PRICES, COMPETITION AND REGULATION IN PHARMACEUTICALS: A CROSS-NATIONAL COMPARISON

Patricia M. Danzon
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SUMMARY[1]

Cross-national differences in manufacturer prices for pharmaceuticals are an important policy concern, both because of the impact on medicine costs to payers and consumers and because price differences are viewed as a measure of the impact of alternative regulatory regimes. Most countries regulate manufacturer prices for pharmaceuticals, either directly (France, Italy) or indirectly through controls on reimbursement (Germany, Japan) or profits (the UK). The consensus view, based on prior studies, is that countries with strict price regulation have lower medicine prices than countries with less restrictive price regulation, such as the UK, or no regulation, as in the US. For example, BEUC (1989b) concluded that drug prices in the UK and the US were, respectively, 20 and 54 percent above the EEC average, whereas those in France and Italy were, respectively, 30 and 28 percent below the EEC average. The US General Accounting Office (GAO, 1992, 1994) concluded that prices in the US in 1992 were 32 percent higher than prices in Canada and 60 percent higher than prices in the UK. A UK Department of Health study (UK DOH, 1997) concluded that US prices were 88 percent higher than the UK in 1992. A recent US study (US H.R. Minority Staff, 1998) reported that drug prices in the US were 70 percent higher than in Canada and 102 percent higher than in Mexico. In the US, these studies have contributed to proposals (so far not enacted) for drug price controls – for example, President Clinton's Health Security Act (1993) and the Prescription Drug Fairness Act of 1999 (US H.R.644). In addition to these comparisons of average price levels, a growing number of countries, including Italy, Spain, the Netherlands, Canada and Japan, use international comparisons in their regulation of prices for individual drugs.

Our study challenges this conventional wisdom, that price differences are large, particularly between the unregulated US and other, more

1 Research support was provided by Pfizer Inc. through a grant to the University of Pennsylvania for the study of international price comparisons. This support is gratefully acknowledged. The views expressed here are those of the authors, and are not necessarily shared by the research sponsors.

regulated markets. It shows that average price differences are smaller than previously suggested, and that prior studies have been biased by use of small, unrepresentative samples and inappropriate methods. These conclusions are based on indexes of manufacturer-level drug prices for seven major markets – the UK, the US, Canada, France, Germany, Italy, and Japan – using comprehensive data and standard index number methods. These price indexes are based on data for all outpatient drug sales in 1992 for all molecules that match across the countries under comparison. For multisource molecules, the molecule price is a weighted average that includes branded products (whether sold by the originator company or a licensee, hereafter 'originator' and 'licensed' products) and generic products, and all formulations, strengths and packs.[2]

Table S1 shows indexes for price per standard unit (a proxy for a dose) for each country relative to the US, using respectively US or comparison country quantity weights. Numbers greater (less) than one imply that the price of a basket of medicines that are available in both countries is higher (lower) in the country in question than in the US. Using the bilaterally matched samples (which include all compounds that are available in each comparison country and the US), the average price differentials relative to the US using US quantity weights are: for the UK –16.6 percent, Canada +2.1 percent, Germany +24.7 percent, France –32.2 percent, Italy –12.9 percent, and Japan –11.6 percent. If, however, the weights used for combining the different medicines' prices are the quantities used in each country, rather than the quantities used in the US, then all of the comparator countries have prices well below those in the US: ranging from 44.0 percent lower in the UK to 67.0 percent lower in France. The sensitivity of the price comparisons to the choice of US or other country weights is an important finding from our

2 The data are from Intercontinental Medical Systems (IMS), a market research firm that collects data on drug sales worldwide. Throughout, 'Germany' refers to former West Germany. 'Branded' here refers to R&D-based products that have at some time had patent protection, whereas 'generics' refers to imitator products that enter after patent expiry of the branded product. Branded and generic products with the same active ingredient are referred to as 'generically equivalent.'

Table S1 **Pharmaceutical price indexes relative to US – 1992**

Sample/Index	Canada	Germany	France	Italy	Japan	UK
Bilateral molecule matches with US						
Price index using US weights	1.021	1.247	0.678	0.871	0.884	0.834
Price index using non-US weights	0.447	0.403	0.330	0.485	0.457	0.560
Seven country molecule matches						
Price index using US weights	0.983	1.193	0.701	0.910	0.943	0.883
Price index using non-US weights	0.694	0.362	0.364	0.543	0.479	0.630

analysis. It highlights the difficulty of making meaningful international comparisons of pharmaceutical prices: patterns of medicines use vary so much from country to country.

The lower part of Table S1 compares the prices in different countries of a more restricted range of medicines, namely just those compounds that were available in all seven countries. Using this basis does not greatly affect the relative prices in different countries except that Canada now has slightly lower, rather than slightly higher, prices than the US when US weights are used.

Table S2 shows similar indexes to those in Table S1 but for each country relative to the UK as base, with both UK quantity weights and comparison country weights. The indexes with UK quantity weights, which are most relevant for the UK perspective, show all countries with prices higher than the UK in 1992, except France which has comparable prices when the sample of 'global' products (i.e. those available in all seven countries) is used.

Note that these measures overstate manufacturer prices for the US because the available data do not reflect discounts given to managed

Table S2 **Pharmaceutical price indexes relative to UK – 1992**

Sample/Index	Canada	Germany	France	Italy	Japan	US
Bilateral molecule matches with UK						
Price index using UK weights	1.433	2.291	1.042	1.792	1.326	1.787
Price index using non-UK weights	0.832	1.044	0.708	0.653	0.719	1.198
Seven country molecule matches						
Price index using UK weights	1.216	1.460	0.993	1.309	1.380	1.589
Price index using non-UK weights	1.064	1.005	0.820	1.053	0.826	1.133

care and government purchasers. Similarly, these estimates of UK prices overstate true manufacturer net prices in the UK because the data do not reflect discounts to pharmacists.

Estimates of price differences can be quite different, depending not only on which country's quantity weights are used but also on whether price is measured per dose or per gram. There is no single, 'right' measure of price differences: the best measure depends on the question and the perspective. In particular, for each country it is probably most appropriate to use price indexes that weight prices of different products by its own utilization weights. The UK-weighted indexes shown in Table S2 can be interpreted as showing the percentage change in the UK's total drug expenditures if it were to adopt another country's prices but make no change in its relative utilisation of different drugs. In reality, if relative prices were to change significantly, consumption would probably shift slowly towards products that became relatively less expensive. The non-UK weighted indexes can be interpreted as showing the percentage change in UK drug expenditures if, say, the UK were to adopt French price levels and French utilisation patterns.

If this seems implausible given differences in medical norms, the most relevant indexes for each country are those that use its own utilisation as quantity weights to reflect the relative importance of different products in total expenditures.

The price comparisons reported here differ significantly from previous estimates. Previous price comparisons have been seriously biased by the use of very small, unrepresentative samples, confined to leading branded products, excluding all generics. Since regulation systematically affects generic market shares and prices, comparisons that omit generics yield biased estimates of the overall average cost of drug therapy under different regulatory regimes. In addition, most previous studies have lacked quantity data and so have reported simple unweighted averages of the prices in the sample. Such unweighted averages are extremely sensitive to the sample and generally give undue weight to the highest priced products.[3]

We have also used the quantity data to calculate indexes of cross-national differences in drug consumption per capita, comparable to price indexes. These quantity comparisons show that, by the most relevant measure (using UK price weights), all countries have higher per capita consumption of pharmaceuticals than the UK (see Table S3).

Having reported more accurate measures of cross-national price and quantity differences, this study examines the extent of competition under alternative regulatory regimes, and the contribution of competition and other factors to the cross-national price differences. Regulation of drug prices is often rationalised by the assumption that price competition is weak: insurance tends to make patients insensitive to prices; physicians who are primary decision-makers may not know product prices and/or may be imperfect agents for patients; patents intentionally limit competition from generically equivalent substi-

3 Some studies use retail rather than manufacturer prices (for example, Minority Staff, 1998; BEUC, 1989a, b). Retail prices reflect wholesale and retail pharmacy margins and Value Added Tax (sales tax), and hence cannot provide an accurate measure of differences in manufacturer prices.

Table S3 **Pharmaceutical quantity indexes (per capita) relative to UK – 1992**

Sample/Index	Canada	Germany	France	Italy	Japan	US
Bilateral molecule matches with UK						
Quantity index using UK weights	2.028	1.288	2.477	2.078	1.292	1.557
Quantity index using non-UK weights	1.177	0.587	1.683	0.757	0.701	1.044
Seven country molecule matches						
Quantity index using UK weights	1.519	1.213	1.818	1.127	0.931	1.513
Quantity index using non-UK weights	1.329	0.835	1.501	0.907	0.557	1.079

tutes; and differentiated compounds are imperfect therapeutic substitutes. Retail pharmacy prices and other aspects of retail pharmacy are also regulated in countries that regulate manufacturer prices. Previous studies have found evidence of price competition in the UK, the US and Germany.[4] However, both theory and casual empirical evidence suggest that strict price regulation may undermine competition. Generic market shares of off-patent products are significantly lower in countries with strict price or reimbursement regulation, such as

4 Reekie (1996), BCG (1993) and Towse and Leighton (1999) show that successive entrants enter at discounts relative to incumbents. Grabowski and Vernon (1992, 1996) provide evidence of post-patent competition from generics in the US after the passage of the Waxman Hatch Act in 1984 and the growth of managed care in the 1990s. Alexander et al. (1994) estimate overall market volume elasticities with respect to price in seven countries for the period 1980-1987. The estimated elasticity (–2.8) is implausibly large, and may be biased by the limited data. Ellison et al. (1997) find significant cross-price elasticities of demand between generically equivalent products in four cephalosporins in the US, with weaker effects for therapeutic substitutes.

France, Italy or Japan, than in the US, the UK, Canada and Germany, which have less strict price regulation.[5] Whether regulation reinforces or undermines competition is an important issue, as different countries evaluate possible changes in their regulatory regimes. Our study uses multivariate statistical analysis to estimate the extent of price competition due to generic and therapeutic substitute products, controlling for other factors, in these seven countries to assess the effects of different regulatory regimes.

The evidence here shows that generic competition significantly lowers prices in countries with free or only moderately regulated pricing (the US, the UK, Germany and Canada), whereas generic competition appears to be ineffective and even counterproductive in countries with strict price regulation (France, Italy and Japan). See Table S4. In Table S4, the US coefficients can be interpreted as the effect of the explanatory variables on the average price per molecule, in percentage or elasticity terms. The coefficient for any other country measures the difference between the impact of that variable in the country concerned and the impact in the US. The net effect for a non-US country is then the sum of the US coefficient and the country-specific coefficient. For example, the US coefficient –0.567 for **Generic Competitors** implies that a doubling of the number of generic competitors in the US is associated with a 56.7 percent decrease in molecule price. The net effect of **Generic Competitors** is not significantly different in Canada, is smaller but still negative for the UK and Germany, but is positive in France, Italy and Japan. One plausible explanation is that in these strict regulatory regimes that drive down

5 The UK permits free pricing of originator products at launch, subject to a rate-of-return constraint on the product portfolio and restriction on post-launch price increases. Germany in 1992 permitted free pricing, with reference price reimbursement for certain products, primarily multisource compounds. The Canadian federal government monitors launch prices, relative to the average in seven foreign countries, and limits post-launch price increases to the rate of increase in the general consumer price index (CPI).

Table S4 **Summary effects of molecule characteristics on prices**
Dependent variable: log price per standard unit (t statistics in parentheses). Coefficients for non-US countries are differentials relative to the US.

Variable	US	Canada	Germany	France	Italy	Japan	UK
Molecule Age (ln)	–0.184 (–3.660)	–0.150 (–2.056)	–0.216 (–2.665)	–0.443 (–5.219)	–0.387 (–4.863)	–0.690 (–6.906)	–0.354 (–3.953)
Global (ln)	0.430 (5.163)	–0.241[a] (–1.493)	–0.341 (–2.016)	–0.645 (–3.170)	–0.820 (–4.102)	–0.617 (–3.589)	–
Generic Competitors (ln)	–0.567 (–14.804)	0.097[a] (1.110)	0.231 (3.391)	0.645 (6.369)	0.756 (9.049)	0.674 (9.100)	0.322 (3.188)

Note:
a p>0.05. All other coefficients are significant with p<0.05.

originator prices over the life-cycle, generic equivalents are often licensed co-marketers or minor 'new' versions of old molecules introduced by manufacturers as a strategy to obtain a higher regulated price. By contrast, in countries with less stringent regulation of manufacturer prices and competitive retail pharmacy regimes that encourage price sensitive purchasing, generic entrants engage in aggressive price competition in order to gain market share. For therapeutic substitutes, the results here confirm previous findings (Reekie, 1996; Towse and Leighton, 1999) that successive molecules to enter a therapeutic category do so at lower prices than those of established entrants.[6]

Countries with strict price regulation (France, Italy and Japan) appear to pay systematically lower prices than do the less regulated countries (the US, the UK, Germany and Canada) for products that attain broad global diffusion. (In Table S4, **Global** measures the number of countries, out of our seven, in which the molecule is available).

