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Impact of European Pharmaceutical Price Regulation on Generic Price Competition
A Review

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Contents

Abstract

Although economic theory indicates that it should not be necessary to intervene in the generic drug market through price regulation, most EU countries intervene in this market, both by regulating the maximum sale price of generics (price cap) and by setting the maximum reimbursement rate, especially by means of reference pricing systems.

We analyse current knowledge of the impact of direct price-cap regulation of generic drugs and the implementation of systems regulating the reimbursement rate, particularly through reference pricing and similar tools, on dynamic price competition between generic competitors in Europe.

A literature search was carried out in the EconLit and PubMed databases, and on Google Scholar. The search included papers published in English or Spanish between January 2000 and July 2009. Inclusion criteria included that studies had to present empirical results of a quantitative nature for EU countries of the impact of price capping and/or regulation of the reimbursement rate (reference pricing or similar systems) on price dynamics, corresponding to pharmacy sales, in the generic drug market.

The available evidence indicates that price-cap regulation leads to a levelling off of generic prices at a higher level than would occur in the absence of this regulation. Reference pricing systems cause an obvious and almost compulsory reduction in the consumer price of all pharmaceuticals subject to this system, to a varying degree in different countries and periods, the reduction being greater for originator-branded drugs than for generics.

In several countries with a reference pricing system, it was observed that generics with a consumer price lower than the reference price do not undergo price reductions until the reference price is reduced, even when there are other lower-priced generics on the market (absence of price competition below the reference price). Beyond the price reduction forced by the price-cap and/or reference pricing regulation itself, the entry of new generic competitors is useful for lowering the real transaction price of purchases made by pharmacies (dynamic price competition at ex-factory level), although this effect is weaker or non-significant for official ex-factory prices and consumer prices in some countries. When maximum reimbursement systems such as reference pricing or similar types are applied, pharmacies are seen to receive large discounts on the price they pay for the pharmaceuticals, although these discounts are not transferred to the consumer price. The percentage discount offered to pharmacies in a country that uses a price-cap system combined with reference pricing is positively and significantly related to the number of generic competitors in the market for the pharmaceutical (dynamic price competition at ex-factory level).

The justification of price regulation in the pharmaceutical market on the grounds of the near absence of competition seems weak when we observe markets with products whose patents have expired. When the patent of a product expires, barriers to entry should disappear, as the composition of an active ingredient becomes public and other firms should have little difficulty in reproducing the production process. The traditional reasons given to defend price regulation when any firm can make a generic to compete with the originator brand-name product can find little justification in economic theory,[1] given that temporary market power of manufacturers has disappeared and the oligopolistic nature of many therapeutic submarkets has been potentially reduced.

A generic drug is a medicinal product that has the same qualitative and quantitative composition in active substances, and the same pharmaceutical form, as the reference medicinal product, and whose bio-equivalence with the reference medicinal product has been demonstrated by appropriate bio-availability studies. Some countries allow international non-proprietary name prescribing (this name identifies the active substance rather than a brand name), whilst others do not, leading to the concept of 'branded generics', which can be promoted to physicians.

Although economic theory indicates that it should be less necessary to intervene in the generic drug market through price regulation, most EU countries intervene in this market both by regulating the maximum consumer price of generics (price cap) and by setting the maximum reimbursement rate, especially by means of reference pricing systems.

In 2007, according to data provided by the European Generic Medicines Association (EGA), 78% of a sample of 27 European countries used some form of direct regulation of generic prices.[2-4] However, some European countries (Germany, the Netherlands, Sweden, UK) apply free or quasi-free pricing to generics, as does the US.[5]

Most countries that apply price-cap regulation systems set the price cap as the average observed price in other countries, a certain percentage below the innovator's price, a maximum price or a negotiated price (price/volume).[3,6]

Austria is an example of price-cap regulation based on the price of the innovator's branded drug. In this country at present, the first generic entry must set the selling price at least 48% lower than that of the originator-branded pharmaceutical (46% lower in 2005 and 44% lower in 2004), the second must be 15% lower than the first generic, and the third must be 10% lower than the second.[7]

In addition to the direct regulation of generic prices, the regulation of the reimbursement rate represents an indirect regulation of generic prices, especially in European markets, where there is a majority public insurer. Thus, 71% of the countries comprising the EGA's sample of 23 European countries apply some form of reference pricing (maximum price the public insurer is willing to pay), and 63% of these apply this system to chemically equivalent drugs (with the same active ingredient). For example, although pricing is free in Sweden, the reimbursement rate is set according to the lowest price, with a system of compulsory substitution with the cheapest drug, updated every 2 months,[8] unless the patient pays the difference. As a result, generic prices were 40% lower in 2005 than in 2003.[9] Even in the UK, a maximum reimbursement rate is applied to a large proportion of the most commonly prescribed generic medicines in primary care.[10]

