1.04	1.02	1.03
(G) Genitourinary system and sex hormones	0.76	1.42	1.29	0.76	1.30	1.27	1.09	1.01
(H) System hormonal preparations	0.83	1.39	1.18	0.83	1.38	1.16	1.00	1.01
(J) Antiinfective for systemic use	0.85	1.13	1.30	0.85	1.13	1.25	1.00	1.04
(L) Antineoplastic & immune modulating agents	0.84	1.54	1.23	0.84	1.54	1.18	1.00	1.05
(M) Musculoskeletal system	0.87	1.12	1.26	0.87	1.11	1.21	1.01	1.04
(N) Nervous system	0.87	1.18	1.45	0.87	1.17	1.39	1.01	1.04
(P) Antiparasitics, insecticides & repellents	0.91	1.31	0.86	0.91	1.31	0.86	1.00	1.00
(R) Respiratory system	0.89	1.26	1.32	0.89	1.23	1.29	1.03	1.02
(S) Sensory organs	0.88	1.94	1.04	0.88	1.88	0.96	1.03	1.09
(V) Various	0.90	1.46	1.27	0.90	1.46	1.25	1.00	1.02

Discussion

This study was initiated to assess the impact of new drugs as a driver of increase drug expenditure in Korea in recent years. The treatment expansion and drug-mix effects of new drugs were examined. To quantify these effects, we analyzed total pharmaceutical expenditure for South Korea over the 5-year period from 2006 to 2010. Previous studies [20-24] considered only changes in price, quantity, and drug mix over time, without segregating observed changes by type of drug. However, these changes were attributable to both new drugs and existing drugs. Our research question was posed to distinguish the effects associated with new and existing drugs. The previous model of Gerdtham and colleagues [20-22] was modified to calculate the treatment expansion effect (Q_N) and drug-mix effect (ε_N). The equation (Equation 3) was also designed to measure the impact of existing drugs in light of changes in price (P_I), quantity (Q_I) and drug mix (ε_I).

The results of this study indicate that existing drugs had a greater effect on the growth of drug expenditure in recent years in Korea than the launch of new premium priced drugs. Although treatment expansion and the drug-mix effect of new drugs positively contributed to the increase in drug spending, the quantified impact was minimal. Existing drugs substantially contributed to increased pharmaceutical expenditure in recent years. Prices for existing drugs decreased slightly over the period (P_I=0.86), but the drug-mix effect (ε_t=1.32) had the most significant impact, followed by quantity increase (Q_t=1.26). Given that increased drug volumes have long been claimed to be the major factor contributing to the growth of Korean pharmaceutical expenditure in recent years [17-19], this study presents different results. Our findings indicate that the drug-mix effect, both for existing and new drugs, had a greater impact on the growth of drug expenditure than increased volumes. Additionally, the growth of expenditure was mainly attributable to existing drugs rather than new drugs. Prices for existing drugs decreased in 2010 in all ATC classes when compared to 2006 prices. However, the overall drug-mix changed in a number of classes increasing overall drug expenditure. The drug mix effect was more significant for ATC classes A, J, M, N and R, with increasing volumes the major factor for increased drug expenditure in the other classes. This is perhaps not surprising since cost containment measures for pharmaceuticals in South Korea have traditionally focused on enforced price cuts rather than demand-side measures. Numerous re-pricing strategies have been implemented, but the price decreases over the 5 years have not been significant [32, 34-35]. The absence of policies that encourage the use of cheaper drugs or more cost-effective prescriptive practices results in the increase utilization of expensive drugs facilitated by the considerable marketing activities of pharmaceutical companies [36]. Therefore, demand-side strategies to address this should be prioritized in order to efficiently control the increase of pharmaceutical expenditure in Korea with increased coverage in four disease areas.

Several policies enacted by the NHIS targeting new drugs, such as the PLS and price negotiation procedure with the single payer, have acted as an entry barrier. However, many of the strategies for drugs that are already listed have focused only on cutting prices, and the effectiveness of these strategies is debatable [37]. Since our findings suggest that existing drugs rather than new drugs have a significant impact on the growth of drug expenditure, policies targeting both cost-effective prescription practices and efficient price controls for existing drugs should be considered. There have been a number of supply- and demand-side measures across Europe to enhance the prescribing of low cost generics in classes where all the drugs are seen as similar in all or nearly all patients [38-42]. These initiatives have released considerable resources without compromised care (summarized in Table 4), with the products in these classes seen as therapeutically similar at appropriate doses demonstrated by meta analyses, registry studies as well as successful therapeutic switching programs [47-53].