6 For more detailed analysis, see Danzon and Chao (1999a, b).

If, as seems plausible, broad global diffusion is an indicator of high therapeutic value, this suggests that regulation is biased against more valuable products.

The findings reported here have important implications for drug price comparisons and for policy. First, as already noted, valid comparison of average price levels requires use of representative samples, including generics as well as originator products, older as well as new products, appropriately weighted to reflect their relative importance in overall drug utilization. Comparisons that are based solely on leading branded products, with unweighted averages, tend to systematically overestimate prices in unregulated or less regulated markets, compared to strictly regulated markets.

Second, regulation clearly undermines competition in the off-patent, multisource sector. This is despite a strong presumption that price competition between generic substitutes of patent-expired drugs is socially beneficial and can yield significant savings to consumers (assuming that the patent term is designed to yield the socially appropriate return on research and development (R&D) investments). Off-patent drugs account for 88 percent of reimbursable packs sold in member states of the EU (European Commission, 1998), and this off-patent share is expected to grow as patents expire on many of the current leading drugs. Increasing competition in the off-patent sector to free up 'headroom' in public budgets to pay for innovative, patent-protected products is one suggestion that has emerged from the Bangemann Round Table discussions on the European single market for pharmaceuticals (European Commission, 1998; Danzon, 1998). Designing regulatory systems to promote competition in the off-patent sector is an important issue for all governments concerned with obtaining maximum value from health spending. The evidence here suggests that useful pro-competitive strategies include: (1) permitting pharmacists to substitute between generically-equivalent products (generic substitution), unless the physician indicates otherwise; and (2) promoting competition in retail pharmacy, including deregulating dispensing fees.

The evidence here shows some forms of competition between ther-

apeutic substitutes. However, the data used here are inadequate to measure the full extent of competition in the on-patent sector. Policy conclusions on the optimal extent of competition in the on-patent sector would require more extensive analysis, weighing the benefits of competition through lower prices to consumers, against the objectives of patent policy, which are to provide an opportunity for originator firms to recoup their R&D investments.[7]

The question of whether observed price differences across countries are appropriate is not addressed here. Economic theory indicates that uniform prices would not be optimal and that price differences (Ramsey pricing) for patented products are the most efficient practical strategy to pay for the common costs of R&D that serve all consumers (Danzon, 1997b, c). The potential for price differences within the EU arises because health care is a national policy prerogative. Different countries have pursued very different policies in controlling their health expenditures. However, these differences have narrowed recently due to the growth of parallel trade – whereby wholesalers import products from lower-priced to higher-priced countries – and the increased tendency for countries to regulate their domestic prices based on foreign prices. Because both parallel trade and regulation based on foreign prices have increased since 1992, a price comparison based solely on recently-launched, branded products might show quite different price differences between EU countries than the price indexes reported here. Our analysis is based on 1992 prices for all drugs available at that time, including older drugs whose prices reflect 1980s regulatory regimes and exchange rates. However, although the cross-national price differentials reported here may not reflect current differentials on newly-launched originator products, this analysis does demonstrate the importance of broader samples to measure average price differences, and to show the effects of regulatory regimes on these overall price levels and on competition.

7 R&D accounts for approximately 30 percent of total costs (Danzon, 1997a). If competition resulted in marginal cost pricing, only 30-50 percent of total cost would be covered.

1 INTRODUCTION AND OVERVIEW

Most countries regulate manufacturer prices for pharmaceuticals, either directly (France, Italy) or indirectly through controls on reimbursement (Germany, Japan) or profits (the UK). It is widely believed that drug prices are lower in countries with strict price regulation than in countries with less restrictive regulation (the UK) or no regulation (the US). For example, the BEUC (1989b) concluded that prices in the UK and the US were, respectively, 20 and 54 percent above the EEC average, whereas those in France and Italy were, respectively, 30 and 28 percent below the EEC average. The US General Accounting Office (GAO, 1992, 1994a) concluded that prices in the US in 1992 were 32 percent higher than prices in Canada and 60 percent higher than prices in the UK. A UK Department of Health study (DOH, 1997) concluded that US prices 88 percent higher than the UK in 1992. A recent US study (US H.R. Minority Staff, 1998) reported that drug prices in the US were 70 percent higher than in Canada and 102 percent higher than in Mexico. In the US, these studies have contributed to proposals (so far not enacted) for drug price controls – for example, President Clinton's Health Security Act (1993) and the Prescription Drug Fairness Act of 1999 (H.R.644). In addition to these comparisons of average price levels, a growing number of countries, including Italy, Spain, the Netherlands, Canada and Japan, use international comparisons in their regulation of prices for individual drugs.

The first purpose of this paper is to report indexes of manufacturer-level drug prices for six major markets – the UK, Canada, France, Germany, Italy, and Japan – relative to the US, using comprehensive data and more appropriate methods than those used in previous studies. Our data are from Intercontinental Medical Systems (IMS), a market research firm that collects data on drug sales worldwide. IMS data for all outpatient drug sales in 1992 are used to construct price indexes based on all molecules that match across the countries under comparison, including branded products (whether sold by the originator company or a licensee, hereafter 'originator' and 'licensed' products) and generic products, and all formulations, strengths and packs.

Standard price indexes, weighted by either US consumption patterns or the comparison country's consumption, are computed. The indexes with US quantity weights show average prices for each country, relative to the US, as follows: the UK –17 percent, Canada +2 percent; Germany +25 percent; France –32 percent; Italy –13 percent; and Japan –12 percent. Thus this analysis, using a comprehensive market basket including generics and appropriate weighting, shows that cross-national price differences are less than suggested by previous studies. The indexes with UK consumption weights show the UK either lowest based on price per gram or third lowest, after France and Italy, based on price per pill. The bias in previous studies for the US is shown to result from selection of very small, unrepresentative samples of leading branded products, exclusion of all generics, and reporting of unweighted averages which give undue weight to the highest priced products. The Appendix to this paper details the differences between our price comparisons and those made by the GAO and BEUC.

The cross-national diversity in range of products available and in patterns of drug consumption implies that there is no single 'correct' measure of price differences. Methodological judgements are unavoidable – in particular, choice of sample, weights and measure of price - and the most appropriate measure depends on the perspective of the analysis. However, while some choices depend on perspective, the analysis here clearly shows that a robust estimate should be based on a representative sample, including generics, and standard weighted indexes, not simple averages, as used in BEUC (1989), GAO (1992) and the OECD Pharmaceutical Purchasing Power Parities (OECD, 1993).

The second purpose of this paper is to examine the extent of competition under alternative regulatory regimes. Regulation is often rationalised by the assumption that price competition is weak because: insurance makes patients insensitive to prices; physicians who are primary decision-makers may not know product prices and/or may be imperfect agents for patients; patents intentionally limit competition from generically equivalent substitutes; and therapeutic substitutes are

imperfect. Retail pharmacy prices and other aspects of retail pharmacy are also regulated in countries that regulate manufacturer prices. Previous studies have found evidence of price competition in the UK, the US and Germany (Reekie, 1996; Towse and Leighton, 1999). However, both theory and casual empirical evidence suggest that strict price regulation may undermine competition. Generic market shares of off-patent products are significantly lower in countries with strict price or reimbursement regulation, such as France, Italy or Japan, than in the US, the UK, Canada and Germany, which have less strict price regulation. Whether regulation reinforces or undermines competition is an important empirical question, as different countries evaluate possible changes in their regulatory regimes. This paper estimates the effects of generic competition, therapeutic competition and other factors in the seven countries with their different regulatory regimes.

The main findings are that generic competition significantly reduces prices in countries with free pricing (the US) and moderately constrained pricing (the UK, Germany and Canada), whereas generic competition is ineffective and may be counterproductive in countries with strict price or reimbursement regulation (France, Italy and Japan). One plausible explanation is that in regulatory regimes that drive down the originator price over the life-cycle, generic equivalents are often licensed co-marketers or minor 'new' versions of old molecules introduced by manufacturers as a strategy to obtain a higher regulated price. By contrast, in countries with free pricing and price sensitive purchasers, generic entrants must compete on price to gain market share. For therapeutic substitutes, the results here confirm previous findings (Reekie, 1996; Towse and Leighton, 1999) that successive molecules to enter a therapeutic category do so at lower prices than those of established entrants.

This analysis has important implications for the methodology of drug price comparisons and for policy. First, robust price comparisons require representative samples and standard indexes. Limiting the sample to leading branded products and use of unweighted averages can yield very misleading results that tend to systematically overestimate

prices in unregulated or less regulated markets, compared to strictly regulated markets.

Second, regulation clearly undermines competition in the off-patent, multisource sector, which is contrary to sound economics and to the stated aim of policy in most countries. Innovative products are appropriately protected from generic competition for the life of the patent, in order to yield a return on R&D investments. However once the patent has expired, price competition between generic substitutes can yield significant savings to consumers and payers. Off-patent drugs account for 88 percent of reimbursable packs sold on average for member states of the EU (European Commission, 1998), and this off-patent share is expected to grow as patents expire on many of the current leading drugs. Increasing competition in the off-patent sector to free up 'headroom' in public budgets to pay for innovative, patent-protected products was suggested by the Bangemann Round Table discussions on the European single market for pharmaceuticals (European Commission, 1998; Danzon, 1998). Designing regulatory systems to promote competition in the off-patent sector is an important issue for all governments concerned with obtaining maximum value from health spending. The evidence here suggests that useful pro-competitive strategies include: (1) permitting pharmacists to substitute between generically-equivalent products (generic substitution), unless the physician indicates otherwise; and (2) promoting competition in retail pharmacy, by deregulating dispensing fees.

For the on-patent sector, policy conclusions are more tentative because the empirical evidence is less robust and because optimal competition policy must weigh the consumer benefits of lower prices against the need to provide an opportunity for originator firms to recoup their R&D investments, which is the intent of patent protection.

Whether pharmaceutical prices should differ between countries and, if so, the appropriate magnitude of such differences, has been addressed elsewhere (Danzon, 1997b, c) and is not discussed in detail here. Economic theory indicates that uniform prices would not be

optimal and that price differences (Ramsey pricing) for patented products are the most efficient practical strategy to pay for the common costs of R&D that serve all consumers. The potential for price differences within the EU arises because health care is a national policy prerogative and different countries have pursued very different regulatory strategies. The growth of parallel trade, whereby wholesalers import products from lower-priced to higher-priced countries has narrowed sustainable differences, particularly on high-volume branded products. Regulation based on cross-national price comparisons has similar effects. Because of both of these factors, a comparison based solely on recently-launched branded products might show smaller differences between EU countries than the differences reported here based on 1992 prices which may still reflect, via the older products, the regulatory regimes and exchange rates that prevailed in the 1980s . Although the price data used here may not accurately reflect current price differentials on newly-launched products, these data do show the methodological issues raised by cross-national price comparisons and the biases in previous comparisons, as well as the broad effects of regulatory systems on competition.

The report is structured as follows. Section 2 describes the data. Section 3 reports price and quantity indexes, and compares the results here with those in previous cross-national price comparisons. Section 4 outlines a simple model of drug prices and the expected effects of regulation. Section 5 describes the empirical model and methods. Section 6 reports product-level regression analysis of product prices and tests for significant differences between countries. Section 7 reports similar analysis for prices at the molecule level, where the molecule price is a weighted average over all products in the molecule. Section 8 concludes.