Table I presents an updated comparison of the main features in the application of reference pricing systems (year started, level of equivalence and maximum reimbursement rate) and generic price regulation systems in the EU countries. Of the 26 EU countries that feature in table I (information is not available for Bulgaria), 14 (54%) apply some form of price regulation to generic drugs, and, in most of these, the price of the generic is set on the basis of the price of the originator-branded pharmaceutical minus a discount. In addition, the maximum reimbursement rate is set officially in 22 countries (85%), in 19 of these by means of a reference pricing system (and in 12 of these, equivalence is determined as medicines with the same active ingredient).

There is growing concern that this widespread application of direct and/or indirect forms of price regulation of generic medicines in the EU, precisely when the barrier to entry constituted by the innovator's patent is removed, restricts price competition.[4,16,17] Furthermore, in some cases competition is found to take the form of pharmacy discounts that do not reach the final consumer/insurer.

Despite price regulation of generic medicines being common in the EU, as is official fixing of their reimbursement rate by means of reference pricing or similar policies, knowledge is scant with regard to the impact of these policies on price competition between generics: to what extent do they encourage price competition between generic firms? To what extent and how rapidly do they bring the consumer price down towards the marginal cost of production and distribution? To what extent do they induce price reductions beyond those imposed by price regulation or maximum reimbursement rates? Is regulation more effective than free price competition in the generic market at bringing the price down towards the marginal cost? As an indication of the lack of research on the impact of these forms of generic regulation, in a recent literature review on the impact of reference pricing and other forms of price regulation,[18] only three of the 12 selected studies referred to European countries, and only two of these three analysed the impact on prices. Furthermore, the review in question made no reference at all to the impact on price competition.

The dynamics of price competition among generic competitors in highly regulated contexts such as European markets have received very little attention to date, especially in comparison with the dynamics of generic prices in countries with free pricing[19] and the dynamics of innovators' prices in the face of competition from generics.[20,21]

In a pioneering study on the relationship between price competition among generics and both direct and indirect price regulation, Danzon and Chao[22] found, with data for 1992, that competition is greater in unregulated or weakly regulated markets (USA, Germany, UK, Canada) than in those that are highly regulated (France, Italy and Japan).

The aim of this article is to analyse the extant knowledge of the impact in Europe on dynamic price competition among generic firms exerted by direct price-cap regulation of generic medicines and the implementation of systems regulating the reimbursement rate, especially by means of reference pricing and similar tools.

Some demand side measures may also potentially enhance the prescribing and dispensing of generics and may also have an impact on the

Table I. Application of reference pricing and generic price regulation systems in the EU[4,6-15] [a]

Country (year reference pricing started)	Level of equivalence	Maximum reimbursement rate	Price regulation of generic medicines
Austria	NA	As of third generic, 60% below price of original product	First generic priced 48% lower than original product; second 15% lower than first; third 10% lower than second; fourth and following, 10% lower than the third
Belgium (2001)	Chemical	30% below price of original product	Generic priced 30% lower than original product
Czech Republic (1995)	Chemical, pharmacological and therapeutic	Lowest price in group	Price ≤55% of price of original product
Denmark (1993)	Chemical	Lowest price in reimbursement or substitution group	Generic priced lower than original product
Estonia (2003)	Chemical	2nd lowest price in group	NA
Finland (2009)	Chemical	Lowest price plus €1.5 (€2 if price >€40)	NA
France (2003)	Chemical	Average of generics with one active ingredient	Generic priced 55% lower than original product
Germany (1989)	Chemical, pharmacological and therapeutic	Price cap 30% of lowest price in price range of group with chemical equivalence	No regulation
Greece (2006)	Pharmacological	Lowest price in group	Generic priced ≤80% of price of original product
Hungary (1997)	Chemical	Price of cheapest product in group	Generic priced 30% lower than original product and no higher than the reference price
Ireland	NA	NA	Generic priced 20% lower than original product
Italy (2001)	Chemical	Lowest price in group	Generic priced at least 20% lower than original product
Latvia (2005)	Therapeutic	Lowest price in group	NA
Lithuania (2003)	Chemical	Lowest price in group	Generic priced 30% lower than original product
Malta	NA	NA	No regulation
Netherlands (1991)	Chemical, pharmacological and therapeutic	Lowest price in group	Price cap based on average of four EU countries
Poland (1998)	Chemical and pharmacological	Lowest price in group	NA
Portugal (2003)	Chemical	Price of most expensive generic	Generic priced 35% lower than original product
Romania (1997)	Chemical	Lowest price in group	NA
Slovakia (1995)	Chemical and pharmacological	Lowest price (per DDD) in group	NA
Slovenia (2003)	Chemical	Price of cheapest generic in group	NA
Spain (2000)	Chemical	Average of price of three cheapest products	Generic priced lower than reference price; untransparent criterion before application of reference pricing
Sweden (discontinued in 2002)	NA	Compulsory substitution with lowest-priced equivalent product	Free pricing, with negotiated purchase agreements
UK (2005, *Drug Tariff* Price)	Chemical	Weighted average price	No regulation

a No information is available for Cyprus and Luxembourg.