A similar finding regarding losartan in Sweden was seen in NHS Bury in England. Initially there was no change in the utilization of losartan post generics. This changed significantly following multiple interventions which were similar to Sweden (Table 4) for patients with hypertension, with losartan utilisation increasing significantly from 26% of all single ARBs to 65% 7 months later [49]. The savings were estimated at eight times the cost of implementing this comprehensive program [49].

Table 4. Combination of supply- and demand-side initiatives among selected European countries and their impact

Country	Class	Initiative and outcomes
Denmark [42]	ARBs	• Delisting of all other ARBs other than losartan from the reimbursed list • Patients could still be prescribed another ARB and have this reimbursed. However, the prescribing physician has to justify the rationale and have this accepted before other ARBs reimbursed – otherwise 100% co-payment • The combination of supply- and demand-side measures in Denmark resulted in a 77% reduction in ARB expenditure over the study period despite a 16% increase in utilisation, leading to estimated savings of over 290million Danish Kroner (€40 million) per annum
Netherlands [38, 41,43]	PPIs and statins	• Under the preference pricing policies only the cheapest generics are reimbursed, with patients having to cover the costs themselves for a non-preferred drug. This has resulted in generic omeprazole and simvastatin a only 2% of pre-patent loss prices • This coupled with extensive multiple demand side measures including educational activities, prescribing targets and physicians financial incentives, to increase the prescribing of generics vs. patented products resulted in reimbursed expenditure for the PPIs falling by 58% in 2010 vs. 2000 despite a 3 fold increase in utilisation (DDDs) and reimbursed expenditure for the statins falling by 14% in

		2010 vs. 2000 despite a 3.8 fold increase in utilisation. As a result, saving considerable resources without compromising care
Scotland [38,40,41, 44,45]	PPIs, statins and ACEIs vs. ARBs	○ Transparency in the pricing of generics, coupled with transparency in the rebates offered to wholesalers and pharmacists, has resulted in prices of high volume generics as low as 2%/ 3% to 12% of pre-patent loss prices ○ Multiple demand-side measures including extensive educational activities, prescribing targets and physician financial incentive schemes to increase the prescribing of generics vs. patented products resulted in expenditure/ 1000 inhabitants/year for the PPIs in 2010 56% below 2001 levels despite a 3 fold increase in utilisation and reimbursed expenditure for the statins increased by only 7% in 2010 compared with 2001 despite a 6.2 fold increase in utilisation. Without these measures, health authority spending on PPIs for the same overall utilization would have been GB£159million higher in 2010 in Scotland for the 5.2million population and GB£290million for the statins ○ Similar multiple demand-side measures vs. Portugal with its limited demand-side measures to encourage the preferential prescribing of generic ACEIs limited ARB prescribing to only 19% of total renin-angiotensin inhibitor drugs in 2007 (DDD basis) vs. 44% in Portugal, leading to stable reimbursed expenditure between 2001 and 2007 vs. over 40% increase in Portugal
Sweden [38,39,41, 46-48]	PPIs, statins and ARBs	• Compulsory generic substitution with the lowest price molecule has resulted in prices for high-volume generics being 4 to 13% of originator pre-patent loss prices by 2009. More recently: ○ all pharmacies are obligated to offer patients the cheapest molecule currently on the market (ATC Level 5) when there are substitutable generic medicines available ○ there are regular monthly auctions for generics in Sweden, with the manufacturer with the lowest price wining the auction. However manufacturers must be able to supply the whole market for the entire period (typically 70% to 80% of sales during the period) ○ Expected savings from the tendering process are estimated at 8billion SEK/ year from 2011 onwards • Multiple demand side measures including extensive educational activities, prescribing targets and physician financial incentives, to increase the prescribing of generics resulted in reimbursed expenditure for the PPIs decreasing by 49% in 2007 vs. 2001 despite utilisation increasing by 53% during this period. Similar combined measures led to a 39% reduction in statin expenditure in 2007 vs. 2001 idespite a 3.2 fold increase in utilisation during this period • Reimbursed expenditure (Euros/ 1000 inhabitants/ year) in Sweden was less than one-tenth of that in Ireland in 2007 with its increased utilisation of patented PPIs and statins following generics as limited demand-side measures to combat company activities (although more co-morbid population) • Similar demand-side measures including encouraging therapeutic substitution of patented ARBs with losartan significantly increased losartan utilisation in recent years. As a result, total single ARB expenditure fell by 26% in recent years in Sweden despite a 16% increase in utilisation. Separate analyses suggest care was not compromised at appropriate ARB doses