2 DATA AND METHODS

Accurate measurement of both cross-national and intertemporal price indexes for drugs is problematic because of the broad range of products, multidimensional quality and rapid technological change.[8] To illustrate the problem of product diversity, for the seven major markets studied here – Canada, France, former West Germany (hereafter referred to simply as 'Germany'), Italy, Japan, the UK and the US in 1992 – less than one third of each country's molecules are present in all seven markets. Moreover, each compound may be marketed by different manufacturers (originator, licensee, parallel import or generic), in different dosage forms, strengths and pack sizes and with either prescription-only or non-prescription (over-the-counter or OTC) status. This diversity within and between countries implies a trade-off: if price comparisons are confined to products that are identical in chemical composition, manufacturer, strength, formulation and pack size, as attempted in previous studies, then only a very small and unrepresentative sample of each country's products can be included, and most generics will be excluded.[9] Most previous cross-national price studies have exacerbated this intrinsic problem of non-matching products by intentionally selecting only leading, branded, prescription products, and excluding all generics despite their substitutability and significant market shares in some countries. Since regulation systematically affects generic market shares and prices, comparisons that omit generics will yield biased estimates of the average cost of drugs under different regulatory regimes.

8 For measurement of intertemporal price change for drugs, see Berndt et al. (1993), who show the bias that results from use of fixed weight indexes, and Griliches and Cockburn (1994) who address the treatment of generics as new drugs rather than new versions of old drugs.

9 Although GAO (1992, 1994) and BEUC (1989a, b) attempted to require matching on all these criteria, compromises were made. For example, BEUC (1989a) imputed prices for missing products, which is inappropriate if differences in products available in different countries reflect systematic differences in regulation, reimbursement, etc.

This study draws on a comprehensive IMS database of all drug sales through retail pharmacies between October 1991 and September 1992. A drug is defined by active ingredient (molecule) and three-digit anatomic therapeutic category (hereafter molecule/ATC) to which the drug is classified, regardless of manufacturer or brand name. Indexes are calculated for two samples. The bilaterally matched sample includes all molecule/ATCs that are available in both the US and the comparison country. These bilaterally matched samples range from 365 molecules for the Japan-US comparison to 438 for the Germany-US comparison. The global sample consists of the 171 molecules that are available in all seven countries.[10] The price for each molecule is defined as a weighted average price, based on all products in the molecule, including originator, licensed, generic and those OTC products that meet the sample criteria.[11] This weighted average price per molecule implicitly assumes that all products with the same active ingredient and for the same indication are substitutes, regardless of originator/generic status, manufacturer, or prescription/OTC status. This assumption of substitutability is consistent with practices of third party payers in the US, Canada, Germany, Sweden and other countries, who set a single reimbursement price for all generically equivalent products (generic reference pricing), regardless of real and

10 These bilateral and global samples are matched across countries using molecule name and ATC3. For a few molecules, different strengths and/or forms are classified by IMS to different ATCs, implying use for different indications, hence possibly different market and regulatory conditions. In fact, indexes based on the simple molecule, regardless of ATC, are very similar to those obtained from molecule/ATC3 matched samples presented here.

11 Excluded are products with sales of fewer than 1,000 packs or less than one kilogram of active ingredient, due to higher risk of sampling and reporting error, and all multiple molecule drugs, because the proportions of the different molecules may differ across countries. Since OTC status is not identified, the sample includes some OTC products, and this is appropriate assuming that they are good substitutes for prescription-only products.

perceived differences between originator and generic products. The UK Drug Tariff applies the same principles to generics.[12]

The IMS prices used here are at the manufacturer level. However, these IMS list prices may significantly overestimate net manufacturer prices for certain products in the US and the UK due to discounts. Specifically, the US price data do not reflect manufacturers' discounts given directly to managed care and public purchasers, or sales through mail order, supermarkets and HMOs. The UK data do not reflect all manufacturer discounts to pharmacists.[13] Thus these list, rather than transactions, prices are expected to underestimate the extent of generic price competition in the UK and underestimate therapeutic competition in the US, as discussed further below.

Indexes are reported for two price measures, price per gram of active ingredient (KG) and price per 'standard unit' (SU), defined by IMS as one tablet, one capsule, 10ml of a liquid etc., as a rough proxy

12 We use the weighted average price over products in the molecule, rather than the lowest price available in each country, because the co-existence of different prices suggests that some consumers or physicians perceive sufficient differences to use the higher priced products – usually a branded version – in the molecule. Taking the weighted average of product prices in the molecule is also consistent with the overall structure of a price index, which volume-weights the products in the market basket. Matching molecules across countries, regardless of each country's within-molecule product mix, implies a stronger assumption of perfect substitutability between products within molecules. This admittedly imperfect assumption seems preferable to the only practical alternative, which is to assume no substitutability between products with the same molecule but different manufacturers. As discussed above, requiring that products match on manufacturer as well as molecule in order to be matched across countries has the effect of excluding most generics and licensed products, yielding a comparison that is based solely on branded products sold by multinational companies. This is a small and unrepresentative sample of the products available in any market and hence yields unrepresentative price comparisons.

13 In the US, the unweighted average 'best price' discounts declined from 42 percent in first quarter 1991 to 33 percent in fourth quarter 1992 (CBO, 1996). The percentage of sales that received some discount is not known. Evidence of discounts in the UK is discussed later (see Section 4.4).

for a dose.[14] Although neither standard units nor grams is an ideal, quality-constant, volume measure, their advantage is that they are defined for all packs, hence a weighted average price for the molecule can be calculated that includes all forms/strengths/packs of that molecule. By contrast, previous cross-national drug price studies have compared prices for a single, supposedly representative, pack – for example, a pack of 100 250mg tablets – with imputation where this particular pack was not available in all countries under comparison. Such comparisons based on a single (possibly imputed) price per pack are likely to be biased because price per pill varies significantly with strength and pack size in some countries, as shown below.

The matching criteria used here require only that two drugs have the same molecule/ATC3 in the US and the comparison country, not the same manufacturer or form/strength/pack. Nevertheless, over 40 percent of total retail pharmacy sales in Germany, France, Italy and Japan are for molecules not available in the US and therefore cannot be included in the price indexes. Whether this results in bias cannot be determined, because to compare the prices of these non-matching molecules would be to compare apples and oranges. The extent to which this heterogeneity in product mix results from the different regulatory systems also remains an unanswered question.

14 Other studies have used price per WHO defined daily dose (DDD), which is not available in these data. DDDs are also imperfect because they are not defined to be equipotent units; do not necessarily correspond to actual daily doses; and ignore differences in duration of treatment (Danzon, 1996). Since DDDs for each drug are defined as grams per day, indexes based on DDDs should be similar to these indexes based on grams, if days of treatment are uniform across countries.

3 PRICE AND QUANTITY INDEXES

Table 1 reports price and quantity indexes for two measures, price per standard unit (SU) and price per gram (KG), for each of the six comparator countries relative to the US. Part A of the table includes the bilaterally matched products. Part B includes only the

Table 1a **Pharmaceutical price indexes relative to US – 1992 Bilateral molecule/ATC3 matches with US**

Variable/Index	Canada	Germany	France	Italy	Japan	UK
Standard Units (SU)						
Laspeyres price index (US weights)	1.021	1.247	0.678	0.871	0.884	0.834
Paasche price index (non-US weights)	0.447	0.403	0.330	0.485	0.457	0.560
Laspeyres quantity index (US weights)[a]	1.989	1.694	2.690	1.583	1.081	0.957
Paasche quantity index (non-US weights)[a]	0.871	0.548	1.311	0.881	0.559	0.642
Paasche index/ Laspeyres index	0.438	0.323	0.487	0.557	0.517	0.671
Grams (KG)						
Laspeyres price index (US weights)	0.866	0.914	0.548	0.696	1.193	0.713
Paasche price index (non-US weights)	0.674	0.597	0.419	0.326	0.484	0.522
Laspeyres quantity index (US weights)[a]	1.320	1.145	2.122	2.353	1.019	1.026
Paasche quantity index (non-US weights)[a]	1.027	0.748	1.621	1.103	0.414	0.752
Paasche index/ Laspeyres index	0.778	0.653	0.764	0.469	0.406	0.733
Population ratio (non-US/US)	0.103	0.244	0.218	0.220	0.473	0.219
Number of molecules	420	438	373	386	365	377

Note:
a Adjusted for population.

Table 1b **Pharmaceutical price indexes relative to US – 1992**
All seven country molecule/ATC3 matches ('global' molecules)

Variable/Index	Canada	Germany	France	Italy	Japan	UK
Standard Units (SU)						
Laspeyres price index (US weights)	0.983	1.193	0.701	0.910	0.943	0.883
Paasche price index (non-US weights)	0.694	0.362	0.364	0.543	0.479	0.630
Laspeyres quantity index (US weights)[a]	1.358	1.966	2.392	1.276	0.936	0.927
Paasche quantity index (non-US weights)[a]	0.959	0.596	1.242	0.761	0.476	0.661
Paasche index/ Laspeyres index	0.706	0.303	0.519	0.596	0.508	0.713
Grams (KG)						
Laspeyres price index (US weights)	0.857	0.887	0.576	0.696	1.163	0.708
Paasche price index (non-US weights)	0.699	0.589	0.427	0.302	0.792	0.553
Laspeyres quantity index (US weights)[a]	1.349	1.207	2.038	2.290	0.566	1.055
Paasche quantity index (non-US weights)[a]	1.100	0.802	1.511	0.995	0.386	0.824
Paasche index/ Laspeyres index	0.815	0.664	0.741	0.435	0.681	0.781
Population ratio (non-US/US)	0.103	0.244	0.218	0.220	0.473	0.219
Number of molecules	171	171	171	171	171	171

Note:
a Adjusted for population.

global products that are available in all seven countries. Values greater (less) than one indicate prices higher (lower) than the US. The Laspeyres indexes weight prices by US consumption quantities, and hence are most relevant from the US perspective, whereas the Paasche indexes weight relative prices by the comparison country's consump-

tion. The Laspeyres indexes can be interpreted as a lower bound estimate of how much the US might save by adopting another country's prices, assuming no change in US consumption. The Paasche indexes are an upper bound estimate of potential savings, under the implausible assumption that the if US adopted another country's prices it would also adopt that country's consumption patterns, and that these changes would leave R&D and availability of new drugs unaffected.

3.1 Price indexes with US as base

The US-weighted (Laspeyres) indexes for price per standard unit show smaller foreign price differences relative to the US than reported in other studies: Canada and Germany, respectively, are 2.1 and 24.7 percent higher than the US; Japan, Italy and the UK are respectively 11.6, 12.9 and 16.6 percent lower than the US; and France is 32.2 percent lower than the US. The comparator-weighted (Paasche) indexes show all countries with lower prices than the US. Thus the magnitude and even the rank ordering of price differentials depend on the weights used. In particular, the Laspeyres indexes (per unit) show the UK with the second lowest prices, after France, whereas based on the Paasche indexes the UK appears second highest for the bilateral sample and third highest for the global sample, after Canada and the US. The Paasche/Laspeyres ratios provide a measure of the effect of different weights on the estimate of price differences.[15]

For given weights, the SU and KG indexes differ significantly for some countries, reflecting systematic difference in strength per unit. For example, strength per dose in Japan is typically weak, partly because doctors commonly prescribe several drugs to be taken together (polypharmacy). Japan thus appears 11.6 percent less expensive than the US based on price per SU, but 19.3 percent more expensive based on price per KG, because more pills are required to yield a given number of grams (Table 1a).

15 For analysis of the factors underlying the large Paasche-Laspeyres differentials, see Danzon and Chao (2000a).

3.2 Price indexes with UK as base

Tables 1c and 1d report prices relative to the UK as the base price, for products that match bilaterally between the UK and each comparison country (1c), and for global products (1d). In these tables, the

Table 1c **Pharmaceutical price indexes relative to UK – 1992 Bilateral molecule/ATC3 matches with UK**

Variable/Index	Canada	Germany	France	Italy	Japan	US
Standard Units (SU)						
Laspeyres price index (UK weights)	1.433	2.291	1.042	1.792	1.326	1.787
Paasche price index (non-UK weights)	0.832	1.044	0.708	0.653	0.719	1.198
Laspeyres quantity index (UK weights)[a]	2.028	1.288	2.477	2.078	1.292	1.557
Paasche quantity index (non-UK weights)[a]	1.177	0.587	1.683	0.757	0.701	1.044
Paasche index/ Laspeyres index	0.581	0.456	0.679	0.364	0.542	0.671
Grams (KG)						
Laspeyres price index (UK weights)	1.385	1.381	0.859	0.984	1.645	1.915
Paasche price index (non-UK weights)	1.091	0.979	0.632	0.880	1.123	1.403
Laspeyres quantity index (UK weights)[a]	1.547	1.374	2.774	1.542	0.828	1.330
Paasche quantity index (non-UK weights)[a]	1.219	0.974	2.040	1.378	0.565	0.974
Paasche index/ Laspeyres index	0.788	0.709	0.735	0.894	0.683	0.733
Population ratio (non-UK/UK)	0.470	1.114	0.995	1.005	2.160	4.566
Number of molecules	376	457	393	412	348	377

Note:
a Adjusted for population.

