Pharmaceutical Care & Health Systems

Zeng, J Pharma Care Health Sys 2015, 2:4
http://dx.doi.org/10.4172/2376-0419.1000141

Review Open Access

Ongoing Initiatives in China to Enhance Prescribing Efficiency: Impact and Proposals for Improvement

Wenjie Zeng[1], Mengying Feng[1], Stephen M Campbell[2,3], Alexander E Finlayson[4] and Brian Godman[5,6,7*]

[1]*School of Management, Chongqing Jiaotong University, China*

[2]*Centre for Primary Care, Institute of Population Health, University of Manchester, United Kingdom*

[3]*NIHR Greater Manchester Primary Care Patient Safety Translational Research Centre, Manchester, UK*

[4]*Green Templeton College, University of Oxford, Oxford, UK*

[5]*Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital Huddinge, Sweden*

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

[7]*School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia*

***Corresponding author:** Brian Godman, Department of Laboratory Medicine, Division of Clinical Pharmacology, Karolinska Institutet, Karolinska University Hospital Huddinge, SE-141 86, Stockholm, Sweden, Tel: 00468 585 81068; Fax: 00468 585 81070; Email: Brian.Godman@ki.se

Received date: June 26, 2015; **Accepted date:** July 09, 2015; **Published date:** July 16, 2015

Abstract

Background: Pharmaceutical expenditure is currently rising by 16% per annum in China, greater in recent years. Initiatives to moderate this growth include drug pricing regulations, essential medicine lists and encouraging generic prescribing. These measures are principally concentrated in hospitals as they account for over 80% of total pharmaceutical expenditure. However, no monitoring of prescribing and perverse incentives enhances irrational prescribing.

Objective: Review the influence of recent measures on subsequent utilization and expenditure of high-volume classes in China to provide future guidance.

Methods: Principally a narrative review of published studies of the proton pump inhibitors (PPIs), statins, renin–angiotensin inhibitor drugs and traditional Chinese medicines (TCMs) between 2004 and 2013 in the largest teaching hospital group in Chongqing District.

Results: Appeciable increase in drug utilisation including TCMs. Generics typically only 30% to 34% of total utilisation for the molecule for CV medicines, with decreasing trends in recent years. Greater utilisation of generic PPIs; however, this includes generic injectable preparations with considerably higher prices. Prices decreased over time, with appreciable reductions for some generics. Overall, considerable opportunities to save resources without compromising care. Restricting the formulary to just one statin, angiotensin receptor blocker or PPI based on the cheapest one would have saved 50-84% of total accumulated expenditures.

Conclusions: Encouraging to see high utilisation of generic PPIs and low prices for some oral generics. However, real progress will only be made by addressing current perverse financial incentives. Potential reforms could include limiting the number of available medicines in a class to enhance the quality and efficiency of prescribing.

Keywords: ARBs; China; Generics; Incentives; PPIs; Reforms; Statins

Background

As a developing and transitional country, China has seen considerable increases in pharmaceutical expenditure in recent years, growing at over 16% per annum during the past decade and over 35% per annum recently [1-4]. This growth has principally been driven by an increase in insurance coverage [4], although a change in the financing of hospitals has also contributed to this growth [5]. For example, the Chinese government introduced three different types of health insurance in recent years targeting different populations, with coverage reaching over 90% of the population by 2011 [3,6-8], although large disparities still exist [9]. The ultimate goal of the authorities in China is universal coverage by 2020 [6-8,10]. As a result of increased coverage, healthcare expenditure increased from 3.5% to 5% of GDP between 1995 and 2010, equating to a ten-fold increase in yearly per capita spending from US$ 21 to 220 [8]. This further increased to US$350 per year in 2011 [4]. Expenditure on pharmaceuticals was 42% of total healthcare expenditure in 2009 [3], amounting to CNY580 billion (US$92 billion) in 2012 and CNY695 billion in 2013 [4].

Consequently, the authorities in China have introduced a number of measures in recent years to help moderate this growth given the continual pressure on resources [1,2,8,9,11]. To date, these measures have principally concentrated on trying to control pharmaceutical prices and expenditure in hospitals since more than 80% of total

pharmaceutical consumption is currently dispensed in public hospitals in China [1,2,12].

Medicines in hospitals are subject to tenders in each province and municipality with each hospital pharmacy deciding on its own procurement list [5]. Studies suggesting these bidding processes reduced the prices of essential medicines by 16.9% between 2009 and 2011 [8]. However, there are no formal pricing policies for generics in China unlike the policies introduced across Europe, which have resulted in low prices in some countries [13-16]. This lack of policies is at least partially responsible for the fact that there are more than 5,000 pharmaceutical manufacturers in China producing mainly generics [1,4,12]. In addition, pharmaceutical expenditure in hospitals accounted for approximately 40% to 50% of their total income during the past decade [1,4,5,17-20]. This arose because the financial support from the Chinese government to public hospitals declined steadily from approximately 60% of hospital revenues in the 1980s to 8.2% by 2003 or lower [5,21]. As a consequence, hospitals in China must necessarily use the revenues from drug procurement and dispensing for their sustainability [3,5,8,17,22]. Even with the various measures to reduce procurement prices over time, the actual mark-up of medicines in hospitals in 2005 averaged approximately 42% [17]. There are also incentives for physicians to overprescribe drugs as well as prescribe drugs that produce the greatest profit for them and the hospital [1,3,5,23,24]. This has resulted in for instance the overuse of antibiotics, especially injectable antibiotics, as well as injections generally [5,20,22,25-27]. This situation is exacerbated by currently low salaries for physicians in China, with many physicians earning 5000 CNY (US$ 780) a month or less [28], and expected to earn up to 30% of their earnings through profit sharing with hospitals [4].

Demand-side measures to enhance the quality and efficiency of care include the development of an essential medicine list, clinical guidance and guidelines [2,4,8,19,29]. However, there are currently few initiatives among public insurers to monitor the quality of prescribing in China [20,23]. There were reforms specifying that prescriptions should be written by generic (INN) name but limited enforcement to date [1,17,21]. As a consequence, physicians tend to write prescriptions with the generic (INN) name and simultaneously indicate the brand or manufacturer's name; alternatively, they simply choose medicines listed in hospitals' information technology (IT) systems with the corresponding brand name or manufacturer [1,17,21]. This situation is not helped by similar patient co-payments for an originator or a generic as well as physicians and hospitals necessarily using the profits from medicine procurement for their sustainability [4,5,21,23].

The objective of this review article is to appraise the influence of the various measures and initiatives introduced in China during the past decade to improve prescribing efficiency among a number of high-volume classes on their subsequent utilization and expenditure. Following this, use the findings to give guidance on potential measures and initiatives that the authorities in China could consider as they strive for universal coverage by 2020. This will be based on measures successfully introduced in Europe, with Europe already attaining and maintaining universal coverage through a variety of initiatives and measures [15,30-33].