NB: ARB = angiotensin receptor blocker, ACEIs = Angiotensin converting enzyme inhibitors, PPIs = Proton Pump Inhibitors

We believe the exemplars in Denmark, the Netherlands, Sweden and the UK (NHS Bury and Scotland) among a range of classes provide guidance for Korea as it contemplates abolishing co-payments in high prevalence disease areas such as cardiovascular and cerebrovascular diseases without appreciably increasing expenditures.

We accept there are limitations with the study design. These include our suggested methodology. However, we believe this approach is justified for the reasons we have given. We also accept that we have not used defined daily doses in our analysis. However, other studies have used different units including IMS units [54] as well as items dispensed [49]. Consequently, we believe our findings are justified and provide direction to the authorities in Korea.

Conclusions

This study used a model to assess the impact of both new and existing drugs on changes in price, quantity, and drug mix over the 5-year period in Korea from 2006 to 2010. Contrary to the results of previous studies, our findings indicate that the drug-mix effect and existing drugs contributed most to the growth of pharmaceutical expenditure. Policies targeting drug mix are not sufficiently implemented in South Korea and reforms to encourage the prescribing use of cost-effective drugs within a class should be emphasized. Measures can also include initiatives to reduce drug volumes where these are considered inappropriately high.

Acknowledgements

We are indebted to the National Health Insurance Corporation for providing the data used for analysis. This work was self-funded.

References

1. Health Insurance Review and Assessment Service (HIRA). Statistical indicators for medical expenses, http://www.hira.or.kr/dummy.do?pgmid=HIRAA020045030000&cmsurl=/cms/information/05/03/03/stats_surface.html [Accessed 10 October 2013].

2. OECD. Health at a Glance 2011. OECD indicators. Available via URL: http://www.oecd.org/els/health-systems/49105858.pdf [Accessed 22 November 2013]

3. OECD (2012), "Pharmaceutical expenditure", in Health at a Glance: Europe 2012, OECD Publishing. http://dx.doi.org/10.1787/9789264183896-55-en [Accessed 22 November 2013].

4. Godman B, Malmstrom RE, Diogene E et al. Dabigatran - a continuing exemplar case history demonstrating the need for comprehensive models to optimize the utilization of new drugs. *Frontiers in pharmacology*. 2014;5:109.

5. Vogler S, Zimmermann N, Leopold C, et al. Pharmaceutical policies in European countries in response to the global financial crisis. *South Med Rev* 2011;4:69-79.

6. Simoens S. A review of generic medicine pricing in Europe *GaBI Journal* 2012; 1(1):8-12.

7. Dylst P, Vulto A, Godman B, et al. Generic medicines: solutions for a sustainable drug market? *Appl Health Econ Health Policy* 2013;11(5):437-43.

8. Godman B, Wettermark B, van Woerkom M et al. Multiple policies to enhance prescribing efficiency for established medicines in Europe with a particular focus on demand-side measures: findings and future implications. *Frontiers in pharmacology*. 2014;5:106.

9. Park SE, Lim SH, Choi HW et al. Evaluation on the first 2 years of the positive list system in South Korea. *Health Policy* 2010;104:32-29.

10. Kim HJ. Pharmaceutical reform in South Korea and the lessons it provides. *Health Affairs* 2008;27(4): w260–9.

11. Ministry of Health and Welfare (MOHW), NHI coverage expansion plan for four severe diseases, Press release, 26 June 2013. South Korea.

12. Morgan SG. Quantifying components of drug expenditure inflation: the British Columbia senior's drug benefit plan. *Health Services Research* 2002 Oct;35(5):1243-1266.

13. Chernew EM, Smith GD, Kirking MD et al. Decomposing pharmaceutical cost growth in different types of health plans. *Am J Managed Care* 2001; 7(7):667-673.