Table 1d **Pharmaceutical price indexes relative to UK – 1992**
All seven country molecule/ATC3 matches ('global' molecules)

Variable/Index	Canada	Germany	France	Italy	Japan	US
Standard Units (SU)						
Laspeyres price index (UK weights)	1.216	1.460	0.993	1.309	1.380	1.589
Paasche price index (non-UK weights)	1.064	1.005	0.820	1.053	0.826	1.133
Laspeyres quantity index (UK weights)[a]	1.519	1.213	1.818	1.127	0.931	1.513
Paasche quantity index (non-UK weights)[a]	1.329	0.835	1.501	0.907	0.557	1.079
Paasche index/ Laspeyres index	0.875	0.688	0.826	0.804	0.598	0.713
Grams (KG)						
Laspeyres price index (UK weights)	1.358	1.327	0.879	0.939	1.673	1.808
Paasche price index (non-UK weights)	1.158	0.985	0.717	0.942	1.227	1.412
Laspeyres quantity index (UK weights)[a]	1.396	1.238	2.079	1.260	0.627	1.214
Paasche quantity index (non-UK weights)[a]	1.190	0.919	1.697	1.263	0.460	0.948
Paasche index/ Laspeyres index	0.853	0.742	0.816	1.003	0.733	0.781
Population ratio (non-UK/UK)	0.470	1.114	0.995	1.005	2.160	4.566
Number of molecules	171	171	171	171	171	171

Note:
a Adjusted for population.

Laspeyres indexes have UK weights and the Paasche indexes use the comparison country weights. These UK Laspeyres indexes are similar in concept to the indexes in DOH (1997). Differences are that: DOH (1997) uses a smaller sample of leading branded-only products, excluding generics, with only one or two formulations per product; and

DOH weights appear to be number of scripts whereas our weights are units or grams. It is unclear whether DOH (1997) prices are per pack or per unit, hence whether they are more comparable to our prices per standard unit or per gram. Comparing price per standard unit for bilaterally matched products, we find all countries more expensive than the UK, with France and Italy 4 percent and 79 percent higher, respectively, whereas comparing price per gram shows France and Italy 14 percent and 2 percent lower than the UK. By contrast, DOH (1997) reports France 9 percent lower and Italy 4 percent lower than the UK. By these UK-weighted indexes, the US is 79-92 percent higher than the UK, similar to the 88 percent difference reported in DOH (1997). However, using US weights (Paasche indexes) the US is only 20 percent higher than the UK for price per unit, 40 percent higher for price per gram. The differences between our results and those of DOH (1997) for France and Italy presumably reflect our larger sample and inclusion of generics, and possibly differences in the measure of price. For the US-UK comparison, our results show that the DOH finding of 88 percent higher US prices in part results from use of UK weights. This differential falls to 20-40 percent when we use US weights.

3.3 Quantity indexes

The quantity indexes in Table 1a-d are normalised by population, and so can be interpreted as differences in quantity per capita. The Laspeyres KG indexes show higher consumption for all countries relative to the US – for example, France and Italy have quantity indexes more than twice the US level – whereas Paasche indexes show only three of the six countries with higher per capita volume than for the US. Differences in KG quantity indexes are generally smaller than differences in SU indexes, suggesting that systematic differences in strength per pill are partially offset by differences in number of pills per capita. The Paasche/Laspeyres ratio is identical for price and quantity indexes. Relative to the UK, all countries have higher volume using UK price weights (except Japan for grams).

In general, these quantity indexes suggest smaller cross-country differences in per capita volume than previously reported. For example, Burstall (1991) estimates per capita drug consumption by deflating total drug expenditures per capita by the BEUC (1989a) price indexes. This method yields estimates of per capita volume, relative to the UK, of 3.06 for France, 2.06 for Italy and 1.53 for Germany, which imply larger differences than most of the measures in Table 1c and d. Previous estimates of volume per capita tend to be upward biased in countries where price estimates have been downward biased. Our indexes avoid these biases. However, quantity indexes, like price indexes, can only be computed for matching molecules, hence conclusions about differences in total drug consumption are tentative. In particular, the molecules included here are a smaller fraction of total drug sales for Germany, France, Italy and Japan than for the UK, the US and Canada. By these indexes, Japan appears to have relatively low per capita consumption for global and bilaterally matched products. Thus if the conventional view, that Japanese drug consumption is very high, is correct then this must reflect high consumption of local products, not the global products that are included in these indexes.

3.4 Bilateral vs global molecules

The US-based price indexes for global molecules generally show slightly smaller price differences between countries than the indexes based on the larger, bilaterally matched samples. Less cross-national price dispersion on global molecules, particularly on price per SU, could reflect either corporate strategies to maintain prices for global products within narrower bands in order to pre-empt parallel trade and/or regulatory cross-national spillovers, or the effects of such spillovers.[16] Quantity indexes also show less dispersion for global products, suggesting more uniform consumption patterns across countries for consensus drugs.

16 Danzon (1997b) discusses manufacturers' incentives to reduce cross-national price differences in response to parallel trade and regulatory use of price comparisons.

4 MEASURING THE EFFECTS OF COMPETITION AND REGULATION ON DRUG PRICES

The previous analysis showed that estimates of cross-national price differences depend on the sample used. One key reason for this is that regulation does not simply lower all prices by a certain percentage, relative to unregulated prices; rather, regulation affects the relative prices for different drugs differently. This is demonstrated in the following sections, which describe a multivariate analysis of the effects of competition and regulation on prices at the individual product level.

In analysing the effects of competition and regulation on manufacturer prices, it is important to control for product characteristics and for other relevant determinants of demand. The demand for drugs depends on the out-of-pocket costs faced by consumers after insurance, and on the incentives and choices of physicians who prescribe and pharmacists who dispense drugs. Since insurance and regulatory regimes affect the incentives and constraints of consumers, physicians and pharmacists, the relevant features of insurance and regulatory regimes as of 1992 are summarised next.[17]

4.1 Consumers and insurance

Coverage of drugs through public and private insurance programs was extensive in all seven countries in 1992, except the US. Although some countries' social insurance nominally includes significant co-payment rates, either as a percentage of the price (France, Italy, Japan) or a fixed payment per script (the UK, Germany), effective marginal co-insurance rates were often lower or nil because of exemptions for the elderly and other needy groups; supplementary insurance that covers co-payments under public schemes (the mutuelles in France); and stop loss limits on out-of-pocket payments (Japan). Moreover, all countries except the US had low or zero co-payments on physician visits, which

17 For a more detailed description of the insurance and regulatory systems, see Danzon (1997a).

can be a significant part of the full price of obtaining prescription drugs.

There are two exceptions to this extensive insurance coverage. First, in 1989 Germany introduced a reference price system (see below), primarily for off-patent, multisource drugs, that requires patients to pay 100 percent of the manufacturer's price above the reimbursement or reference price. This reference price system accounted for 40 percent of expenditures in 1992 (VFA, 1997); however, the great majority of affected products were priced at or below the reference price (REMIT, 1991; Ulrich and Wille, 1996). Second, in the US roughly 50 percent of outpatient drug expenditures was paid directly out-of-pocket by patients, because many traditional indemnity insurance policies did not cover outpatient drugs. People with managed pharmacy benefits typically have generic substitution programmes, which set a maximum allowable charge (MAC) for generically equivalent drugs and require the patient to pay any excess if the manufacturer's actual price exceeds the MAC, as in Germany's reference price system.

Given the extensive insurance coverage, consumer demand is expected to be price-inelastic, with no significant difference across countries, with the possible exception of the US and multisource drugs in Germany.

4.2 Physician agents

Theory and evidence indicate that physicians are imperfect agents and that their prescribing choices reflect their own financial incentives as well as patient concerns.[18] However, as of 1992, physicians in most countries in our sample were not at financial risk for costs or profit

18 Danzon and Liu (1998) develop a model of imperfect physician agency and provide empirical evidence on the effects of Germany's reference price system and drug budgets. Hillman et al. (1999) show the interaction between patient and physician incentives in US managed care.

from the drugs that they prescribed, and hence had little personal incentive to be price sensitive.[19] One exception is the UK where, from April 1991, fundholding general medical practitioners (GPs) received drug budgets and could redirect or reinvest any savings, although they were not at risk for budget overruns. However, as of 1992 few GPs were fundholders. The majority were non-fundholders who faced only 'indicative' drug budgets, with monitoring but no financial penalties for overruns.[20] In Japan, physicians dispense drugs and can profit from the margin between the reimbursement price and the acquisition cost. Japanese physicians are thus expected to be sensitive to the profit margin; however, absolute margins are often lower on low-priced drugs, so physicians may in fact prefer high-priced drugs (Ikegami et al., 1998). In conclusion, as of 1992 cross-national differences due to patient co-payments and physician incentives were small, with exceptions noted for the US, UK, Germany and Japan, compared to differences in pharmacy and price regulation, which are described next.

4.3 Generic substitution and pharmacy regulation

The extent to which pharmacists are authorised to substitute between drugs and make price conscious choices is a further potential influence on the incentives of drug manufacturers to compete on price. Pharmacists are authorised in some countries to substitute between generically equivalent products to fill a prescription. In the UK, pharmacists may substitute a generic if the prescription is generically writ-

19 Germany adopted a national spending limit for drugs, with physicians at risk for overruns, in 1993. In the US, capitation of physicians for drug costs by managed care plans was relatively uncommon in 1992.

20 Baines et al. (1997) find that the main effect of fundholding was to encourage generic substitution. In the UK, roughly 10 percent of (mostly rural) physicians directly dispense drugs and profit from the reimbursement – acquisition cost margin, as in Japan, and hence are expected to be price sensitive, particularly for generics.

ten (that is, the molecule is described by chemical name rather than brand name), which occurs in over 60 percent of GP prescriptions (Pharma Pricing Review, 1998). The pharmacist retains the margin between the Drug Tariff reimbursement price and the acquisition cost of the product dispensed, which creates incentives for manufacturers to offer discounts to pharmacists on multisource products. In the US, by the 1990s all states authorised generic substitution by pharmacists unless the physician explicitly writes 'dispense as written'. Most managed care and Medicaid plans reimburse only a maximum allowable charge (MAC) or reference price for generically equivalent products. The US pharmacist captures the difference between the MAC and the manufacturer price (net of the wholesale margin), which makes demand for generically equivalent products highly price elastic in the US. Generic substitution programmes also exist in most Canadian provinces. In Germany, pharmacists are permitted to substitute between generically equivalent products where the script is generically written, but this occurred in less than 5 percent of scripts (Schoffski, 1996). German generics are typically branded and compete by promoting a brand image, in contrast to US generics, which are typically unbranded and compete primarily on price. In France, Italy and many other European countries, generic substitution by pharmacists was not permitted at this time.

In addition to restrictions on generic substitution, Germany, France, Italy and many other countries regulate retail pharmacy dispensing margins and impose other barriers to competition in retail pharmacy. These regulatory systems undermine pharmacists' incentives to be price conscious purchasers, which in turn undermines competitive pricing by manufacturers. For example, the regulated pharmacist's absolute margin usually increases with drug price, even if the percentage margin declines, such that pharmacists have little incentive to substitute cheaper products even if authorised, which makes demand inelastic. France, Italy and Germany prohibit pharmacists from splitting large packs (unit pack dispensing), which undermines manufacturers' incentives to compete by offering volume

discounts as occurs commonly in less regulated markets. Retail price competition between pharmacies is further discouraged by requirements that each pharmacy be owned by a licensed pharmacist, restrictions on branch pharmacies, etc.[21] Although OTC prices are not regulated, OTCs are subject to retail price maintenance in most countries. Thus, regulations that restrict price competition between retail pharmacists and make them price-insensitive tend to undermine the incentives for competition at the manufacturer price level.

These cross-national differences in generic substitution and pharmacy regulation are predicted to generate significant cross-national differences in the price sensitivity for multisource products. Specifically, demand is expected to be highly price elastic for generically equivalent products in the UK, the US and Canada, where substitution is permitted and profitable for pharmacists. Conversely, regulation and barriers to price competition between pharmacists are expected to result in inelastic demand for generics in France, Italy and possibly Germany; however, this is mitigated in Germany by the incentives for patients and physicians under reference pricing.