DDD = defined daily dose; **NA** = not applicable.

prices of generics but are not discussed further in this paper.[23]

1. Literature Review

1.1 Methods

We performed an objective and reproducible search for published papers in the EconLit, PubMed, and databases of the Centre for Reviews and Dissemination (CRD) databases (Database of Abstracts of Reviews of Effects, National Health Service Economic Evaluation Database and Health Technology Assessments Database), with the search terms 'reference price' and 'pharmaceutical'; 'reference pricing' and 'pharmaceutical'; 'generic', 'pharmaceutical' and 'reimbursement'; 'generic', 'pharmaceutical' and 'price competition'; 'generic', 'pharmaceutical' and 'discount'; and 'generic', 'pharmaceutical' and 'rebate'.

In order to identify working papers and grey literature, a complementary search was conducted on Google Scholar. We also conducted a manual review of the bibliographical references of the papers selected from the two databases mentioned above, and we personally contacted some of the leading researchers in this area. The search included papers published in English or Spanish in the period January 2000 to July 2009.

The criterion used for inclusion was that the studies presented empirical results of a quantitative nature for EU countries of the impact of price capping and/or regulation of the reimbursement rate (reference pricing or similar systems) on price dynamics in the generic drug market corresponding to pharmacy sales. We only included quantitative empirical studies analysing price competition between generic firms or between all producers (of branded and generic medicines together) that make and market the same active ingredient, once the patent has expired or the period of legal protection has finished.

The studies included were required to contain (as one of their outcome variables, relative either to generics or to branded and generic pharmaceuticals together) the price paid by the final consumer to the pharmacy (with or without taxes), the price paid by the pharmacy to the wholesaler, or the price paid by the wholesale distributor to the manufacturer, with the price quoted in terms of either presentation or defined daily dose (DDD). This price could be the price of the individual pharmaceutical form (manufacturer, active ingredient, dose and number of units) or the average price of the active ingredient or the presentation (active ingredient, dose and number of units) paid by the insurer. We also included papers in which the outcome variable was the discount received by pharmacies on their purchases from distributors and manufacturers on top of the official reimbursement rate.

In addition, we included papers analysing the individual impact of specific regulation policies and papers analysing the overall impact of concurrent policies, as long as the latter employed some statistical technique allowing the estimation of the isolated impact of each policy (regression models). In order to be included, those studies in which price was the outcome variable were required either to conduct a before-and-after comparison of the intervention (price and/or reimbursement rate regulation) or to make a comparison between a group affected by the intervention and a control group, by means of time-series or panel data. In the case of studies in which the outcome variable was the discount received by pharmacies, we also included those that used cross-sectional data to compare the acquisition cost with the official price reimbursed by the insurer. We included both studies published in journals and working papers posted on websites.

We excluded studies of a qualitative nature and those of a quantitative nature that only analysed the impact of generic entry on the price of originator-branded pharmaceuticals (and/or the ratio between brand and generic price) or that analysed the purchase price in hospitals. Studies with cross-sectional data that made price comparisons between countries were excluded. We also excluded studies on the evolution of prices in the absence of price or reimbursement rate regulation and those that only analysed the impact of policies other than price-cap or reimbursement rate regulation (reference pricing).

Finally, we excluded studies of an exclusively theoretical nature without any quantitative

empirical analysis using real data. This ruled out reviews, comments, editorials and letters to the editor or director.

Two reviewers (Iván Moreno and Jaume Puig-Junoy) examined the abstracts of the studies obtained by the search strategy and selected those studies that met the inclusion criteria. When it was not possible to determine their inclusion or exclusion on the basis of the information provided in the abstract, we obtained the full text in order to make the final decision. We read the full text of the papers previously selected on the basis of the abstract review, and then decided on their definitive inclusion.

We used a data collection form that allowed us to collect the information in the studies in a uniform manner. The variables collected for each selected study were (i) author and year of publication; (ii) country of reference; (iii) time period; (iv) scope (group of medicines analysed); (v) outcome variable; (vi) policies evaluated in the study; (vii) method used to analyse the impact of the policies; (viii) source of the data used; and (ix) main results related to the policies evaluated (according to wording of the original text in the results section of the selected studies).