14. Patented Medicine Price Review Board (PMPRB), Pharmaceutical trends overview report: Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, and First Nations and Inuit Health Branch of Health Canada 1997-1998 to 2003-2004. Report, Canada, June 2006.

15. Merlis M. Explaining the growth in prescription drug spending: a review of recent studies. Department of Health and Human Services Conference on Pharmaceutical Pricing Practices, Utilization and Costs. August 8-9. 2000 Washington, DC. http://www.aspe.hhs.gov/health/reports/drug-papers/merlis/merlis-final.htm [Accessed 12 October 2013].

16. Bernt ER. Pharmaceuticals in US health care: determinants of quantity and prices. *J Econ Perspect* 2002;16:45-66.

17. Bae EY. Decomposition analysis on contributing factors to drug expenditures. Report, Health Insurance Review and Assessment Service (HIRA), Korea, March 2007.

18. Jang SM, Park CM, Choi YJ et al. Analysis of determinants of inpatient drug expenditure in NHI. *The Korean Journal of Health Economics and Policy* 2010;16(3):115-137.

19. Hurh SM, Jung JC, Lee HY, A Study of the reasonable drug expenditures, Report, National Health Insurance Corporation(NHIC), Korea 2006.

20. Gertham UG, Johannesson M, Gunnarsson B et al. The effect of changes in treatment patterns on drug expenditure. *Pharmacoeconomics*1998;13(1-2):127-134.

21. Gerdtham UG, Lundin D. Why did drug expenditure increase during the 90's?- A decomposition of Swedish expenditure data. *Pharmacoeconomics* 2004;22:29-42.

22. Gerdtham UG, Lundin D. How did drug expenditure change for different age groups during the 90's? - Evidence from Sweden. *Expert Review of PharmacoEconomics & Outcomes Research* 2004;4:343-351.

23. Addis A, Magrini N. New approaches to analyzing prescription data and to transfer pharmacoepidemiological and evidence-based reports to prescribers. *Pharmacoepidemiology and Drug Safety* 2002;11:721-726.

24. Hsieh CR, Sloan AF. Adoption of pharmaceutical innovation and the growth of drug expenditure in Taiwan: Is it cost-effective? *Value Health* 2008;11(2):334-344.

25. Dubois RW, Chawla AJ, Neslusan CA et al. Explaining drug spending trends: does perception match reality? *Health Affairs* 2000;19(2):231-239.

26. Kwon HY. *Competitive diffusion, budget impact and reimbursement and pricing of new drugs.* PhD Dissertation, Seoul National University, South Korea, 2012.

27. Newhouse JP. Medical care costs : how much welfare loss? *J Econ Perspect* 1992;6:3-21.

28. Mullins CD, Wang J, Palumbo FB et al. The impact of pipeline drugs on drug spending growth. Health Affairs 2001;20(5):210-215.

29. Yang BM, Kwon HY, Kim S et al. Enhancing public roles in manufacturing and supplying Medicines in Korea. Report, Seoul National University & National Health Insurance Corporation, Korea, March 2013.

30. Yim EY, Lim SH, Oh MJ, et al. Assessment of pharmacoeconomic evaluations submitted for reimbursement in Korea. *Value Health* 2012 Jan-Feb;15(1 Suppl):S104-10.

31. Ha D, Choi Y, Kim DU et al. Comparative analysis of the impact of a positive list system on new chemical entity drugs and incrementally modified drugs in South Korea. *Clin Ther* 2011; 33(7):926-32.

32. Ministry of Health and Welfare (MOHW). *Facts and Statistics for Health Insurance Policy*, Report for the Department of Health Insurance Policy, April 2010. Seoul.

33. WHO Collaborating Centre for Drug Statistics Methodology. ATC / DDD index 2011. WHO, Oslo. http://www.whocc.no/atc_ddd_index/ [Accessed 11 October 2013].

34. Kwon HY, Hong JM, Godman B, Yang BM. Price cuts and drug spending in South Korea : The case of Antihyperlipidemic agents *Health policy.* 2013;112:217– 226

35. Lee SY, Pricing & re-pricing of the reimbursable drugs, *The Journal of Korean Pharmaceutical Policy* 2008;3(2):6-23.