4.4 Price and reimbursement regulation

Although each country's system for regulating manufacturer prices for drugs is different, countries can be categorised into those with strict price or reimbursement regulation for individual drugs (France, Italy, Japan), those with indirect or limited price regulation (Canada, the UK, Germany) and the largely unregulated US. In the first group, France and Italy require regulatory approval of the manufacturer's launch price before a drug can be reimbursed by the social insurance scheme. Post-launch price increases are usually not allowed and decreases may be mandated. In Japan, the government negotiates the initial reimbursement price at launch but manufacturers are free to

21 Scherer (1997) discusses barriers to competition in retail pharmacy in the US; for other countries see Reekie (1997).

charge a lower price. Manufacturers compete by cutting price below the reimbursement price to gain market share by increasing the profit margin to dispensing physicians. Every two (now one) years, the government revises the reimbursement price downwards, based on a survey of actual manufacturer prices plus an allowed margin (15 percent in 1992, 2 percent in 1999).

These regulatory systems have two common characteristics that are expected to affect competition and the measurement of competition. First, regulation forces down the real price of an originator (patented) drug over the patent term in France, Italy and Japan.[22] The lower the originator price when the patent expires, the smaller the potential profit margin for a generic competitor pursuing a price competition strategy and hence the less attractive is the market for competitive generic entry. This is exacerbated if the demand facing a potential generic entrant is price inelastic, due to regulated pharmacy margins and absence of generic substitution programmes.

Second, in France, Italy, Japan – and Canada except for truly innovative drugs (see below) – prices of established products serve as a regulatory benchmark for setting new products' prices. The relationship is approximate: some comparator products are more relevant than others; the new product may obtain a mark-up for improved efficacy or usefulness; and the regulated launch price may be higher if a firm makes a significant local investment, co-markets the product with a domestic firm or has other influence. Nevertheless, this regulatory approach implies that if prices of established products decline with time on the market, launch prices of successive entrants will be

22 The inflation-adjusted Divisia price index for drugs for 1981-1992 in Japan is –6.8 percent per year, –4.3 for Italy, –0.25 for France (Danzon and Kim, 1996). (This chain-weighted index adjusts the weights to reflect the product mix available in each pair of adjacent years). In France and Italy this reflects denial of inflation adjustments; in Japan, the downward spiral results from superimposing regulation on a market with competition for physician demand. The UK also does not permit post-launch price increases.

inversely related to the number of competitor products already on the market, other things being equal. This effect is expected to be less negative in Canada, which permits inflation adjustments for established products, than for France, Italy, and Japan (and the UK), which do not permit inflation adjustments. In unregulated markets, since new entrants must also compete with established products, a similar relationship may hold. However, if markets and regulators differ in their evaluation of product differences, then differences between price-regulated and more competitive regimes are expected.

It is sometimes argued that regulatory systems in France, Italy and Japan, by driving down prices over the life-cycle, create incentives for local manufacturers to introduce a continual stream of minor new products in order to obtain a higher price, and that this has undermined their competitiveness in truly innovative R&D.[23] If true, this implies that a new product typically receives a somewhat higher price than established products, despite the downward pressure that results from tying prices for new product to prices for existing products.

Among the less regulated countries, Canada's Medicines Review Board monitors prices to assure that launch prices are 'reasonable' relative to prices in other countries (for innovative products) or relative to prices of established products (for non-innovative products). Post-launch price increases are limited to the rate of inflation. Provincial plans impose additional constraints, although less so in 1992 than now.

The UK and Germany permit relatively free pricing. The UK permits free pricing of a new, patented product at launch, subject to a limit on the company's rate of return on capital in the UK for all products sold to the NHS. Price increases require approval, which is rarely given. After patent expiration and generic entry, the Drug Tariff defines a maximum reimbursement or reference price for multi-source

23 Consistent with this, these three countries have lagged less regulated countries in the development of innovative new drugs although not in the total number of new drugs including minor extensions of existing molecules (Barral, 1995).

products. Manufacturers compete by offering price discounts off list prices to pharmacists. The Drug Tariff is periodically revised downward based on actual supply prices but with a lag. For example, the April 1992 Pharmacist Discount Enquiry showed discounts on generic medicines on average 47.7 percent below the NHS drug tariff (of which 12.5 percent is the wholesale margin). Following deep reductions in NHS prices, the April 1993 Enquiry survey found average discounts of 26 percent.[24] Thus the IMS list prices used in our analysis may significantly overestimate actual manufacturer prices for multisource products in the UK.

In Germany, manufacturer prices were unregulated until 1989, when a reference system of reimbursement was introduced.[25] Phase 1 applied to multisource compounds with several generic competitors, while Phases 2 and 3 extended the system to therapeutically similar molecules. Although manufacturer prices remain unregulated, a price above the reference price usually results in significant loss of market share because the patient must pay the excess and the physician is required to explain to the patient why the excess is necessary, which implies an unreimbursed time cost.[26] For non-reference priced products, prices remained unregulated in Germany as of 1992.

In the US, manufacturer prices are unregulated, but competitive pressures have increased with the growth of managed pharmacy benefits since the mid-1980s, through health maintenance organisations

24 Department of Health Pharmacist Discount Enquiry (April 1992 and 1993). The pharmacists' reimbursement is the Drug Tariff price net of a 'clawback' which is intended to reflect the average discount obtained by retail pharmacists on generic and parallel imported products.

25 A reference price system classifies drugs into groups that are considered close substitutes and sets a single reference price for each group as the maximum reimbursement for all drugs in the group.

26 REMIT (1991) reports that brand prices generally dropped to the reference price. Danzon and Liu (1998) find that German reference pricing reduced the weighted average molecule price and accelerated the rate of price decline.

(HMOs) and stand-alone pharmacy benefit managers (PBMs) that manage drug coverage for other health plans. Pharmacy benefit managers create formularies of 'preferred' drugs which physicians and patients are encouraged to use through monitoring, differential co-payment, etc. The ability of PBMs to shift demand towards 'preferred' products implies increased price elasticity of demand, which enables them to negotiate discounts from list prices for branded products, particularly in crowded therapeutic categories. Since 1991, Medicaid requires discounts off list prices equal to 15 percent or the 'best price' given to any private purchaser. This 'best price' provision has tended to reduce the discounts given to private purchasers. Between 1991 and 1993, the median 'best price' discount declined from 24 percent to 14 percent for HMOs (GAO, 1994b); unweighted average 'best price' discounts declined from 42 percent in first quarter 1991 to 33 percent in fourth quarter 1992 (CBO, 1996). Although these discounts probably applied to under 50 percent of sales, since deep discounting is concentrated in crowded therapeutic categories, the list price data used in our analysis will underestimate the extent of therapeutic competition in the US.

5 METHODS AND VARIABLE DEFINITIONS

5.1 Empirical model of drug pricing

The empirical analysis of drug prices here is structured to test certain simple hypotheses about the effects of competition and other factors on drug prices. Drug markets are assumed to be imperfectly competitive, and prices may be affected by quality attributes. Specifically, the price of a drug is expected to be positively related to quality attributes such as effectiveness and convenience; negatively related to the number of generic competitors, with greater impact from post-patent 'true' generics than from licensed, co-marketed products; and negatively related to the number of substitute molecules in the therapeutic category, although the competitive effect of therapeutic substitutes is expected to be less than for generic substitutes.

The empirical estimation here has three potentially significant limitations, due to lack of data. First, as noted earlier, the price data do not reflect discounts to managed care and Medicaid in the US and discounts to pharmacists in the UK.

Second, the available data cannot control for manufacturers' promotional investments that may influence market demand. Promotion is expected to be greater for on-patent products, where any demand expansion accrues primarily to the firm that undertakes the investment, than for off-patent products, where increased demand for the molecule may be largely captured by other generic competitors.[27] However, even for on-patent drugs, one firm's promotion may increase awareness of the product class, with demand-expanding spillover effects to other drugs in the same class. If (unobserved) promotion is positively correlated with number of substitute molecules in the class, our measures will underestimate the competitive effects of substitute molecules on price. Note that demand-shifting effects of promotion may be associated with both higher price and volume in unregulated

27 Consistent with this, Caves, Whinston and Hurwitz (1991) find that originator firms reduce promotional investment before patent expiration.

markets, whereas in price-regulated markets, promotion can only affect volume.[28] This is further discussed below.

Third, this analysis treats the number of competitors as given, although in reality the number of both generic and therapeutic competitors plausibly reflects prior expectations about profitability, which may be correlated with the observed prices. To the extent that a reverse relationship exists, such that higher (expected) prices encourage greater entry of generic and therapeutic substitutes, this is an additional reason why the present estimates may underestimate the competitive effects of generic and therapeutic substitutes on prices.

5.2 Sample

The two subsamples – global and bilaterally-matched molecules – are used to study competition at the product and the molecule level. The global molecule sample includes all molecules that are available in all seven countries.[29] Although the molecules are the same in all countries, the products in any given molecule may differ across countries, including possibly the originator brand, licensees, parallel imports and generics. After deleting observations with missing data, the global sample includes 171 global molecules with a total of 5,690 products. Analysis of this sample is at the level of the individual product, defined by molecule, manufacturer, and product name, with aggregation over all pack sizes in the product.[30]

28 Indeed, in France the regulated price was often reduced if volume exceeded a target level. Recent regulatory changes are intended to grant manufacturers higher prices in return for lower volumes.

29 Multiple molecule (combination) products are excluded because the relative mix of different molecules may differ, which reduces comparability across countries and renders ambiguous such variable definitions as strength or number of generic competitors.

30 Following IMS usage, the analysis here defines a new dosage form – for example, a delayed release tablet – as a new product rather than a new form of an old product if it has a different product name. Thus Procardia XL is a distinct product from Procardia.

The bilaterally matched sample includes all molecules that are available, pairwise, in each comparison country and the US, and ranges from 365 molecules for Japan to 438 for Germany. This larger, bilaterally-matched sample is used for analysis at the molecule level, with all variables defined as weighted averages over the values for all products in the molecule.

5.3 Variable definitions

Price – For each product, the average price per standard unit is the volume-weighted average price per standard unit for all forms/strengths/packs in the product. The molecule price is similarly the volume-weighted average price over all products in the molecule. All analysis is in US dollars, using the values reported by IMS, who convert foreign currency to US dollars using quarterly 1992 exchange rates. Since the price distributions are approximately log normal, the dependent variable in the regression analysis is the log transform of price per standard unit. Log transforms are also applied to all explanatory variables where proportional effects are expected. Coefficients in the log on log regressions can be interpreted as elasticities, that is, the proportional effect of the explanatory variable on the dependent variable.

Quality – Several 'quality' characteristics are included as proxy variables for the product's effectiveness or convenience, which may affect price. Indicators for 13 one-digit IMS therapeutic categories (ATC1) are included as controls for the primary medical indication of the product, which may influence therapeutic value and/or insurance coverage, and hence price – for example, cardiovascular drugs (the omitted category), dermatologics, etc.[31]

31 Therapeutic category may also be an indicator of insurance coverage, since insurance coverage in most countries is more complete for 'medically necessary' drugs than for 'comfort' drugs.

Strength, defined as average grams of active ingredient per standard unit, is expected to be positively related to price per unit if stronger products typically have higher prices. However, since some highly potent molecules may have weak strength per pill but command high prices, the price-strength relationship for a market basket of molecules is uncertain.

Molecule Age, measured as (log) months from September 1992 (the last observation month) to the country-specific launch date of the first product in the molecule, is an inverse indicator of therapeutic effectiveness, assuming that more recent compounds are generally more effective.[32] Molecule Age is the same for all products in the molecule in a given country, but may differ across countries if the molecule's launch dates differ. Molecule Age may also reflect life cycle pricing and age-related regulatory effects.

The Number of Forms of the product is included as a measure of choice of formulation and hence convenience for patients. The coefficient is expected to be positive, if manufacturers develop new forms only where the expected increase in price is sufficient to cover the development costs.

None of these 'quality' variables provides a good measure of effectiveness, comparable to a willingness-to-pay or quality-adjusted life year (QALY) measure. Omitting an important variable from a regression model in general reduces the model's overall explanatory power. However, coefficients of the variables that are included should be unbiased, unless they are correlated with the omitted variable. In this case, estimates of differences in effects between each comparison country and the US should be unbiased, since effectiveness is an omitted variable for all countries and the same molecules are included in each bilateral US-foreign comparison.

32 Since most of the molecules in the sample are well-established, the Molecule Age coefficient should reflect value after several years of experience, but may be biased for very recent products, if they tend to be undervalued initially.