Methodology

The authors conducted a narrative review of multiple publications written by themselves and others regarding generics, injectables and Traditional Chinese Medicines (TCMs) in China and across Europe. These included the angiotensin receptor blockers (ARBs), cerebrovascular and cardiovascular (CV) medicines including TCMs, proton pump inhibitors (PPIs) and statins. The authors did not undertake an extensive systematic review of the literature regarding ongoing reforms to enhance the prescribing of low cost generics to give guidance to the authorities in China since such reviews have already been undertaken [30,34-43]. They employed a similar methodology in other review publications regarding generics that they have been involved with [16,30-32,35,44-47]. No attempt has been made to assess the quality of the referenced papers using for instance a modified Jadad scale as a number of the cited publications involved the coauthors.

The following definitions are used in this paper:

Originator products: These include products from multinational companies imported into China or manufactured by joint ventures in China founded by multinational pharmaceutical companies. Since these medicines have the original intellectual property and are considered by some to have better quality, they typically command premium prices versus generics.

Generic products: These are produced by enterprises with local investment, including state-owned and private enterprises. Their quality has improved in recent years with a number of different measures to enhance manufacturing standards, e.g. in 2009, all medicines on the Chinese essential medicine list were required to undergo quality sampling and testing at the provincial level at least annually and at the central level at least every three years [8]. Good Manufacturing (GMP) standards were also revised in 2011 to further improve the quality of generics manufactured in China [8].

Traditional Chinese medicines (TCMs): Usually prepared from herbs or other traditional sources, with some preparations including chemical substances. The main delivery route is via an injection. The characteristics of TCMs are multi target and multi utility, and they are believed to provide comprehensive treatment of patients with chronic cardiovascular and cerebrovascular diseases enhanced by a high degree of acceptance among both physicians and patients. They are also believed for instance to improve blood circulation and remove blood stasis and activate collaterals [48,49].

Medicine utilisation in the principal studies was typically measured in defined daily doses (DDDs), with the latest DDDs used in line with international guidance [50,51]. The only exception were medicines to treat cerebrovascular and cardiovascular diseases. Here, the unit of utilisation employed were package units as there is currently no reliable source for DDDs for traditional Chinese medicines, most physicians use the package unit as the charging unit when calculating their patients' expenditure and the specifications of the products typically did not change during the study period [49,52]. The Chinese currency Renminbi "yuan" (CNY) was used in these four studies to determine expenditure over time [21,49,53,54]. Expenditure was typically not converted to either US$ or Euros in the quoted studies as the authors did not want pricing data influenced by currency fluctuations especially during the recent financial crises in Europe and the US. Expenditure figures were also not adjusted for inflation or deflation as the authors wanted to compute actual changes over time as a result of tendering process [21,49,53,54].

Results

The findings for cardiovascular and cerebrovascular medicines including TCMs, ARBs, statins, and the PPIs process [21,49,53,54] will first be displayed in a consolidated table (Table 1) before describing the research findings in more detail. This will also consider potential savings if the authorities in China were to adopt measures that have been successfully introduced in Europe.

Product Class	Number of products	Total utilisation	Total Expenditure	Price	Generics	Implication
CV medicines (2006 to 2012) [49]	Medicines: 48 TCM: 52	Total increase- 3.3 fold. TCMs higher at 4.41 fold	Increased overall 4.85 fold. TCMs 7.78 fold	New products (typically injectables) with higher prices increased overall expenditure–higher than utilisation	Generics utilisation was 29% to 31% of total utilisation for 12 identified CV medicines Steady growth in the utilisation of originator products despite generics being available at reduced prices (up to 64% to 82% lower prices, e.g. 18% to 36% of originator 2006 prices)	Four models were subsequently identified to explain utilisation patterns
ARBs (2006-2012) [54]	Single ARBs: 5, FDCs : 3	12 fold increase	Rising 9.8 fold to 9.87million CNY in 2012	Price reductions (combined): (i) Single generics: 44% reduction (ii) Single originators: 7% reduction (iii) Generic FDCs: 49% reduction (iv) Originator FDCs: 21% reduction	Variable use of generics led to their overall utilisation increasing from 24% of total single ARBs in 2006 to 31% in 2008 before falling to between 22% and 24% between 2010 and 2012 This was despite increasing availability of generic ARBs	Overall limited utilisation of generics either single or as FDCs despite increasing availability. Utilisation driven by higher list prices
Statins (2004-2013) [53]	6 statins available in two hospital groups	Increasing 32 fold in one hospital group and and 54 fold in the other	Increasing 24 fold in one hospital group and 39 fold in the other	23% reduction in one hospital group for originator statins vs. 38% for generics (combined) Limited price reduction for generics (combined) in the other hospital group (3%) Greatest price reduction for generic simvastatin (91% and 74% reduction)	In one hospital group, generic utilisation increased from 18% of total statins in 2004 to 28% in 2013 In the other, generic statins accounted for only 9% to 10 % of total statin utilisation	Initiatives have resulted in low costs statins (simvastatin) Limited utilisation of generics have increased expenditure inappropriately
PPIs (2004-2013) [21]	6 PPIs were available	Rising 10.4 fold Greatest increase (15.7 fold) for injectable PPIs	Rising10.1 fold. Greater for injectable than oral PPIs As a result, injectables 74% of total PPI expenditure in 2013	Injectables 4.2-6.8 fold more expensive than orals - injectable lansoprazole at 13.4-18.0 fold higher than oral formulation between 2010 and 2013 Price for oral PPIs combined decreased by 34% vs. 19% for injectables	Generic oral PPIs reached 84% of total oral PPIs by 2013 Steady growth in generic injectable PPIs reaching 93% of total injectable utilisation in 2013 Utilisation of lansoprazole grew 28.4 fold especially after the launch of generic injectable lansoprazole in 2010	Utilisation of injectible PPIs is higher than the WHO guidelines for injections among developing countries This needs to be addressed to save resources
NB: CV medicine = cerebrovascular and cardiovascular medicines; ARBs = angiotensin receptor blockers; FDCs = fixed dose combinations; PPIs = proton pump inhibitors; CNY = Renminbi "yuan" ; TCM = Traditional Chinese Medicines						

Table 1: Findings for cardiovascular and cerebrovascular medicines, ARBs, statins and PPIs among hospitals in the Chongqing District of China.