1.2 Results

From a maximum number of papers reported in the search (EconLit = 16, Pubmed = 602, CRD databases = 26, and 4 from other sources), we identified 16 that met our criteria (figure 1). Of the 16 studies included in this systematic review of the literature, 12 examine the impact of the regulation of prices (price capping) and of the reimbursement rate applied to prices (reference pricing) and four analyse this same impact on the discount on pharmacy purchases in relation to the official reimbursement rate (discounts).

2. Impact of Reimbursement Rate Regulation on Dynamic Price Competition

The results of the literature review on the impact of price cap and reference pricing regulation on the trend in generic prices are shown in table II.

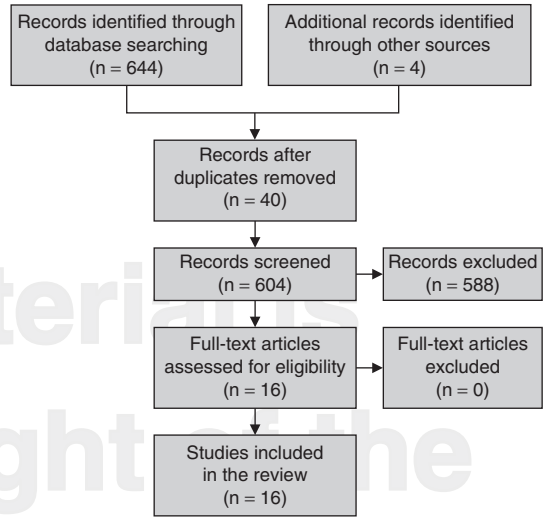

Fig. 1. Flow diagram of study selection process.

Of the 12 studies that analysed the time trend of prices under price cap and/or reference price, three correspond to Germany, three to Spain, two to Italy and two to Norway. One study was found for each of the following countries: France, Netherlands, Slovenia, Sweden and the UK; there was also one study that covered a group of 17 EU countries (some studies refer to more than one country).

The time period analysed in these studies ranged from 3 to 13 years.[25,28,33] This time period started in 2000 or later in seven studies; four studies analysed a period spanning the turn of the century; and one study analysed a time period that ended before 2000.

The number of active ingredients analysed in these studies varied enormously: from only three active ingredients[24,25] to 122.[17] Eight of the 12 studies only examined the time trend of prices of off-patent active ingredients that have undergone (or may undergo) generic entry, whereas the other four also included patented drugs.

Eight studies evaluated the effect of reference pricing. Three studies analysed the joint effect of price-cap regulation and reference pricing. The European Commission study[17] analysed,

Table II. Selected studies on the impact of the regulation of prices (price cap [PC]) and the reimbursement rate (reference pricing [RP]) on dynamic price competition in Europe

Study, country (period)	Scope (policies evaluated)	Outcome variable	Method and data	Main results
Pavcnik,[24] Germany (1986–96)	Oral antidiabetics and antiulcers, subject and not subject to RP (RP)	Average quarterly consumer price per DDD per presentation	Regression analysis with fixed effects and panel data. Private IMS data	Major price reductions for branded and generic drugs, with a larger reduction for branded drugs. The additional competition of new generics is related to lower prices; however, prices of branded drugs fall more with more generic competitors
Boersma et al.,[25] Netherlands (1996–2001)	Enalapril, fluoxetine, ranitidine (PC and RP)	Average quarterly consumer price per DDD of active ingredient (branded and generic), untaxed	Graphical analysis of time series before/after patent expiry and entering RP. Aggregate consumption data for 300 000 pts at active ingredient level	Price per DDD falls for all three ingredients, but significantly only for enalapril and fluoxetine
Ghislandi et al.,[26] Italy (2001–3)	Most sold presentation of ticlopidine, nimesulide and ranitidine (RP)	Monthly consumer price of each presentation	Graphical analysis of time series before/after RP. The source of the data is not specified	Prices tend to fall. Major reductions for nimesulide and ticlopidine when the maximum reimbursement rate is adjusted, whereas ranitidine prices began to fall with the entry of the first generic
Andersson et al.,[27] Sweden (1986–2002)	Five ATC4 groups subject to RP (RP)	Average monthly consumer price per DDD of equivalent group (branded and generic), untaxed	Segmented linear regression analysis. Aggregate monthly data at ATC4 level	The introduction of RP was associated with a reduction in the cost/DDD slope for all medicines affected
Puig-Junoy,[28] Spain (2001–4)	Statins [five active ingredients] (PC and RP)	Monthly consumer price per presentation	Graphical analysis of time series of prices. Official data for consumer PCs	The reduction in the consumer price of generics is not related to potential competition from lower-priced entries but rather to arbitrary details of the RP system. Generic prices higher than the RP fall to this level immediately when RP is applied, but RP is not effective for reducing the price of generics initially priced lower than the RP
Podnar et al.,[29] Slovenia (2002–4)	14 pharmaceutical forms of seven active ingredients subject to RP (RP)	Monthly consumer price of two pharmaceutical forms of each presentation	Before-and-after descriptive analysis with descriptive data. Private IMS data	After application of RP, generic prices settle at the reference level, but not below it
Brekke et al.,[30] Norway (2001–4)	24 off-patent active ingredients subject and not subject to RP (RP [index pricing] replacing PC)	Average monthly price per DDD of each active ingredient paid by pharmacies	Regression analysis with fixed effects and panel data. Private Farmastat data	In comparison with PC regulation, RP reduces the price of branded and generic drugs, but the effect is greater on branded drugs;