Competition – Pack Size (average number of units per pack) is included to test the joint hypothesis of scale economies in packaging and competition. Assuming scale economies in packaging, the price-pack size relationship is expected to be negative in countries with competitive retail pharmacy (US, UK, Canada), where manufacturers have incentives to compete by passing on to pharmacists the packaging economies through volume discounts. In countries that require unit dispensing (France, Germany, Italy), the range of pack sizes is expected to be smaller and the price-pack size relationship is expected to be less negative.

Generic Competitors is the number of products in the molecule, including originator, licensed and parallel import products as well as post-patent true generics.[33] For a single source molecule, sold only by the originator manufacturer, Generic Competitors takes a value of one. The different types of generic competitors differ in competitive impact, but unfortunately the data do not distinguish between them. The expected effect of true generic imitators on manufacturer prices is negative in markets where prices are unregulated, particularly where retail pharmacy is unregulated and pharmacists are permitted to substitute between generically equivalent products[34]; a negative effect is also expected in Germany due to reference pricing. However, price competition is expected to be less intense between originator and licensee firms, because firms that co-market or co-promote have aligned incentives to avoid price competition and, in regulated markets, usually receive the same regulated price. Moreover, in regulated markets a multinational firm may allegedly agree to co-market with a

33 The results are invariant to measuring Generic Competitors as number of products or number of manufacturers, because most manufacturers produce only one product per molecule. Parallel imports occur when wholesalers import the originator product from a low price country to a higher price country in the EU (see Danzon, 1997b).

34 The UK permits substitution if the script is generically written; the US and some provinces in Canada permit substitution unless the physician indicates that a particular brand is required.

local firm in return for a higher regulated price. This is an additional reason for expecting a less negative effect of the Generic Competitors variable on price in regulated markets than unregulated markets.

Our measure of therapeutic competition, Therapeutic Substitute Molecules, is the total number of molecules in the three-digit therapeutic category (ATC3). This is an imperfect measure of therapeutic competition because substitutability differs between molecules in a therapeutic category, and drugs in other categories may also be substitutes.

The number of Products per Therapeutic Substitute Molecule is also included, to test the hypothesis that the cross price elasticity between molecules increases as the number of producers per molecule increases.

Previous studies have found evidence of a first mover advantage and that followers enter at lower prices relative to the market leader, in pharmaceuticals and in other industries (for example, Reekie, 1996; Towse and Leighton, 1999). The within-molecule and between-molecule effects are distinguished in this paper. Generic Entry Lag is the (log) number of months between the product's own launch date and the launch date of the first product in the molecule (plus one). This ranges from one for the originator product to large positive values for late entrants.[35] The expected sign is negative, under the hypothesis that the originator product has a first mover advantage relative to later generic producers of the same molecule who offer little or no therapeutic advantage.

Therapeutic Substitute Molecule Entry Lag is (log) months from the launch of this molecule to the launch of the first molecule in the therapeutic category. The sign could be negative or positive, depending on whether first mover advantage of the pioneer molecule in a class dominates or is dominated by superior efficacy of later molecules.

35 Patent expiry dates are not available in our data, so time since patent expiry as used in previous studies cannot be used here.

6 EMPIRICAL RESULTS

6.1 Differences in means

To show cross-national differences in the average characteristics of these 171 global molecules, Table 2 reports mean values for each variable and t-tests for significant difference from the US. The unit of observation is the molecule, and the value for each molecule is a weighted average over products in that molecule.

Although the sample of molecules is the same for all countries in Table 2, there are significant differences in average attributes. Mean Molecule Age is significantly higher in the UK, Germany, France and Italy than in the US, which is consistent with a regulatory lag in launch in the US in the 1960s and 1970s.[36] The average age of over 20 years for all countries is influenced by a few very old molecules, but also reflects the fact that global diffusion takes time, hence a sample of global molecules cannot include the newest molecules.

The average number of Generic Competitors per molecule, including licensees and generic imitators, is 11.1 in the US, compared to 6.6 in Germany, 4.5 in Japan, 3.3 in Canada, 3.0 in Italy, 2.4 in France and 2.3 in the UK. This large number of generic equivalent products per molecule reflects the fact that global molecules tend to be the most valuable and hence attract the most products per molecule. Consistent with this, the mean number of Products per Therapeutic Substitute Molecule, which includes all molecules – non-global and global – in the category, is consistently lower than the mean Generic Competitors for the global molecules. However, the pattern across countries is the same, with the US having more than twice as many Products per Therapeutic Substitute Molecule as all other countries.

36 Dranove and Meltzer (1994) estimate that the average time from a drug's first worldwide patent application to its approval by the FDA rose from 3.5 years in the 1950s to almost six years in the 1960s and 14 years in the mid-1980. Wardell and Lasagna (1975) report that the US lagged behind each major European country in new drug introductions. For molecules launched since 1980 there is no evidence of US regulatory lag, which probably reflects both reduction in regulatory delay in the US and possibly some lengthening in some other countries.

Table 2 **Cross-country comparison of variables and t-tests for differences relative to the US – 1992**
Unit of observation: 'global' molecules, retail pharmacy.

Variable		US	Canada	Germany	France	Italy	Japan	UK
Price per unit	Mean	0.903	0.857	0.746	0.396	0.504	0.672	0.485
	SD	1.816	2.349	1.314	0.678	0.920	1.598	1.033
	t		0.201	0.912	3.419	2.562	1.248	2.612
Quality								
Strength	Mean	0.190	0.171	0.203	0.241	0.290	0.142	0.158
	SD	0.367	0.288	0.378	0.633	1.024	0.346	0.336
	t		0.536	0.315	0.904	1.197	1.242	0.852
Molecule Age	Mean	240.994	259.620	312.380	268.135	282.082	257.497	283.409
	SD	143.717	144.527	191.182	138.625	157.405	136.463	142.418
	t		1.195	3.903	1.777	2.521	1.089	2.741
Number of Forms	Mean	3.830	3.135	3.895	2.579	2.643	3.012	3.392
	SD	2.473	1.863	2.228	1.669	1.552	1.652	2.001
	t		2.939	0.253	5.484	5.317	3.599	1.803
Competition								
Pack Size	Mean	118.715	168.008	63.222	39.490	37.784	397.973	93.942
	SD	82.804	156.517	43.290	52.154	59.431	353.162	108.050
	t		3.640	7.766	10.587	10.383	10.067	2.380
Generic Com-petitors	Mean	11.146	3.275	6.608	2.368	3.000	4.544	2.333
	SD	12.694	3.304	7.720	2.391	3.249	4.548	2.262
	t		7.847	3.994	8.886	8.130	6.403	8.938
Generic Entry Lag	Mean	116.588	66.863	113.602	51.640	45.704	63.726	44.369
	SD	119.734	83.723	133.654	82.764	89.177	79.005	76.211
	t		4.451	0.218	5.835	6.209	4.819	6.654
Therapeutic Substitute Molecules	Mean	7.286	6.014	10.443	9.214	9.457	9.586	6.800
	SD	4.976	4.241	7.573	6.510	7.619	8.044	5.216
	t		1.627	2.915	1.969	1.997	2.034	0.564
Products per Therapeutic Substitute Molecule	Mean	6.389	2.225	3.023	1.520	2.111	2.578	1.651
	SD	4.317	1.391	2.540	0.613	1.044	1.191	0.978
	t		12.007	8.788	14.604	12.595	11.129	14.000
Therapeutic Substitute Molecule Entry Lag	Mean	163.608	139.760	230.099	179.532	168.123	154.965	146.187
	SD	151.896	143.927	232.834	163.241	136.214	133.571	132.541
	t		1.490	3.128	0.934	0.289	0.559	1.130
N		171	171	171	171	171	171	171

By contrast, the mean number of Therapeutic Substitute Molecules in the ATC3 is higher in Germany, France, Italy and Japan than in the US, the UK or Canada. This suggests that the much larger number of generic competitors in the US than in other countries is not attributable simply to the larger US market size. The large number of non-global molecules in Germany, France, Italy and Japan is consistent with traditional incentives under their regulatory systems for local manufacturers to develop many, minor products that do not diffuse globally.[37]

The average lag between the entry of the originator and follower products in the molecule (Generic Entry Lag) is roughly 10 years for the US and Germany compared to five years or less for the other countries.[38] The higher mean Generic Entry Lag in the US and Germany reflects more late generic entrants and possibly differences in patent term and ease of generic entry.[39] Relatively low Generic Entry Lag for Italy, Japan and France is consistent with casual evidence that generically equivalent products in these regulated systems are disproportionately licensees rather than competitive generics, and with a relatively large number of single source molecules after patent expiry. In analysis not reported here of molecules launched since 1980, we found the same pattern across countries although lower means for generic entrants.

Average Pack Size is significantly lower in Germany, France and Italy, which require unit pack dispensing, than in the US, Canada, the

37 For molecules launched since 1980, the US has more molecules per therapeutic category, suggesting that the influence of old regulatory traditions is changing.

38 Since Generic Entry Lag cannot exceed Molecule Age, the shorter mean Molecule Age in the US would imply shorter mean Generic Entry Lag in the US, other things equal.

39 In the US, the 1984 Waxman Hatch Act gave patent holders up to five years of patent extension, but also accelerated generic manufacturers' access to the data needed for prompt post-patent entry. The EU adopted patent extension later and granted the originator firm data exclusivity for 6-10 years, compared to five years in the US (European Commission, 1998).

UK and Japan, where pharmacists and/or dispensing physicians are permitted to purchase in bulk and dispense smaller volumes to individual patients. This limits the potential for volume discounts in the unit pack dispensing countries, as shown below.

6.2 Product-level regression analysis

The estimation procedure used here pools the data for all seven countries but permits all coefficients to differ across countries, using the US as base. In this form, the US coefficients measure the effects in the US and the coefficients for other countries measure the country-specific differentials between the effect of each variable in that country and its effect in the US. The US is used as the base country because it is the least regulated market for both manufacturer prices and pharmacy margins. This 'pooled and fully interacted' model yields the same coefficient estimates as would be obtained from separate, country-specific regressions. The advantage of this specification is that the t-statistics for comparison country interactions test directly for coefficient differences between that country and the US. Entries '–' in the tables indicate that a variable's coefficient was constrained to be the same in the country in question as the US coefficient, because preliminary analysis showed not even marginally significant difference (t-statistic less than one).[40] The discussion here focuses first on the results from the product-level analysis for the global molecules (Table 3), then turns to similarities and differences in the molecule-level analysis for the bilaterally matched molecules (Table 4). The coefficients in these log on log regressions can be interpreted as elasticities.

40 The constraints improve the efficiency of the estimates. The F statistic for the joint hypothesis that the constrained interactions are zero is 0.35, which suggests that any bias from imposing the constraints is small.

Table 3 **Product-level regressions: 'global' molecules – 1992**
Dependent variable: log price per standard unit (t statistics in parentheses). Coefficients for non-US countries are differentials relative to the US.