Medicines to treat cardiovascular and cerebrovascular diseases

Total utilisation increased 3.3 fold between 2006 and 2012, greatest for TCMs at 4.41 fold [49]. Total procured expenditute increased by 4.85 fold. This was greatest for TCMs at 7.78 fold, helped by a 1.77 fold increase in procured prices over time. This was facilitated by the launch of new products with higher prices, relatively limited competition, and typically administered via injection. As a result, the share of expenditure on TCMs on total CV medicines increased from 35% in 2006 to 57% in 2012.

There was also steady growth in the expenditure of originator products with procured values of more than one million CNY in 2012 (Table 2). Telmisartan is included in view of its rapid rise in recent years.

	2006	2007	2008	2009	2010	2011	2012
Nifedipine	408492	634433	1059304	850230	1316610	1161800	1731451
Felodipine	95357	230576	428861	671820	1008336	1182072	1731600
Amlodipine	303142	338616	353088	715638	952956	860417	1378092
Benazepril	307854	400865	528242	775505	826081	1114124	1348217
Losartan	426804	796349	1369708	1661338	2660355	2395552	2738551
Irbesartan	226915	506012	698425	1124449	1721435	1812780	2349528
Valsartan	77222	185410	618854	913311	1026720	1618663	2301978
Telmisartan	54881	122496	286860	304960	396140	507059	894730
Atorvastatin	162092	168840	357763	1393600	2106480	2204728	2631632
Simvastatin	365627	790921	1579420	1726296	1702398	1907784	1420866
Metoprolol	208246	256202	297993	357173	445450	823460	1416130
Bisoprolol	265392	433904	565653	544171	1062686	1121249	1242144

Table 2: Total procured expenditure of 12 originator cardiovascular and cerebrovascular medicines in CNY in the Chongqing District 2006 to 2012 [49].

There was variable utilisation of generics over the years (Figure 1), with overall utilisation of generic CV medicines stabilising at 29% to 31% of total utilisation for the 12 cardiovascular products in recent years (Table 1 and Figure 1).

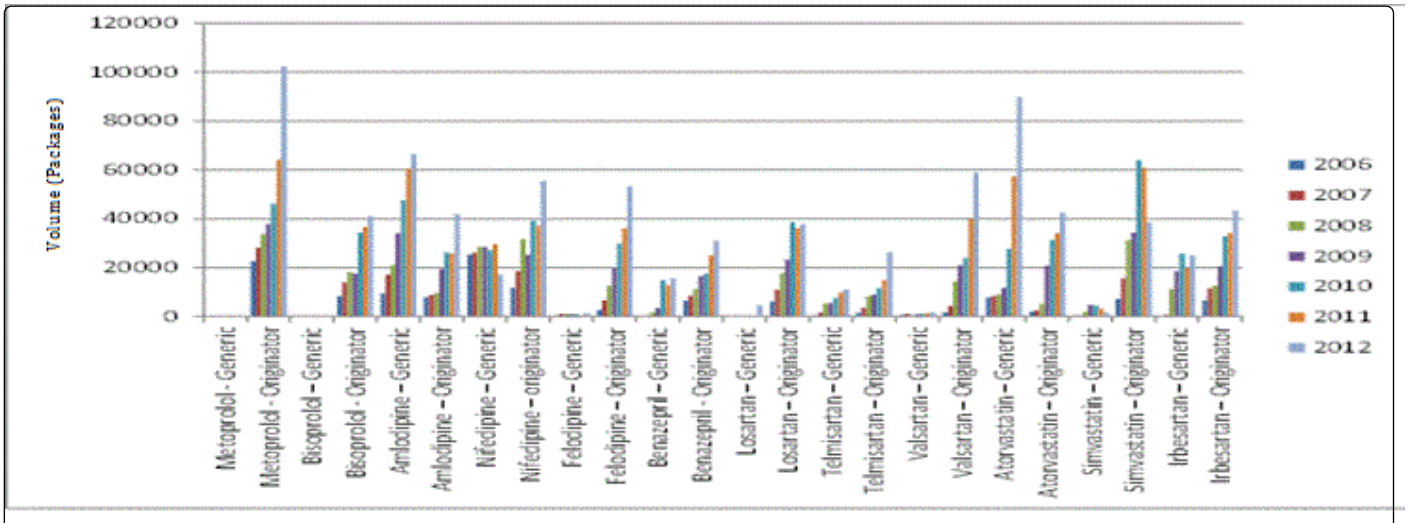

Figure 1: Utilisation of originator and generic CV medicines in the Chongqing hospital group 2006 to 2012 [49].

Concerns with irrationality in prescribing were further confirmed by the continued growth in the utilisation of originator medicines despite generics being available at lower prices (Table 1) [49].

Based on the findings, there appears to be four different models in operation for CV medicines in China. These are [49]:

Model 1 – a substantial drop in prices adversely affects subsequent use (with higher prices translating into higher profitability for the hospitals). This is illustrated by some products no longer procured or with limited procurement after an appreciable price decline, e.g. limited utilisation of generic versus originator simvastatin with a 67% price reduction for generic simvastatin over the study period (originator price only decreased by 29%).

Model 2 – a small decrease in procured prices, e.g.10%, does not appear to typically change utilisation trends (may also be an increase). One explanation for this could be that the whole supply chain,

including manufacturers and prescribing doctors, adjust their profitability mix accordingly. This is illustrated by generic benazepril and telmisartan as well as both originator and generic atorvastatin, with increased utilisation over time despite limited decreases in procured expenditure/ unit.

Model 3 - Some medicines maintain a relatively high price and their consumption substantially increases, e.g. originator bisoprolol, metoprolol and oxiracetam. Other products with relatively stable prices over time also increased their volume in line with market growth, e.g. amlodipine besylate.

Model 4 - "CNY 20 phenomenon", i.e. when the procurement price per pack drops to near or below CNY 20, utilization rates usually decreases/ stops increasing. Examples include generic nifedipine, generic enalapril and generic simvastatin (Figure 1).

Angiotensin receptor blockers

As documented in Table 1, the prescribing of ARBs alone or as FDCs in the Chongqing hospital group increased 12 fold between 2006 and 2012 [54]. This greatest increase was seen with telmisartan and valsartan among the single ARBs and irbesartan among fixed dose combinations (FDCs) (Table 3). Total ARB expenditure (single and FDCs) increased appreciably from just over 1million in 2006 to 9.87million CNY in 2012) (Table 3).