36. Godman B, Gustafsson LL. A new reimbursement systems for innovative pharmaceuticals combining value-based and free market pricing. *Applied Health Economics and Health Policy* 2013; 11:79–82.

37. Kwon HY, Yang BM. Fixed budget for pharmaceuticals, *The Korean Journal of Health Economics and Policy* 2011;17(1):25-46.

38. Godman B, Campbell S, Suh HS et al. Ongoing measures to enhance prescribing efficiency across Europe: implications for other countries. J Health Tech Assess 2013;1:27-42

39. Godman B, Shrank W, Andersen M et al. Policies to enhance prescribing efficiency in Europe: findings and future implications. *Frontiers Pharmacol*. 2011; 1 (141): 1-16 doi:

10.3389/fphar.2010.00141

40. Vončina L, Strizrep T, Godman B et al. Influence of demand-side measures to enhance renin–angiotensin prescribing efficiency in Europe: implications for the future. *Expert Rev Pharmacoeconomics and Outcomes Res* 2011; 11: 469-79

41. Godman B, Bennie M, Baumgärtel C et al. Essential to increase the use of generics in Europe to maintain comprehensive healthcare? Farmeconomia: *Health Economics and Therapeutic Pathways* 2012; 13 (Suppl 3): 5-20

42. Hesse U, Godman B, Petzold M et al. Impact of delisting ARBs, apart from losartan, on ARB utilisation patterns in Denmark; implications for other countries. *App Health Econ Health Policy* 2013; 11:677–685

43. van Woerkom M, Piepenbrink JF, Godman B et al. Ongoing measures to enhance the efficiency of prescribing of PPIs and statins in the Netherlands; influence and future implications. *Journal of Comparative Effectiveness Research* 2012; 1: 527-38.

44. Godman B, Bishop I, Finlayson AE et al. Reforms and initiatives in Scotland in recent years to encourage the prescribing of generic drugs, their influence and implications for other countries. Expert Rev. Pharmacoecon. Outcomes Res. 2013; 13(4): 469–82.

45. Bennie M, Godman B, Bishop I et al. Multiple initiatives continue to enhance the prescribing efficiency for the proton pump inhibitors and statins in Scotland. *Expert Review Pharmacoeconomics and Outcomes Research* 2012;12:125-130.

46. Godman B, Wettermark B, Hoffman M et al. Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden; global relevance. *Expert Rev Pharmacoeconomcis Outcomes Research* 2009; 9:65-83.

47. Godman B, Wettermark B, Miranda J et al. Influence of multiple initiatives in Sweden to enhance ARB prescribing efficiency following generic losartan; findings and implications for other countries. *Int J Clin Pract* 2013; 67: 853–62

48. Moon J, Godman B, Petzold M et al. Different initiatives across Europe to enhance losartan utilisation post generics: impact and implications. *Frontiers in pharmacology*. 2014;5(Article 219):1-10.

49. Martin A, Godman B, Miranda J et al. Measures to improve angiotensin receptor blocker prescribing efficiency in the UK: findings and implications. *Journal of Comparative Effectiveness Research 2014;3(1):41-51.*

50. Usher-Smith J, Ramsbottom T, Pearmain H et al. Evaluation of the clinical outcomes of switching

patients from atorvastatin to simvastatin and losartan to candesartan in a primary care setting: 2 years on. *International journal of clinical practice*. 2008;62(3):480-4.

51. Sakshaug S, Furu K, Karlstad O et al. Switching statins in Norway after new reimbursement policy: a nationwide prescription study. *British journal of clinical pharmacology*. 2007;64(4):476-81.

52. Norman C, Zarrinkoub R, Hasselstrom J et al. Potential savings without compromising the quality of care. *International journal of clinical practice*. 2009;63(9):1320-6.

53. Weng TC, Yang YH, Lin SJ et al. A systematic review and meta-analysis on the therapeutic equivalence of statins. *Journal of clinical pharmacy and therapeutics*. 2010;35(2):139-51.

54. Gobernado M, Valdés L, Alós JI et al. Spanish Surveillance Group for Urinary Pathogens. Antimicrobial susceptibility of clinical Escherichia coli isolates from uncomplicated cystitis in women over a 1-year period in Spain. *Rev Esp Quimioter.* 2007;20(1):68-76.