Variable	US	Canada	Germany	France	Italy	Japan	UK
Intercept	4.989	0.371	–1.245	0.076	–0.895	1.697	–1.363
	(15.442)	(0.644)	(–2.473)	(0.118)	(–1.535)	(2.912)	(–1.893)
Quality							
Strength (ln)	0.103	–0.076	0.071	–	0.029	–	0.091
	(10.150)	(–2.945)	(3.658)	–	(1.107)	–	(3.170)
Molecule Age (ln)	–0.027	–0.465	–0.264	–0.757	–0.664	–0.783	–0.440
	(–0.481)	(–4.919)	(–3.139)	(–7.160)	(–7.709)	(–8.103)	(–3.796)
Number of Forms (ln)	–0.005	–	0.181	0.130	0.201	0.361	0.177
	(–0.163)	–	(3.232)	(1.483)	(2.322)	(4.914)	(1.910)
Competition							
Pack Size (ln)	–0.946	0.110	0.392	0.323	0.395	0.375	0.427
	(–39.497)	(2.517)	(9.385)	(5.369)	(7.146)	(10.046)	(8.378)
Generic Competitors (ln)	–0.503	0.249	0.083	0.346	0.557	0.444	0.144
	(–16.103)	(3.648)	(1.740)	(4.263)	(8.188)	(7.116)	(1.647)
Generic Entry Lag (ln)	–0.104	0.088	0.072	0.180	0.187	0.182	0.189
	(–6.786)	(3.508)	(3.429)	(6.466)	(6.814)	(7.339)	(6.333)
Therapeutic Substitute Molecules (ln)	0.130	0.258	–	–	–0.155	–0.200	–0.110
	(4.549)	(3.146)	–	–	(–2.048)	(–3.697)	(–1.289)
Products per Therapeutic Substitute Molecules (ln)	–0.220	–	0.079	–0.207	0.547	–0.236	0.155
	(–5.699)	–	(1.197)	(–1.324)	(4.173)	(–2.402)	(1.210)
Therapeutic Substitute Molecule Entry Lag (ln)	–0.027	0.029	0.032	–0.035	–	0.039	0.079
	(–2.517)	(1.198)	(1.762)	(–1.270)	–	(1.731)	(2.738)

Table 3 **Product-level regressions:** *continued*

Variable	US	Canada	Germany	France	Italy	Japan	UK
Therapeutic categories							
A	–1.526	0.532	1.181	1.394	1.755	1.603	0.918
	(–15.587)	(3.181)	(8.425)	(7.171)	(10.603)	(10.892)	(4.194)
B	–1.098	–	0.886	1.148	1.335	0.591	0.507
	(–9.573)	–	(4.061)	(3.997)	(4.843)	(2.587)	(2.070)
D	–0.885	–0.392	0.440	0.180	0.465	0.245	0.535
	(–8.885)	(–1.873)	(2.650)	(0.782)	(2.242)	(1.395)	(2.365)
G	–0.170	0.539	–	0.492	0.442	–	0.614
	(–1.560)	(2.017)	–	(1.633)	(1.887)	–	(1.928)
H	0.193	–0.449	0.369	0.992	0.389	0.526	0.650
	(1.447)	(–1.623)	(1.796)	(3.363)	(1.240)	(2.285)	(2.565)
J	0.629	–0.142	–0.300	–0.499	–0.430	–0.712	–0.520
	(8.361)	(–0.918)	(–2.359)	(–2.749)	(–2.420)	(–5.086)	(–2.710)
L	0.289	–	1.066	–	0.522	0.841	–
	(1.650)	–	(3.846)	–	(1.247)	(2.316)	–
M	0.261	–	–0.861	–0.660	–0.430	–0.482	–0.403
	(3.245)	–	(–6.524)	(–2.794)	(–2.437)	(–3.165)	(–1.902)
N	–0.266	–1.047	–0.829	–0.517	–	–0.294	–0.540
	(–4.579)	(–8.230)	(–7.592)	(–3.319)	–	(–2.255)	(–3.233)
P	–0.313	–	–	–	1.512	–1.564	–2.142
	(–0.895)	–	–	–	(1.545)	(–1.593)	(–2.173)
R	0.596	–0.771	–0.207	–0.625	–0.584	–0.122	–
	(7.013)	(–3.880)	(–1.546)	(–3.099)	(–2.933)	(–0.672)	–
S	–3.100	–0.616	0.557	–	1.411	–	–
	(–15.628)	(–1.191)	(1.460)	–	(2.760)	–	–
N=5,690 Adjusted R^2=0.6223							

Note:
t>1.960 implies significance with p<0.05.

Table 4 **Molecule-level regressions: bilateral molecules – 1992**
Dependent variable: log price per standard unit (t statistics in parentheses). Coefficients for non-US countries are differentials relative to the US.

Variable	US	Canada	Germany	France	Italy	Japan	UK
Intercept	3.260	1.203	1.008	1.601	1.743	4.197	0.389
	(10.334)	(2.428)	(1.769)	(2.726)	(3.203)	(6.266)	(0.742)
Quality							
Strength (ln)	0.124	–0.022	0.089	–	0.052	–0.066	–
	(9.597)	(–0.798)	(3.766)	–	(1.924)	(–2.542)	–
Molecule Age (ln)	–0.184	–0.150	–0.216	–0.443	–0.387	–0.690	–0.354
	(–3.660)	(–2.056)	(–2.665)	(–5.219)	(–4.863)	(–6.906)	(–3.953)
Number of Forms (ln)	0.273	–	–	–0.170	–	–	–0.145
	(6.778)	–	–	(–1.558)	–	–	(–1.451)
Global (ln)	0.430	–0.241	–0.341	–0.645	–0.820	–0.617	–
	(5.163)	(–1.493)	(–2.016)	(–3.170)	(–4.102)	(–3.589)	–
Competition							
Pack Size (ln)	–0.705	–0.088	0.180	–	–	–	0.106
	(–29.931)	(–1.609)	(3.358)	–	–	–	(1.898)
Generic Competitors (ln)	–0.567	0.097	0.231	0.645	0.756	0.674	0.322
	(–14.804)	(1.110)	(3.391)	(6.369)	(9.049)	(9.100)	(3.188)
Therapeutic Substitute Molecules (ln)	0.069	–	–0.279	–0.216	–0.188	–0.144	–0.200
	(1.326)	–	(–3.118)	(–2.189)	(–2.135)	(–1.616)	(–2.137)
Therapeutic Substitute Molecule Entry Lag (ln)	–0.037	–	0.074	0.041	0.037	0.057	0.056
	(–2.097)	–	(2.286)	(1.157)	(1.110)	(1.591)	(1.617)

Table 4 **Molecule-level regressions:** *continued*

Variable	US	Canada	Germany	France	Italy	Japan	UK
Therapeutic categories							
A	–0.736	–	–	0.704	0.694	0.572	0.237
	(–7.887)	–	–	(3.719)	(3.792)	(3.025)	(1.305)
B	–0.293	–	0.272	0.555	0.510	0.403	–
	(–1.773)	–	(0.851)	(1.744)	(1.637)	(1.216)	–
D	–0.965	–	0.486	0.704	0.910	–	0.316
	(–9.617)	–	(2.562)	(3.443)	(4.258)	–	(1.603)
G	0.275	–0.361	–0.609	–	–	–0.348	–
	(2.423)	(–1.481)	(–2.674)	–	–	(–1.314)	–
H	–0.179	–	0.593	0.600	–	–	–
	(–1.265)	–	(1.851)	(1.743)	–	–	–
J	0.611	–0.530	–	–0.445	–	–	–
	(6.754)	(–2.626)	–	(–2.211)	–	–	–
L	0.742	–	0.436	–	–	–	–
	(6.184)	–	(1.617)	–	–	–	–
M	0.021	–	–0.579	–	–	–0.292	–
	(0.205)	–	(–2.607)	–	–	(–1.184)	–
N	0.216	–0.535	–0.623	–0.468	–0.304	–0.550	–0.401
	(1.794)	(–3.165)	(–3.470)	(–2.366)	(–1.595)	(–2.910)	(–2.093)
P	–0.234	–0.448	–0.474	–	–	–1.377	–1.077
	(–1.027)	(–0.954)	(–1.109)	–	–	(–1.334)	(–2.535)
R	–0.290	–	–	0.351	0.389	–	0.237
	(–2.738)	–	–	(1.449)	(1.575)	–	(1.037)
S	–2.230	–0.564	–	–	0.482	–	–
	(–17.798)	(–2.064)	–	–	(1.597)	–	–
N=2,987 Adjusted R^2=0.6224							

Note:
t>1.960 implies significance with p<0.05.

Quality

Price is increasing in **Strength**, as expected if therapeutic value increases with strength.

Price is independent of **Number of Forms** in the US and Canada, whereas for other countries, the average price increases with number of forms and this effect is greatest in Japan. This is consistent with the hypothesis that introducing line extensions is a strategy to obtain a higher price in countries where regulation drives down prices over the life-cycle as in Japan, where price decline with molecule age is most severe (Danzon and Kim, 1996).

Price is negatively related to **Molecule Age** for most countries, consistent with the hypothesis that newer molecules are on average of higher relative quality, hence receive higher prices, and with regulatory restrictions on price increases in most countries. However, there are significant differences across countries in the price-Age relationship, which are consistent with differences in regulatory and competitive environments. For the US, the price-Molecule Age relationship is insignificant in the product level analysis, which plausibly reflects the tendency for competitive generic prices to approximate the marginal cost of production, which may be unrelated to the drug's therapeutic value, and the predominance of generics in this sample. (For the molecule-level analysis in Table 4, US prices are lower for older Molecule Age.) The Molecule Age elasticity is most negative (–0.69 or greater) for France, Italy and Japan, which have the strictest price regulation.

Note that to estimate the full effect of age on a product's price in this analysis requires combining the effect of its Molecule Age, its Therapeutic Substitute Molecule Entry Lag (relative to the first molecule in the class) and its product-specific Generic Entry Lag relative to the first product in that molecule. Since the Therapeutic Substitute Molecule Entry Lag and Generic Entry Lag coefficients are significantly more negative for the US than for other countries, the net effect of age for, say, a late generic entrant in a crowded therapeutic category, may imply a very low price. This decomposition of the overall age effect on product prices indicates that competition is the more potent force in the unregulated US market,

whereas regulation is the dominant effect in strictly regulated markets, and the moderately regulated markets are in between.

Many of the ATC **therapeutic category** dummies are significant at conventional levels relative to cardiovasculars (the omitted category), and some country-ATC interaction terms are significant. These findings imply that therapeutic category influences prices, after controlling for competition and the quality measures used here, and that these effects differ across countries, due to such factors as medical norms, insurance, regulation and the OTC share of the market.

Competition

Product prices are significantly negatively related to number of **Generic Competitors** in less regulated markets (the US, Germany, the UK, Canada), but not in strictly regulated markets (France, Italy and Japan). The elasticity estimates imply that doubling the number of Ggeneric Competitors reduces the average product price by 50 percent in the US, other things equal; 42 percent for Germany; for the UK 36 percent; and Canada 25 percent. All of these countries encourage price competition between generics through some form of reference pricing for multisource drugs. Recall that for the UK these data may underestimate the effect of generic competition because they do not reflect discounts to pharmacists, which were large in 1992 (see above) and probably greatest for compounds with multiple generic suppliers. By contrast, average price is positively related to the number of Generic Competitors in Italy (+5 percent), with a negligibly small negative effect in Japan (–6 percent) and France (–16 percent).

In France and Italy, the absence of price competitive effects of generics plausibly reflects the lack of incentives for price sensitivity on the part of patients, physicians or pharmacists in 1992.[41] For Japan, physicians are sensitive to the margin between reimbursement and product price, but this is often higher for newer, higher-priced products

41 Co-payments have since been increased in Italy and have significantly affected demand (see Anessi, 1997).

(Ikegami et al., 1998). This evidence of lack of generic competition in France, Italy and Japan is also consistent with other evidence that multisource products in these countries are disproportionately either licensed co-marketers with little incentive to compete on price, or new forms of old molecules that are introduced to obtain a higher regulated price when prices of older forms are low. Some of these new versions of old molecules may offer real quality improvements, such as a delayed release form. However, such quality improvements occur in all countries. The difference is that in countries that promote price competition, the price-increasing effect of new formulations is dominated by the price-decreasing effect of competitive generics, whereas the reverse is true in the highly regulated markets of France, Italy and Japan.

As further evidence on this, the negative elasticity of price with respect to **Generic Entry Lag** (–0.10) in the US implies that successive generic entrants receive lower prices than prior entrants. For Canada and Germany price differentials based on time of entry are still negative but smaller. For France, Italy, Japan the later entrants appear to receive positive price premiums, which is consistent with expected regulatory effects in these countries. For the UK, these data appear to show no evidence of price reductions by successive generic entrants. However, as noted earlier, these IMS data do not reflect manufacturer discounts off list prices, which may be relatively large for later entrants trying to gain market share. In fact the UK has relatively few generic entrants (mean Generic Competitors per molecule is 2.3 in the UK versus 6.6 in Germany and 11.1 in the US) and relatively few late generic entrants (mean Generic Entry Lag is 44 months in the UK versus 117 months in the US, see Table 2).

These cross-national differences in the effects of Generic Competitors cannot be attributed to reverse causation (if generic entry responds to expected prices which are positively correlated with observed prices) because this potential bias exists in all countries. Indeed, if entry response to expected high prices does bias downward our estimates of competitive effects, this downward bias is probably greatest in less regulated markets. In that case, these estimates may

understate the true extent to which regulation undermines price competition between generically equivalent drugs.