Utilisation (DDDs)	2006	2007	2008	2009	2010	2011	2012
Candesartan	36960	62580	70560	60480	30880	52400	83190
Irbesartan	46550	84700	156602	255240	384850	358200	452400
Losartan	61740	114597	182700	252210	414400	379400	495740
Telmisartan	23912	71218	191968	203420	268800	345072	523250
Valsartan	18060	38150	103663	154560	179200	290080	424235
Irbesartan FDC	2800	27314	71610	116060	178080	216720	301280
Losartan FDC	19306	38850	78400	79100	122990	131600	173250
Valsartan FDC			350	1960			
Expenditure (CNY)							
Candesartan	199459	281139	304114	260669	132613	173592	275783
Irbesartan	212367	377438	655902	1068325	1619697	1450664	1808932
Losartan	300385	540814	859548	1146623	1886528	1677952	2102293
Telmisartan	60594	178430	473949	502192	663812	746167	1126164
Valsartan	93891	209218	624353	920495	1056180	1640615	2329578
Irbesartan FDC	14548	144646	354734	573381	866556	904673	1241512
Losartan FDC	126419	255535	510160	514715	787467	755792	990422
Valsartan FDC			2437	13647			

Table 3: Utilisation (DDDs) and expenditure (CNY) of ARBs in the Chongqing hospital group 2006 to 2012 [54].

The lesser increase in total expenditure (9.8 fold) versus utilisation (12 fold) was helped by reduced expenditure/ DDD for the various ARBs over the study period [54]. This was greatest for single generics (44% reduction over time vs. only 7% for single originator ARBs) resulting in an overall 17% price reduction for single ARBs combined over time. However, there was a greater procured price reduction for combined originator FDCs at 21% [54]. Expenditure/ DDD for generic FDCs combined were lower by 49% in 2012 versus combined originator prices in 2006.

The variable use of generic ARBs led to their overall utilisation increasing from 24% of total single ARBs in 2006 to 31% in 2008 before falling to between 22% and 24% between 2010 and 2012. This was despite increasing availability of generic ARBs (there were over 250 generic ARBs in China in 2013). There was though increased utilisation of generic ARB FDCs, reaching 19% of total ARB FDCs in 2012 (54). Overall there were [54]:

- A 21.5 fold increase in ARB FDC utilisation between 2006 and 2012 (DDD based), greatest for irbesartan FDC (Table 3) leading to increased use of ARB FDCs as a % of total ARBs.
- Variable use of generic ARBs, i.e. a rapid increase in the utilisation of generic irbesartan peaking at 44% of total irbesartan in 2009 before declining to 33% by 2012 (DDD based). There was a similar pattern for telmisartan, with generics peaking at 40% of total telmisartan in 2011 before falling to 30% in 2012.
- There was also increased utilisation of generic candesartan in 2012 vs. 2006, although this varied by year, resulting in its share of total single ARBs falling from 20% in 2006 to between 2% to 4%

between 2010 and 2012. No originator candesartan was procured between 2006 and 2012.

- Considerable variation in procured price reductions for generics by the end of the study. This ranged from -22% for generic valsartan to -39% for candesartan and -54% for telmisartan. This resulted in variable differences in procured prices for generic versus originator single ARBs over time. This greatest for valsartan reaching -59% in 2012. This compares to a maximum of -32% for irbesartan in 2012, with the difference steadily growing over time.

Statins

There was an appreciable increase in the prescribing of statins, 32 fold from 2004 to 2013 in the Third Military Medical University (TMMU) hospitals and 54 fold among the Chongqing Medical University (CMU) hospitals (Table 1). There was a lower increase in total expenditure (24 fold in the TMMU hospital and 39 fold in the CMU hospital) compared with utilisation, helped by reducing expenditure/ DDD for the various statins [53].

In the TMMU hospitals, there were lower price reductions (-23%) for originator statins combined in 2013 vs. 2004 versus a 38% decrease for generics (combined), which was greatest for generic simvastatin (-74%). This resulted in an overall 27% price reduction for combined statins between 2004 and 2013. In the CMU hospitals, there was also considerable variation in the price reductions for individual generic and originator statins over time. The greatest price decline was seen with generic simvastatin (-91%). As a result, generic simvastatin in TMMU hospitals in 2013 was 49% below 2013 originator prices and 86% below 2013 originator prices in CMU hospitals [53].

Overall, there was variable uses of generic statins in both hospital groups. In the TMMU hospitals, there was a rapid increase initially in generic utilisation, e.g. generic atorvastatin was 97% of total atrovastatin utilization in 2004 (DDD based) before declining to 22% in 2009 and subsequently increasing to between 45% and 55% in recent years. A similar pattern was seen with generic pravastatin once procured, peaking at 50% of total pravastatin in 2009 before falling to 24% in 2010 and subsequently increasing to between 41% and 57% in recent years. However, there was limited utilisation of either generic pitavastatin and rosuvastatin in recent years. This variable use of generic statins resulted in their overall utilisation increasing from 18% of total statins in 2004 to 28% in 2013 among TMMU hospitals [53] (Table 4).

Utilisation (DDDs)	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Total PPIs	242113	346445	474146	824062	1151371	1390171	1765443	2113162	2427049	2509195
Total oral PPIs	195845	273527	361071	559003	669415	800366	1036979	1386099	1770332	1783799
Total injectable PPIs	46268	72918	113075	265059	481956	589805	728464	727063	656717	725396
Total oral generics	125062	210854	286192	465703	579033	671671	849779	1164225	1533132	1500439
Total oral originators	70783	62673	74879	93300	90382	128695	187200	221874	237200	283360
Total injectable generics	21136	35518	64355	207003	420023	485530	620657	679463	612917	672176
Total injectable originators	25132	37400	48720	58056	61933	104275	107807	47600	43800	53220
Expenditure (CNY)										
Total PPIs	5602189	7964638	9950311	18866503	26448571	31885597	41341064	47260383	49822102	56692311
Total Oral PPIs	2418344	3256961	4187360	5831530	6583875	7795656	10351461	12805046	14380231	14554888
Total Injectable PPIs	3183845	4707677	5762952	13034973	19864696	24089941	30989603	34455337	35441872	42137423
Total Oral Generics	1112037	2151927	3043505	4325122	5242342	6117648	7842938	9519056	10792929	9777624
Total Oral originators	1306307	1105034	1143854	1506409	1341533	1678008	2508523	3285991	3587301	4777264
Total Injectable Generics	1343950	2066840	2581308	9281646	16013580	17603745	24252075	30871591	32091311	37892385
Total Injectable Originators	1839896	2640837	3181644	3753328	3851116	6486196	6737528	3583746	3350561	4245038

Table 4: Utilisation (DDDs) and expenditure (CNY) of PPIs in the Chongqing hospitals 2004 to 2013 [21].

In the CMU hospitals, decreasing utilisation of generic atorvastatin resulted in generic statins accounting for only 9% to 10 % of total statin utilisation (DDD based) in 2012 and 2013 [53].

Proton pump inhibitors

PPI utilisation among the Chongqing hospitals increased 10.4 fold betwen 2004 and 2013, greatest for injectable PPIs at 15.7 fold (Table 1) [21]. At one stage (2008 and 2009), injectable PPIs accounted for 42% of total PPI utilisation before falling to below 30% in recent years (Table 4).