Continued next page

Table II. Contd

Study, country (period)	Scope (policies evaluated)	Outcome variable	Method and data	Main results
				RP reduces the average price of each active ingredient by 30%
Kanavos et al.,[31] Germany, UK, France, Italy, Spain (2000–5)	12 active ingredients (RP)	Average quarterly consumer price of generic per active ingredient; quarterly consumer price of cheapest generic	Regression analysis with fixed effects and panel data estimated using generalized least squares. Private IMS data	RP does not affect average prices per active ingredient. At ex-factory level, RP results in a price reduction, although a small one for generics. The number of competitors has a significant negative impact on price in France and Spain only
Augurzki et al.,[32] Germany (1994–2005)	All presentations under RP (RP)	Monthly ex-factory price of each pharmaceutical form	Regression analysis with fixed effects and panel data. Data for all prescriptions	A 1% reduction in the RP results in a 0.3% change in the price. The price adjustment is rapid and takes place mostly during the first month of application of RP. In addition, the introduction of RP for the first time reduces the prices of affected products by approximately 7%
Brekke et al.,[33] Norway (2001–4)	30 most sold active ingredients (including patented products) subject and not subject to RP (RP [index pricing] replacing PC)	Average monthly price per DDD of each active ingredient paid by pharmacies	Regression analysis with fixed effects and panel data. Private Farmastat data	RP causes a large reduction in the prices of products covered, with a greater effect on branded drugs (18–19%) than on generics (7–8%). This confirms that RP encourages price competition within the group of products included. RP is more effective than PC regulation for reducing prices
Puig-Junoy and Moreno,[34] Spain (1997–2009)	Eight active ingredients subject to RP (PC and RP)	Monthly consumer price and average price of each presentation paid by the NHS	Calculation of consumer price variation rates before/after RP. Official data for consumer PCs	For most presentations of a pharmaceutical form with a consumer price greater than the RP, this price falls to the RP level when RP is introduced or adjusted. With RP, successive generic entries at a lower consumer price than the pharmaceutical forms already on the market did not cause notable voluntary reductions in the consumer price of the latter, except in the case of ibuprofen
European Commission,[17] 17 EU countries (2000–7)	122 active ingredients, off patent in 2007; from 15 to 91 ingredients in each	Average annual ex-factory price per DDD of	Regression analysis with panel data. Private data from IMS and	PC policies affect price competition negatively. The number of generic entries

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Table II. Contd

Study, country (period)	Scope (policies evaluated)	Outcome variable	Method and data	Main results
	country (PC, lowest price policy, frequent adjustment [RP], compulsory substitution [RP], differential co-payment [RP])	each active ingredient minus estimated discount	pharmaceutical companies	contributes slightly to price reduction. Frequent adjustment, compulsory substitution, maximum reimbursement based on the lowest price and, to a lesser extent, differential co-payment, have a positive effect on price competition

ATC4 = level 4 of the Anatomical Therapeutic Chemical classification; **DDD** = defined daily dose; **NHS** = national health system; **pts** = patients.

for 17 European countries, the impact of both PC regulation and maximum reimbursement systems, distinguishing their particular characteristics: reimbursement policies taking the lowest-priced product as a reference; frequent adjustment of the maximum reimbursement rate; compulsory substitution with a cheaper generic; and differential co-payments.

According to the selection criteria used in this review, the outcome variable of the 12 studies was the price of generics or that of off-patent drugs (both branded and generic). Eight studies analysed the price paid by the insurer or the patient (consumer price), while the other four focussed on the pharmacy purchase price (ex-factory price). Of the four studies[17,29,31,32] that analysed the time trend of the ex-factory price, three used official price lists that did not take into account the possible existence of competitive discounts offered by manufacturers to pharmacies (or to wholesalers for transfer to pharmacies). Only the European Commission study[17] used ex-factory price data corresponding to real transaction prices, although, for a large number of the countries in the sample, these were estimated using a conversion factor for which no more information or justification was provided.