This utilisation of injectible PPIs is considerably higher than the WHO guidelines for injections among developing countries, and appreciably higher than the suggested limited use generally given the effectiveness of oral PPIs [27,55,56].

Total PPI expenditure increased steadily during the study period, rising 10.1 fold between 2004 and 2013 (Table 4).

The growth in expenditure was also greater for injectable than for oral PPIs, resulting in expenditure on injectable PPIs increasing from 57% of total injectable PPI expenditure in 2004 to 71% to 74% between 2008 and 2013 (Tables 1 and 4) [21].

Utilisation of oral generic PPIs grew at a faster rate than oral originators, resulting in the utilisation of oral generic PPIs growing from 64% of total PPIs in 2004 (DDD basis) to between 82% and 87% between 2007 and 2013 (Table 4). There was also greater growth for generic versus originator injectable PPIs, enhanced by these typically being produced by domestic manufacturers. As a result, the utilisation of generic injectable PPIs grew from 46% of total injectables in 2004 to 93% between 2011 and 2013. Utilisation of lansoprazole grew 28.4 fold during the course of the study, especially after the launch of generic injectable lansoprazole in 2010, with the utilisation of pantoprazole declining from 2010 onwards due to falling utilisation of generic injectable pantoprazole [21].

Price reductions were seen for the various PPI formulations over time. These were greater for oral formulations combined (-34%) than injectable formulations combined (-19%) [21]. The greatest procured price reduction was seen with generic oral omeprazole. In 2010, prices were 87% below the 2004 originator price (expenditure/ DDD). The price of generic injectable omeprazole in 2013 was 80% below the 2004 originator price (expenditure/ DDD). However, this was accompanied by limited utilisation [21]. Injectable PPIs were typically 4.2 to 6.8 fold more expensive (CNY/ DDD) than their equivalent oral formulations. The greatest difference was seen with injectable lansoprazole at 13.4 to 18.0 fold higher than the equivalent oral formulation between 2010 and 2013 [21].

Potential savings

Overall, there are considerable opportunities for savings within the Chongqing District as there was typically greater utilization of more expensive originator CV medicines versus generics as well as greater utilization of more expensive injectable than oral PPIs (Table 4).

Table 5 documents the potential savings based on experiences among European countries to obtain low prices for generics and enhance their utilisation versus originators and patented products in a class [13-16]. This also includes limiting the number of available products within a class based on the experiences of Stockholm County Concil [13,57,58].

Class	Potential savings
ARBs [54,59-63]	Restricting the formulary to just one ARB and one ARB FDC based on the cheapest ARB (telmisartan for single ARBs and irbesartan for FDCs) would have saved an accumulated 17million CNY for this hospital group alone between 2006 and 2012 with limited differences between the ARBs at therapeutically equivalent doses. In addition, no concerns with reduced outcomes or persistence from generics versus originators Total expenditure on ARBs (alone and FDCs) was 9.87million CNY in 2012
Statins [15,53,58,64-67]	Restricting the formulary to just one statin based on the cheapest statin (simvastatin) with limited differences between the statins at therapeutically equivalent doses, and no concerns with patient outcomes with generics versus originators, would have saved an accumulated 27 million CNY for the TMMU hospital group alone between 2004 and 2013 (Total statin expenditure was 15.3 million CNY in 2013). Accumulated savings could increase to 49 million CNY with the attainment of generic prices similar to low prices achieved in some Western European countries Simvastatin is recommended in the 'Wise List' in Stockholm County Council. In addition, SIGN (Scottish Intercollegiate Guidelines Network) in Scotland advocate the use of only 40 mg simvastatin for the prevention of cardiovascular disease as well as for primary prevention of cardiovascular disease in patients with Type 1 diabetes. In addition, 40mg simvastatin or 10mg atorvastatin for the prevention of cardiovascular disease in patients with Type 2 diabetes irrespective of starting lipid levels
PPIs [21,57, 58,68]	Restricting hospital procurement to just one oral PPI, i.e. generic omeprazole, following similar initiatives among European countries and regions, e.g. the 'Wise List' in Stockholm Metropolitan Healthcare Region and Germany placing all PPIs in a Jumbo class as no perceived clinical differences between them, and (i) assuming its procured price in 2010 continued to the end of the study and (ii) limiting the utilisation of injectable generic PPIs to just 5% of total PPIs – generic omeprazole (cheapest) - at its procured price each year, would have saved an accumulated estimated 249.65 million CNY for this hospital group during the study period This amounts to 84% of total accumulated PPI expenditure

Table 5: Potential savings among the hospitals in the Chongqing district from greater use of generics.

Discussion

We believe there are a number of key points arising from the findings (Tables 1 to 5 and Figure 1) to provide future guidance to the authorities in China as they strive for universal coverage. Positive findings include the considerable price reductions for some generics over time, e.g. 87% to 91% price reductions for generic omeprazole and generic simvastatin respectively during the study period (Table 1) [21,53]. This is similar to the low prices for high volume generics seen among a number of European countries, e.g. Netherlands, Sweden and the UK [13-15,69], showing that competition among generic companies is working to lower prices. There was also appreciable utilization of generic oral PPIs at 82% to 87% of total oral PPI utilisation between 2007 and 2013 [21]. This is similar to the high utilisation of generics versus originators among a number of European countries [14,15,36,37,44,45,59]. For instance in Scotland, generics accounted for between 98% to 99% of total utilisation across a range of molecules, aided by high voluntary INN prescribing [15].

However, there were a number of areas of concern providing opportunities for the future. These include firstly typically greater utilization of more expensive originators versus generics among the cardiovascular medicines as well as still appreciable utilization of TCMs despite often limited evidence (Table 1). The latter is facilitated by the launch of new TCMs with higher prices, relatively limited competition, and the fact that they are typically administered by injection (Table 1) [21,49,53,54]. Secondly, there was high and unsupportable utilization of injectable versus oral PPIs (Table 1) [21].

Thirdly, the findings from the research into the utilization and expenditure on cardiovascular and cerebrovascular medicines in the Chongqing District resulted in the 4 postulated models which are a potential concern (Table 1) [49]. Models 1, 2 and 4 are a particular concern and need to be addressed to enhance universal coverage. However, we acknowledge that these postulated models need to be researched in more detail to be able to provide comprehensive and robust guidance to the Chongqing District in particular and China in general in future years, although we are already seeing a reduction in the utilization of TCMs [49]. This will be the subject of future research activities.

We believe the considerable differences in the utilisation of oral generic PPIs versus originators, and compared to the findings with cardiovascular medicines including ARBs and statins (Figure 1 and Table 1), can be explained by a number of factors [21,49,53,54].These include the fact that diseases of the cardiovascular system are seen as having greater importance in China compared with acid-related stomach disorders, and originator medicines are thought to have a more consistent effect in treating cardiovascular diseases than generics. Secondly, there are few TCMs to treat peptic ulcer diseases unlike cardiovascular and cerebrovascular diseases [49]; consequently, domestic generic oral manufacturers have less competition. Lastly, it is believed some physicians think that doubling the dose of oral generic PPIs could lead to the same effectiveness as the originators at the standard dose, and this is acceptable in this situation [21]. However, we cannot say this with certainty without further research in this area.

Potential measures that could be considered by the authorities in Chongqing District and elsewhere in China to enhance patient access to medicines without prohibitive increases in expenditure include firstly enhancing INN prescribing, building on earlier measures. This could become compulsory if needed [30,70]. Secondly, measures to enhance the rational use of medicines, building on the essential medicine list concept [8,58]. This includes encouraging the preferential prescribing of evidenced based low cost and equally effective generics versus more expensive originators [16,57,58]. Thirdly, introducing measures to restrict prescribing choices within a class. This was seen with the ARBs among European countries including Austria, Belgium, Croatia, Lithuania and Sweden [47,59,71-73].

Limiting physician choices enhances their familiarity with the medicines they prescribe, potentially reducing adverse drug reactions and drug: drug interactions. This was the philosophy behind the generation of the 'Wise List' in the Stockholm Metropolitan Healthcare Region, which contains approximately 200 drugs including first and second line choices covering most of the therapeutic needs in ambulatory care [57,58]. High adherence rates at 80 to 90% of all utilization in ambulatory care to the voluntary 'Wise List' are achieved by the involvement of prescribers in the selection process, robust methodologies for selecting the medicines based principally on published evidence of effectiveness and safety, a comprehensive communication programme as well as physician trust in the guidance and regular feedback [57,58,74]. Research findings have also shown that increased adherence to the 'Wise List' reduces costs without compromising care [13,58,75]. There are similar examples in Spain and Scotland [15,57,76]. Other initiatives include potentially introducing prescribing quality indicators, which are increasingly used in healthcare as a tool to achieve safe and quality clinical care and cost-effective therapy, as well as for professional learning, remuneration, and accreditation along with financial incentives [74,77-79]. Adoption of such measures will realise considerable savings in the Chongqing District without compromising care (Table 5).

However, real progress to enhance the rational use of medicines in China will only be made by addressing the current perverse financial incentives for both physicians and hospitals that have translated into high utilization of more expensive originators than generics as well as high and unjustified utilization of TCMs and injectable medicines when effective oral medicines are available (Table 1). This is starting to happen [3].

In conclusion, the authors believe that despite the limitations in their research including no formal systematic review for the reasons stated, the findings from the various disease areas and classes provide guidance to the authorities in China on potential ways forward to enhance the quality and efficiency of future prescribing. This has been achieved by reviewing a number of cases histories and comparing the findings with those from a number of different European countries. We are already seeing countries learning from each other especially in Europe, and this will grow.

Acknowledgment

We thank the publishing company of the Journal of China Pharmacy for providing us with the datasets used in the various studies. Part of the analysis and writing of this paper was supported by a grant from Karolinska Institute. There are no additional funding sources.

Conflicts of Interest

The authors declare that they have no conflicts of interest apart from those stated. No writing assistance was utilized in the production of this manuscript.

References:

1. Zeng W (2013) A price and use comparison of generic versus originator cardiovascular medicines: a hospital study in Chongqing, China. BMC Health Serv Res 13: 390.
2. Lu C, Ross-Degnan D, Stephens P, Liu B, Wagner A (2013) Changes in use of antidiabetic medications following price regulations in China (1999–2009). Journal of Pharmaceutical Health Services Research 4: 3-11.
3. Tang S, Tao J, Bekedam H (2012) Controlling cost escalation of healthcare: making universal health coverage sustainable in China. BMC Public Health 12 Suppl 1: S8.
4. Daemmrich A, Mohanty A (2014) Healthcare reform in the United States and China: pharmaceutical market implications. J Pharm Policy Pract 7: 9.
5. Han S, Liang H, Su W, Xue Y, Shi L (2013) Can price controls reduce pharmaceutical expenses? A case study of antibacterial expenditures in 12 Chinese hospitals from 1996 to 2005. Int J Health Serv 43: 91-103.
6. Li X, Zhang W (2013) The impacts of health insurance on health care utilization among the older people in China. Soc Sci Med 85: 59-65.
7. Meng Q, Xu L, Zhang Y, Qian J, Cai M, et al. (2012) Trends in access to health services and financial protection in China between 2003 and 2011: a cross-sectional study. Lancet 379: 805-814.
8. Barber SL, Huang B, Santoso B, Laing R, Paris V, et al. (2013) The reform of the essential medicines system in China: a comprehensive approach to universal coverage. J Glob Health 3: 010303.
9. Wang XQ, Chen PJ (2014) Population ageing challenges health care in China. Lancet 383: 870.
10. Ling RE, Liu F, Lu XQ, Wang W (2011) Emerging issues in public health: a perspective on China's healthcare system. Public Health 125: 9-14.
11. Yang G, Wang Y, Zeng Y, Gao GF, Liang X, et al. (2013) Rapid health transition in China, 1990-2010: findings from the Global Burden of Disease Study 2010. Lancet 381:1987-2015.
12. Yu X, Li C, Shi Y, Yu M (2010) Pharmaceutical supply chain in China: current issues and implications for health system reform. Health Policy 97: 8-15.
13. Godman B, Wettermark B, Hoffmann M, Andersson K, Haycox A, et al. (2009) Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. Expert Rev Pharmacoecon Outcomes Res 9: 65-83.
14. Woerkom M, Piepenbrink H, Godman B, Metz J, Campbell S, et al. (2012) Ongoing measures to enhance the efficiency of prescribing of proton pump inhibitors and statins in The Netherlands: influence and future implications. Journal of comparative effectiveness research 1:527-538.
15. Godman B, Bishop I, Finlayson AE, Campbell S, Kwon HY, et al.(2013) Reforms and initiatives in Scotland in recent years to encourage the prescribing of generic drugs, their influence and implications for other countries. Expert review of pharmacoeconomics & outcomes research 13:469-482.
16. Godman B, Acurcio F, Guerra Júnior AA, Alvarez-Madrazo S, Faridah Aryani MY, et al. (2014) Initiatives among Authorities to Improve the Quality and Efficiency of Prescribing and the Implications. Jn Pharma Care Health Sys1:15.
17. Sun Q, Santoro MA, Meng Q, Liu C, Eggleston K (2008) Pharmaceutical policy in China. Health Aff (Millwood) 27: 1042-1050.
18. National Health and Family Planning Commission of China (2011) China Health Statistics Annuals 2011.
19. Chen Y, Schweitzer SO (2008) Issues in drug pricing, reimbursement, and access in China with references to other Asia-Pacific region. Value Health 11 Suppl 1: S124-129.
20. Wagstaff A, Lindelow M (2008) Can insurance increase financial risk? The curious case of health insurance in China. J Health Econ 27: 990-1005.
21. Zeng W, Finlayson AE, Shankar S, de Bruyn W, Godman B, et al. (2015) Prescribing efficiency of proton pump inhibitors in China: influence and future directions. BMC Health Serv Res 15: 11.
22. Li Y, Xu J, Wang F, Wang B, Liu L, et al. (2012) Overprescribing in China, driven by financial incentives, results in very high use of antibiotics, injections, and corticosteroids. Health Aff (Millwood) 31: 1075-1082.
23. Mao W, Tang S, Chen W (2013) Does perverse economic incentive lead to the irrational uses of medicines? Expert Rev Pharmacoecon Outcomes Res 13: 693-696.
24. Hu S, Tang S, Liu Y, Zhao Y, Escobar ML, et al. (2008) Reform of how health care is paid for in China: challenges and opportunities. Lancet 372: 1846-1853.
25. Reynolds L, McKee M (2009) Factors influencing antibiotic prescribing in China: an exploratory analysis. Health Policy 90: 32-36.
26. Reynolds L, McKee M (2011) Serve the people or close the sale? Profit-driven overuse of injections and infusions in China's market-based healthcare system. Int J Health Plann Manage 26: 449-470.
27. Tang Y, Zhang X, Yang C, Yang L, Wang H, et al. (2013) Application of propensity scores to estimate the association between government subsidy and injection use in primary health care institutions in China. BMC health services research 13:183.
28. Jingang A (2013) Which future for doctors in China? Lancet 382: 936-937.
29. Tian X, Song Y, Zhang X (2012) National Essential Medicines List and policy practice: a case study of China's health care reform. BMC Health Serv Res 12: 401.
30. Godman B, Wettermark B, van Woerkom M, Fraeyman J, Alvarez-Madrazo S, et al. (2014) 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 5:106.
31. Godman B, Campbell S, Suh HS, Finlayson A, Bennie M,et al. (2013) Ongoing measures to enhance prescribing efficiency across Europe: implications for other countries. J Health Tech Assess 1: 27-42.
32. Godman B, Abuelkhair M, Vitry A, Abdu S, Bennie M, et al. (2012) Payers endorse generics to enhance prescribing efficiency; impact and future implications, a case history approach. GaBI Journal 1: 21-35.
33. Vogler S, Zimmermann N, Leopold C, de Joncheere K (2011) Pharmaceutical policies in European countries in response to the global financial crisis. South Med Rev 4: 69-79.
34. Dylst P, Vulto A, Simoens S (2014) Analysis of European policy towards generic medicines. Generics and Biosimilars Initiative Journal 3: 34-35.
35. Dylst P, Vulto A, Godman B, Simoens S (2013) Generic medicines: solutions for a sustainable drug market? Appl Health Econ Health Policy 11: 437-443.
36. Simoens S (2012) A review of generic medicine pricing in Europe. GaBI Journal 1: 8-12.
37. Dylst P, Vulto A, Simoens S (2013) Demand-side policies to encourage the use of generic medicines: an overview. Expert Rev Pharmacoecon Outcomes Res 13: 59-72.
38. Hassali MA, Alrasheedy AA, McLachlan A, Nguyen TA, Al-Tamimi SK, et al. (2014) The experiences of implementing generic medicine policy in eight countries: A review and recommendations for a successful promotion of generic medicine use. Saudi Pharm J 22: 491-503.
39. Hassali MA, Thambyappa J, Saleem F, Haq Nul, Aljadhey H (2012) Generic Substitution in Malaysia: Recommendations from a Systematic Review. Journal of Applied Pharmaceutical Science 2:159-164.
40. Moe-Byrne T, Chambers D, Harden M, McDaid C (2014) Behaviour change interventions to promote prescribing of generic drugs: a rapid evidence synthesis and systematic review. BMJ Open 4: e004623.
41. Acosta A, Ciapponi A, Aaserud M, Vietto V, Austvoll-Dahlgren A, et al. (2014) Pharmaceutical policies: effects of reference pricing, other pricing, and purchasing policies. The Cochrane database of systematic reviews 10: Cd005979.