Six studies[17,24,25,27,30,33] analysed the average price trend at the active ingredient level (average price per DDD of active ingredient), whereas another four[26,28,31,32] analysed price at the presentation level (average price of pharmaceutical forms with the same presentation and active ingredient), and the remaining two studies[29,34] analysed the price trend at the level of each pharmaceutical form.

As regards the sources of the data used in the 12 selected studies, seven used private data provided by IMS,[17,24,29,31] Farmastat in Norway[30,33] and Apoteket AB in Sweden.[27] One used the turnover of an undetermined number of pharmacies as provided by the Dutch Inter-Action Database.[25] The European Commission study[17] used, in addition to private IMS data, private information collected directly from pharmaceutical companies. Two studies used data obtained from official regulated price registers as their main source of information.[28,34] Lastly, two studies did not explicitly state the source of their data.[26,32]

Of the 12 studies in table II, five only used descriptive statistical techniques to analyse the impact of regulation on prices: three studies only performed a graphical analysis of the time series of prices,[25-26,28] one presented the values of the time series of prices without any other statistical analysis[29] and another presented price variation rates before and after changes in regulation.[34] Of the five descriptive studies, only one[34] allowed separate analysis of forced price variation, attributable to the regulation as such, from voluntary variation (the effect of competition, beyond the direct effect of the regulation).

The remaining seven studies used regression analysis to evaluate the impact of regulation: one used a segmented linear regression analysis to detect changes in the slope and/or the constant of the time series of prices,[27] whereas the other six studies (50% of those selected) used regression analysis with fixed effects and panel data. In all the studies that used regression analysis with

panel data (with the exception of Augurzki et al.[32]), we observed the inclusion of the number of manufacturers competing in the market of the same product as one of the potentially explanatory variables, in addition to the regulatory variables. This variable is indicative of the effect of competition on price after controlling for the effect of the regulation.

The only study that individually analysed the impact of price-cap regulation on price in 17 European countries[17] indicated that it has a negative influence, such that, under generic price-cap regulation, the ex-factory price tends to level off at a higher price than in the absence of this regulation.

In all the studies selected we observed a price reduction associated with reference pricing regulation (whether in isolation or in conjunction with price cap); this is obvious in view of the fact that the public insurer is the main buyer in the European countries analysed.

The data provided by these studies on the magnitude of the reduction associated with the application of reference pricing are not directly comparable, and therefore it is not possible to reach a conclusion regarding any differential impact on the ex-factory price or the consumer price. The impact on price reduction seems to be greater for originator-branded pharmaceuticals than for generics,[24,30-31,33] which again is fairly obvious, as the price of originator-branded drugs prior to the introduction of reference pricing is likely to have been higher than that of generics.

Owing to the limited nature of the method, the results of the five descriptive studies on the impact of reference pricing on the consumer price can only show the price reduction after the application of reference pricing, which tends to occur very rapidly or even almost immediately. Three of these studies[29,28,34] indicated that the consumer price only falls to the reference level, and two of these, for the Spanish case, observed that the consumer price of generics priced lower than the reference level does not fall until the insurer lowers this maximum reimbursement rate, despite the entry of new generic competitors at lower prices. This result is indicative of the near absence of price competition (voluntary price reductions aside from reductions imposed by the legislation) in a market in which reference pricing regulation is combined with regulation of the maximum price of generics (price cap).

The results of two of the three studies that used regression analysis to examine the impact of reference pricing on the consumer price[24,31] allow us to draw conclusions about the effect of the entry of new generic competitors on the reduction of the consumer price, after controlling for the application of the reference pricing system (pure effect of price competition). Pavcnik[24] indicated that, in Germany, a larger number of generics is associated with a lower price, although the consumer price of originator-branded drugs falls more than that of generics. Kanavos et al.[31] show that, beyond the effect of reference pricing, a larger number of competitors slightly reduces the price of generics in France and Spain, but not in Germany, the UK and Italy.

The two studies on the impact of the replacement of the system of price-cap regulation with reference pricing in Norway[30,33] show that the number of generic competitors has no significant influence on the official (undiscounted) ex-factory price of generics. However, the study on the observed or estimated ex-factory price in real transactions in 17 EU countries reports a significant and slightly positive impact of the number of generics on price reduction. The existence of discounts on the official price paid by pharmacies (see section 3) may help to explain why evidence of price competition is found when real transaction prices are observed at the ex-factory level, unlike in other studies that use the official ex-factory price or the consumer price as their outcome variable.