42. Vogler S (2012) The impact of pharmaceutical pricing and reimbursement policies on generics uptake: implementation of policy options on generics in 29 European countries-an overview. GaBI Journal 1: 93-100.
43. Toverud EL, Hartmann K, Håkonsen H (2015) A Systematic Review of Physicians' and Pharmacists' Perspectives on Generic Drug Use: What are the Global Challenges? Appl Health Econ Health Policy.
44. Godman B, Shrank W, Andersen M, Berg C, Bishop I,et al.(2010) Comparing policies to enhance prescribing efficiency in Europe through increasing generic utilization: changes seen and global implications. Expert review of pharmacoeconomics & outcomes research 10:707-722.
45. Godman B, Shrank W, Andersen M, Berg C, Bishop I, et al. (2011) Policies to enhance prescribing efficiency in europe: findings and future implications. Front Pharmacol 1: 141.
46. Godman B, Bennie M, Baumgärtel C, Sovic Brkicic L, Burkhardt T, et al. (2012) Essential to increase the use of generics in Europe to maintain comprehensive healthcare? Farmeconomia: Health Economics and Therapeutic Pathways13: 5-20.
47. Godman B, Malmstrom R, Bennie M, Sakshaug S, Burkhardt T, et al. (2012) Prescribing restrictions - a necessary strategy among some European countries to enhance future prescribing efficiency? Reviews in Health Care 3: 5-16.
48. Jin S ZY, Du L, Huang K (2013) Analysis of the drug use in 34 hospitals of Chongqing area from 2009 to 2011. China Pharmacy 24:1643-1647.
49. Zeng W, Zhen J, Feng M, Campbell SM, Finlayson AE, et al. (2014) Analysis of the influence of recent reforms in China: cardiovascular and cerebrovascular medicines as a case history to provide future direction. Journal of comparative effectiveness research 3: 371-386.
50. VlahoviÄ-Palcevski V, Gantumur M, RadoseviÄ N, Palcevski G, Vander Stichele R (2010) Coping with changes in the Defined Daily Dose in a longitudinal drug consumption database. Pharm World Sci 32: 125-129.
51. WHO (2003) Introduction to Drug Utilisation Research.WHO International Working Group for Drug Statistics Methodology, WHO Collaborating Centre for Drug Statistics Methodology, WHO Collaborating Centre for Drug Utilization Research and Clinical Pharmacological Services, Norway.
52. Teng L, Xin HW, Blix HS, Tsutani K (2012) Review of the use of defined daily dose concept in drug utilisation research in China. Pharmacoepidemiol Drug Saf 21: 1118-1124.
53. Zeng W, Xi H, Godman B, Finlayson AE, Malmstrom RE (2014) Ongoing initiatives to improve prescribing efficiency in China; statins as a case history. GaBI Journal 3:122-32.
54. Zeng W, Gustafsson LL, Bennie M, Finlayson AE, Godman B (2015) Review of ongoing initiatives to improve prescribing efficiency in China; angiotensin receptor blockers as a case history. Expert Rev Pharmacoecon Outcomes Res 15: 157-169.
55. Jiang Q, Yu BN, Ying G, Liao J, Gan H, et al. (2012) Outpatient prescription practices in rural township health centers in Sichuan Province, China. BMC Health Serv Res 12: 324.
56. Armstrong D (2005) Intravenous proton pump inhibitor therapy: a rationale for use. Rev Gastroenterol Disord 5 Suppl 2: S18-30.
57. Björkhem-Bergman L, Andersén-Karlsson E, Laing R, Diogene E, Melien O, et al. (2013) Interface management of pharmacotherapy. Joint hospital and primary care drug recommendations. Eur J Clin Pharmacol 69 Suppl 1: 73-78.
58. Gustafsson LL, Wettermark B, Godman B, Andersen-Karlsson E, Bergman U, et al. (2011) The 'wise list'- a comprehensive concept to select, communicate and achieve adherence to recommendations of essential drugs in ambulatory care in Stockholm. Basic & clinical pharmacology & toxicology 108: 224-233.
59. Moon J, Godman B, Petzold M, Alvarez-Madrazo S, Bennett K, et al. (2014) Different initiatives across Europe to enhance losartan utilisation post generics: impact and implications. Frontiers in pharmacology 5:1-10.
60. Martin A, Godman B, Miranda J, Tilstone J, Saleem N, Olsson E, et al. (2014) Measures to improve angiotensin receptor blocker prescribing efficiency in the UK: findings and implications. Journal of comparative effectiveness research 3: 41-51.
61. Corrao G, Soranna D, La Vecchia C, Catapano A, Agabiti-Rosei E, et al. (2014) Medication persistence and the use of generic and brand-name blood pressure-lowering agents. J Hypertens 32: 1146-1153.
62. Corrao G, Soranna D, Merlino L, Mancia G (2014) Similarity between generic and brand-name antihypertensive drugs for primary prevention of cardiovascular disease: evidence from a large population-based study. European journal of clinical investigation 44: 933-939.
63. Kesselheim AS, Misono AS, Lee JL, Stedman MR, Brookhart MA, et al. (2008) Clinical equivalence of generic and brand-name drugs used in cardiovascular disease: a systematic review and meta-analysis. JAMA 300: 2514-2526.
64. Scottish Intercollegiate Guideline Network (SIGN) (2010) Management of diabetes - quick reference guide.
65. Weng TC, Yang YH, Lin SJ, Tai SH (2010) A systematic review and meta-analysis on the therapeutic equivalence of statins. J Clin Pharm Ther 35: 139-151.
66. Usher-Smith J, Ramsbottom T, Pearmain H, Kirby M (2008) 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 62: 480-484.
67. Corrao G, Soranna D, ArfÃ¨ A, Casula M, Tragni E, et al. (2014) Are generic and brand-name statins clinically equivalent? Evidence from a real data-base. Eur J Intern Med 25: 745-750.
68. Godman B, Schwabe U, Selke G, Wettermark B (2009) Update of recent reforms in Germany to enhance the quality and efficiency of prescribing of proton pump inhibitors and lipid-lowering drugs. Pharmacoeconomics 27: 435-438.
69. Bennie M, Godman B, Bishop I, Campbell S (2012) Multiple initiatives continue to enhance the prescribing efficiency for the proton pump inhibitors and statins in Scotland. Expert review of pharmacoeconomics & outcomes research 12:125-130.
70. Garuoliene K, Godman B, Gulbinovič J, Wettermark B, Haycox A (2011) European countries with small populations can obtain low prices for drugs: Lithuania as a case history. Expert Rev Pharmacoecon Outcomes Res 11: 343-349.
71. Godman B, Bucsics A, Burkhardt T, Schmitzer M, Wettermark B, et al. (2010) Initiatives to enhance renin-angiotensin prescribing efficiency in Austria: impact and implications for other countries. Expert review of pharmacoeconomics & outcomes research 10:199-207.
72. Bucsics A, Godman B, Burkhardt T, Schmitzer M, Malmstrom RE (2012) Influence of lifting prescribing restrictions for losartan on subsequent sartan utilization patterns in Austria: implications for other countries. Expert review of pharmacoeconomics & outcomes research 12:809-819.
73. Simoens S, De Bruyn K, Miranda J, Bennie M, Malmström RE, et al. (2013) Measures to enhance ARB prescribing efficiency in Belgium following generic losartan: impact and implications for the future. Journal of Pharmaceutical Health Services Research 4:173–181.
74. Wettermark B, Pehrsson A, Juhasz-Haverinen M, Veg A, Edlert M, et al. (2009) Financial incentives linked to self-assessment of prescribing patterns: a new approach for quality improvement of drug prescribing in primary care. Qual Prim Care 17: 179-189.
75. Norman C, Zarrinkoub R, Hasselström J, Godman B, Granath F, et al. (2009) Potential savings without compromising the quality of care. Int J Clin Pract 63: 1320-1326.
76. Coma A, Zara C, Godman B, Agustí A, Diogène E, et al. (2009) Policies to enhance the efficiency of prescribing in the Spanish Catalan region: impact and future direction. Expert Rev Pharmacoecon Outcomes Res 9: 569-581.
77. Wettermark B, Godman B, Jacobsson B, Haaijer-Ruskamp FM (2009) Soft regulations in pharmaceutical policy making: an overview of current approaches and their consequences. Appl Health Econ Health Policy 7: 137-147.

78. Doran T, Fullwood C, Gravelle H, Reeves D, Kontopantelis E, et al. (2006) Pay-for-performance programs in family practices in the United Kingdom. N Engl J Med 355: 375-384.

79. Campbell SM, Godman B, Diogene E, Fürst J, Gustafsson LL, et al. (2015) Quality indicators as a tool in improving the introduction of new medicines. Basic Clin Pharmacol Toxicol 116: 146-157.