The European Commission[17] study enables us to compare the magnitude of the impact of varying reference pricing regulatory designs in each member state: the price reduction is slightly greater with compulsory generic substitution measures and frequent adjustment of the maximum reimbursement rate than with differential co-payments or the adoption of the lowest price as a reference.

3. Impact of Reimbursement Rate Regulation on Competitive Discounts to Pharmacies

Table III presents the data of the four studies[35-38] that analyse the existence of competitive discounts to pharmacies. These studies refer to France, the UK and Spain (two studies) for cross-sectional data corresponding to moments in time between 2005 and 2008.

The existence and magnitude of pharmacy discounts is estimated for the presentations of a relatively small number of active ingredients: between 8 and 16. Furthermore, as discounts in the generic market is an untransparent phenomenon, the information used in these studies comes from a very small number of agents (pharmacies, wholesalers and manufacturers): between six[35-36] and ten.[38]

In all cases, a descriptive analysis was performed by estimating the average, minimum and/or maximum value of the observed percentage discount off the real acquisition price of the generics for pharmacies, versus the official price used as the basis for the reimbursement system. The percentage discount was calculated on the ex-factory price in three studies,[36-38] and on the wholesale price and the ex-factory price in the remaining one. Only one of the studies[38] conducted a regression analysis with cross-sectional data for the purpose of analysing the factors determining the variability of the discounts observed in different presentations of each active ingredient.

Table III. Selected studies on the impact of reimbursement rate regulation on competitive pharmacy discounts in Europe[a]

Study, country (period)	Scope	Method and data	Main results
Kanavos and Taylor,[35] France (beginning of 2005)	Presentations of 11 active ingredients	Calculation of average % discount on official ex-factory and wholesale prices. Data from interviews with four pharmacies and two wholesalers	Discounts are mostly price related and generally vary from 20% to 70% off the wholesale selling price, on top of the officially allowed 10.74%. Discounts on the ex-factory price are much lower, typically around 7.5%
Kanavos,[36] UK (May 2005)	31 presentations of 12 active ingredients	Calculation of maximum % discount on the official *Drug Tariff* price. Price lists of three wholesalers and three generic firms	In 20 of the product presentations, maximum discounts exceeded 60% of the *Drug Tariff* price
Borrell and Merino,[37] Spain (January 2003 to May 2005)	262 pharmaceutical forms of 16 active ingredients	Calculation of average % discount on the official ex-factory price. Data provided by 'pharmaceutical sector agents'	The average value of the discount was 34% over the period as a whole. The smallest discount was 17%, for diclofenac, and the largest, 50%, was for paroxetine in January 2005. The null hypothesis of equality of discounts over the period analysed cannot be rejected
Puig-Junoy,[38] Spain (January 2005 and first quarter of 2008)	68 presentations (179 pharmaceutical forms) of eight active ingredients	Calculation of average, minimum and maximum % discount on the official ex-factory price. Explanatory econometric model of variability in the % discount for 175 pharmaceutical forms. Price lists of ten wholesalers and manufacturers	The discount on each generic presents an average value of 40.8% of the ex-factory price, ranging from a minimum value of 10% to a maximum of 70%. The discount rate on the ex-factory price at which pharmacies acquire generics with the same active ingredient is higher for pharmaceuticals whose consumer price has declined less in relation to that of the branded drug before generic entry. The discount rate on the ex-factory price at which pharmacies acquire generics is higher for presentations in which there is a larger number of generic competitors

a The outcome variable of all the studies is the percentage discount on the maximum ex-factory price (regulated price) for pharmacy purchases and corresponds to the impact of reimbursement rate regulation systems (reference pricing or similar, such as the *Drug Tariff* price in the UK).

The magnitude of the competitive discounts to pharmacies on the official price seen in these studies presents notably high values: 20–70% in France; up to just over 60% in the UK; 17–34% in Spain in the period 2002–5 and 10–70% in 2008. The magnitude of the discounts as estimated in these studies is indicative that, under a reference pricing-type maximum reimbursement system, price competition reduces the acquisition price for pharmacies (ex-factory price or wholesale price) much more than the consumer price.

The study by Puig-Junoy[38] analysed the impact of the number of generic competitors on the magnitude of the average discount for 179 pharmaceutical forms in Spain in 2008, and revealed that the only variable that displays a significant and positive relationship with the percentage discount is the number of generics on the market. This result indicates the existence of notable competition in the acquisition price for pharmacies under reference pricing that is not transferred to the consumer price.

4. Critical Review of the Included Studies

In contrast with the widespread use of reference pricing and price-cap policies in European generic markets, the studies in this review are few and are subject to a considerable number of limitations that need to be taken into account when interpreting their results and overcome in future research.[39]

The main limitations of the studies that examined the impact of price regulation of generics in Europe are as follows.

First, descriptive analysis using cross-sectional data that do not allow a before-and-after comparison or regression analysis without controlling for the effect of concurrent measures or other factors influencing price, are of little use for understanding the impact of regulation on dynamic price competition.

Second, in countries where there is one predominant majority buyer, it is almost obvious that reference pricing systems (with or without price cap) give rise to price reductions, and it is much more interesting to analyse the magnitude and the duration of the effect on prices, distinguishing the effect on the consumer price and on the real transaction price of pharmacies' purchases (ex-factory price minus pharmacy discounts). Contrary to the conclusions reached in some of the studies reviewed (e.g. Boersma et al.[25]), in order to demonstrate the efficiency of reference pricing it is not enough to observe a significant price reduction after its application; it is necessary to obtain evidence that the price falls progressively until it lies close to the marginal cost (dynamic price competition).

Third, a significant negative impact of the application of reference pricing on price is often interpreted in the conclusions of the studies as evidence of an increase in competition,[32-33] when in fact the reduction may be limited to the short-term impact enforced by the regulation, which may have little to do with competition. To draw useful conclusions on dynamic price competition, it is essential to find evidence that, in addition to the price reduction that is almost forced by the regulation, the increase in the number of generic competitors (or some other measure of competition) causes a significant progressive reduction in the price.

Fourth, the existence of high percentage discounts on the official ex-factory price under maximum reimbursement (reference pricing) regulation systems makes it essential to analyse dynamic price competition at both ex-factory and consumer price level, as one does not follow on from the other.

Fifth, when the reference pricing is determined (as occurs in most countries) at the level of each pharmaceutical form, it is inappropriate to design reference pricing impact studies using the average price of the active ingredient as the outcome variable.[31]

Those studies that address the magnitude of the discounts offered by manufacturers and wholesalers to pharmacies likewise present some limitations that should be taken into account.

First, in general, because of the untransparent and/or 'alegal' (if not actually illegal) nature of discounts, data and sources of information are too limited geographically and temporally to guarantee that they provide a proper representation of the entire generic market.

Second, analysis of the influence of competition on the magnitude and trend of pharmacy discounts, and of how they vary when the institutional details of the reference pricing system are modified (compulsory substitution, frequent adjustment of the reference pricing rate, etc.), deserve considerably more attention than they have been given to date in the literature.

5. Discussion

This literature review on dynamic competition in the prices of generic medicines in Europe has yielded some results of relevance to the adoption and revision of price regulation policies in generic markets.

First, price-cap regulation leads to a levelling off of generic prices at a higher level than would occur in the absence of this regulation. This result coincides with the observations of Anis et al.[40] for Ontario (Canada). Price-cap regulation began to be applied to generics in Ontario in 1993: the price of the first generic entry could be no higher than 70% of the price of the branded product, and that of subsequent entries could be no higher than 90% of that of the first. The effect of this policy was price convergence at the highest regulated level and a smaller price reduction as new competitors entered the market.

Second, reference pricing systems cause an obvious and almost compulsory reduction in the consumer price of all pharmaceuticals subject to this system, to a varying degree in different countries and periods, the reduction being greater for originator-branded drugs than for generics.

Third, in several countries with a reference pricing system, it is observed that generics with a consumer price lower than the reference price do not reduce their price until the reference price is reduced, even when there are other lower-priced generics on the market (absence of price competition below the reference price).

Fourth, beyond the price reduction forced by the price-cap and/or reference pricing regulation itself, the entry of new generic competitors is useful for lowering the real transaction price of purchases made by pharmacies (dynamic price competition at ex-factory level), although this effect is weaker or non-significant for official ex-factory prices and consumer prices in some countries.

Fifth, when maximum reimbursement systems such as reference pricing or similar types are applied, pharmacies are seen to receive large discounts on the price they pay for the pharmaceuticals, although these discounts are not transferred to the consumer price.

Sixth, the percentage discount offered to pharmacies in a country that uses a price-cap system combined with reference pricing is positively and significantly related to the number of generic competitors in the market for the pharmaceutical (dynamic price competition at ex-factory level).

6. Conclusions

The results observed in the literature on the impact of price-cap regulation of the price of generic medicines and the reference pricing systems that predominate in Europe indicate that the application of these policies, although they lead to price reductions with respect to the price before patent expiry, may constitute a barrier to dynamic competition in consumer prices, with the result that insurers and consumers do not reap all the potential benefits of generic competition.

The impact on dynamic price competition and welfare of other market-oriented measures that could be implemented in order to obtain more competitive generic drug prices (such as price deregulation or different designs of competitive tendering) will have to be monitored and evaluated in the near future.

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