The elasticity of unit price with respect to **Pack Size** for the US is –0.95, whereas the elasticities for all other countries are at least one third lower, except Canada. This implies more significant volume discounts to pharmacists for bulk purchasing in the US than in other countries, which is consistent with highly price sensitive pharmacy purchasers in the US.[42] Other analysis suggests that these extreme volume discounts in the US are concentrated in generics, which is plausible since these are the products for which pharmacists are price-sensitive.[43] In Germany, France and Italy the weak volume discounts are not surprising given unit pack dispensing requirements and other impediments to price competition in retail pharmacy, which undermine incentives for competition at the manufacturer price level through discounts. These findings suggest that unit pack dispensing and other barriers to competition in retail pharmacy lead to significant foregone pack size economies. There may also be other costs not estimated here, associated with providing a greater number of different pack sizes and possibly more waste if the available packs are larger than required for some individual prescriptions. Volume discounts for large packs also appear to be small in the UK, relative to the US and Canada, but again this estimate may be biased if the discounts that are not reflected in these data are largest for large packs.

The evidence of price competition between **Therapeutic Substitute Molecules** is weaker than between Generic Competitors, which is partially expected since molecules in the same therapeutic

42 Note that mean pack size is larger in Canada and Japan than the US, hence the greater US price-pack size discounts cannot be attributed to larger average pack size in the US.

43 For molecules aged 15 years or younger, which have fewer generics, the pack size elasticity for the US is only –0.35 compared to –0.95 for the full sample. For other countries, the pack size elasticities are similar for both samples, indicating less difference between generics and originator drugs. The molecule level regressions in Table 4 provide further evidence that the extreme pack size discounts in this product level sample reflect the large number of generics.

class may be much less substitutable than generic equivalents. Number of Therapeutic Substitute Molecules has a small positive association with product price in the US and Canada, and a significant negative differential but negligibly small net effect for Japan and Italy.

However the price elasticity with respect to **Products Per Therapeutic Substitute Molecule** is significantly negative (-0.22) for the US, with no significant difference for the UK, Germany, Canada and France, a more negative effect for Japan (-0.46) and a net positive effect in Italy (0.33). Thus generic competition appears to enhance competition between therapeutic substitute molecules, in addition to the direct effects of within-molecule competition by generic competitors, except in Italy. This general conclusion is robust to changes in specification (see Danzon and Chao, 1999a).

Although number of molecules in the therapeutic class does not appear to have a competitive effect on price, successive molecules in a class do receive lower prices, which is consistent with price competition. The estimates imply that, on average for this sample of global molecules, successive entrants to a therapeutic class entered at a discount of 3 percent per month of lag relative to the first entrant in the class. Differences across countries are small and not highly significant except for a small positive differential for the UK. Less negative effects for **Therapeutic Substitute Entry Lag** than for **Generic Entry Lag** is not surprising, since later molecules in a class can provide real improvements over the first entrant, whereas generic imitators offer little or no improvement over the originator product.

This evidence suggesting apparent lack of competition based on number of Therapeutic Substitute Molecules is contrary to other evidence[44] and may be misleading, reflecting several limitations of our

44 Boston Consulting Group (1993) reports that later entrants to a therapeutic category entered at an average 14 percent discount in list price relative to the market leader, and the mean discount in more crowded therapeutic categories was over 30 percent. Ellison et al. (1997) find fairly high cross-price elasticities between generic substitutes, and smaller but sometimes significant elasticities between therapeutic substitutes in their study of cephalosporins in 1985-1991.

data. First, reverse causation may bias upward our estimates of competition between therapeutic substitutes if, as discussed earlier, entry of substitute molecules is positively related to expected and actual prices. Second, if promotional investment by originator products expands the total market rather than simply eroding each other's sales, this unobserved promotion effect is likely to be positively correlated with number of molecules in a class, leading to underestimation of the true effect of therapeutic competitors on price. Third, the US data used here do not capture competition through discounts to managed care purchasers, which is a major channel for therapeutic competition.[45] Moreover, these 1992 data would almost certainly understate therapeutic competition in the late 1990s, as therapeutic categories have become more crowded, managed care has spread in the US, and the UK and Germany have adopted physician incentive programmes to induce more price sensitive prescribing.

In summary, there is clear evidence of competition between therapeutic substitutes in the form of lower prices for successive entrants. Controlling for this, the number of molecules in a class does not appear to add a net competitive effect but this estimate may be biased, because these data are inadequate to control for the reverse effect of prices on entry; for demand-shifting promotional investment; and for competitive discounts off list prices in the US and the UK. The results for Italy and Japan are of particular interest because these are two countries where strict regulation depresses prices most severely over the lifecycle, with real prices falling at –6.8 percent per year for Japan and –4.3 percent for Italy (Danzon and Kim, 1996). The estimates here suggest that, relative to the US and other less regulated countries, these countries have more negative price effects from Therapeutic Substitute Molecules than from Generic Competitors, although generics are much closer medical substitutes. The more negative effects for Therapeutic Substitute Molecules in heavily regulated countries

45 The UK data omit discounts to pharmacists, but these discounts are expected to be concentrated on multisource products for which pharmacists are price sensitive.

may reflect the tendency for regulators to base prices for new compounds on the prices of established products that are already on the market, which have declined in real terms. The positive differentials for generic products could reflect reverse causation: that only those generics are introduced that are expected to obtain a higher price.

In absolute terms, the net effect of competition is not significantly different from zero for both Generic Products and Therapeutic Substitute Molecules in Japan and Italy. Thus the net effect is that these strict regulatory systems appear to provide indistinguishable price incentives for investment in innovative and imitative R&D. These findings are thus consistent with the evidence (Barral, 1995) that these two countries have produced a large number of minor new products but few molecules that are sufficiently innovative to become global products.

7 MOLECULE-LEVEL PRICE ANALYSIS

The analysis so far has been at the level of the individual product, which effectively gives more weight to molecules with more products. These estimates thus tend to reflect the experience of multisource molecules with numerous generics. In Table 4, the molecule rather than the product is the unit of observation, which may be more intuitive. Price per unit for the molecule is the weighted average of prices per unit for all products in the molecule. Similar weighted averages are used for other variables, such as Strength, which differ across products in a molecule. The sample includes all molecules that match bilaterally with the US, as in the price indexes in Table 1.

The structure of this molecule-level analysis follows that of the product-level analysis, measuring the effect on molecule price (weighted average over all products) of quality characteristics, and the number of generic and therapeutic competitors. The main difference is that, since the sample of bilaterally matched molecules is not the same for all countries, a measure of Global penetration is included, defined as the number of these seven countries in which each molecule is available (in logs). Global penetration has been used in previous studies as a measure of therapeutic value.[46] The implicit assumption is that, having incurred the fixed costs of drug development, a manufacturer will market a drug in any country in which its expected revenue exceeds the marginal cost of launch. Differences across molecules in Global penetration thus reflect differences in expected therapeutic value, assuming that expected revenue reflects expected value perceived by consumers and/or physicians, and that the costs of launch are similar across products.

The results for the molecule price equations in Table 4 are generally similar to those for the product level equations in Table 3. Thus effects of product and market characteristics on drug prices are generally robust, whether the focus is on molecule or product level prices. The discussion here focuses on differences between the molecule and product level results.

46 Barral (1995) shows that global penetration is positively related to medical measures of therapeutic value. See also Thomas (1996).

7.1 Quality

The main new finding in these molecule-level results is for **Global** penetration. In the US, the UK, Canada (and Germany to a lesser extent), prices are higher for drugs that have achieved broad global penetration, consistent with the joint hypothesis that global penetration is an indicator of (unobserved) broad therapeutic value and that more valuable drugs obtain higher prices in the absence of strict price regulation. The US elasticity of 0.43 implies that a drug that is present in, say, six of these major markets would obtain a 43 percent higher price than a drug that has only diffused to three of these markets, other things equal. Of course, other things are not equal, because the drug that diffuses to six rather than three markets is likely to do so because it is a more valuable drug. It is this unmeasured therapeutic value that the Global penetration variable seeks to capture and that is the reason for the higher price. By contrast, for the three most strictly regulated countries (France, Italy and Japan) prices are actually lower for drugs with high Global penetration than for more narrowly diffused products, with a negative price elasticity with respect to Global for France (-0.22), Italy (-0.39) and Japan (-0.19). These results do not permit us to say whether the higher relative prices for global drugs in the no/low regulation countries are too high or too low. However, we can conclude that regulation reduces the prices of global drugs disproportionately relative to more minor drugs, compared to less regulated markets. Analysis of the reasons for this difference is an important topic for future research.

Molecule price is negatively related to **Molecule Age** in less regulated markets, consistent with the hypothesis that newer molecules offer improved therapeutic quality. However, strictly regulated markets have significantly more negative Molecule Age effects, greatest for Japan, followed by France, Italy and the UK. The ranking of these Molecule Age effects – more negative for France, Italy and the UK than for Germany and Canada – is consistent with the fact that regulatory systems in the first three countries do not permit post-launch inflation adjustments, such that real prices fall over the molecule's life,

whereas Canada permits increases in line with the consumer price index. The negative Molecule Age effect in Germany may reflect the reference price system introduced in 1989, which targeted older molecules. The extremely negative age effect in Japan reflects the interaction between competition and regulation, and is consistent with other studies (Danzon and Kim, 1996; Ikegami et al., 1998). Note that these are pure age effects, controlling for the increase in generic and therapeutic competition that occurs with molecule age.

7.2 Competition

The US elasticity of molecule price with respect to number of **Generic Competitors** is –0.57, consistent with the findings for the product level analysis and with other evidence (Grabowski and Vernon, 1992; Ellison et al., 1997). Generic Competitors also have a negative but smaller effect on molecule price in Canada (–0.47), Germany (–0.34) and the UK (–0.25). However, the net effect of generic equivalents on molecule price is positive for France (0.08), Italy (0.19) and Japan (0.11), consistent with the product level results. This is also consistent with other evidence that multisource suppliers are typically licensed co-marketers or firms that enter to obtain a higher regulated price, rather than true generics that compete for market share on the basis of price as in less regulated markets.

The evidence for therapeutic competition is similar to the previous product-level analysis. Number of **Therapeutic Substitute Molecules** appears to have no significant effect on price in the US and Canada. On the other hand, the significant negative effect of **Therapeutic Substitute Molecule Entry Lag** implies that successive entrants to a class enter at lower prices, with a 3.7 percent per month price reduction for each month of entry lag after the first molecule in a class in the US and Canada. These estimates of therapeutic competition are almost certainly biased by the lack of data on discounts to managed care, in addition to inability to control for promotional expense and reverse causation, as discussed earlier.

Number of Therapeutic Substitute Molecules appears to have small but significant negative effects on price in France, Italy, Germany and the UK, but the interpretation is unclear. Since France and Italy show no evidence of competitive effects of generics, which are closer substitutes, the most plausible explanation of the negative Therapeutic Substitute Molecules coefficients is that regulators use a form of implicit reference pricing, setting prices for new products based on prices of established products, which are inversely related to age due to a regulatory bar on inflation adjustments. Thus this implicit price setting mechanism would result in the observed inverse relation between price and number of Therapeutic Substitute Molecules in a class. In most countries the price reduction by successive entrants is less than in the US and Canada, which partially offsets the weaker effect of number of Therapeutic Substitute Molecules in these two countries.

7.3 Quantity equations

The analysis so far has examined the effects of number of competitors on price, ignoring quantity. Another standard measure of competitiveness is the price elasticity of demand, which measures the percentage change in quantity sold in response to a percentage change in price. Measuring demand elasticities for outpatient drugs is difficult because, for a given medical condition, demand may depend on patients, physicians, pharmacists and third party payers, each of whom may face different implicit prices and financial incentives. The estimates here are demand elasticities with respect to manufacturer-level prices, which are relevant if at-risk physicians, pharmacists and payers are key decision-makers. By contrast, most prior studies estimate more conventional consumer demand elasticities with respect to patient co-payment, as discussed below.

Table 5 reports estimates of price elasticities using these data, from equations in which the dependent variable is the (log) quantity of standard units sold per capita and the main explanatory variable is the

Table 5 **Second stage of molecule-level two stage least squares regressions: bilateral molecules – 1992**
Dependent variable: log of standard units per capita (t statistics in parentheses).

	US	Canada	Germany	France	Italy	Japan	UK
Intercept							
Coefficient	–10.532	0.744	0.381	1.745	1.923	0.498	–0.059
t	(–42.295)	(1.848)	(0.966)	(3.914)	(4.585)	(1.195)	(–0.140)
Log price per SU (LPSU)							
Coefficient	–1.294	–0.047	–0.130	0.625	0.932	0.532	0.383
t	(–16.556)	(–0.355)	(–0.831)	(4.250)	(6.312)	(3.961)	(2.508)

Notes:
Coefficients for LPSU are price elasticities of demand for the molecule.
Coefficients for non-US countries are differentials relative to the US.
t>1.960 implies significance with p<0.05.

price per standard unit for the molecule.[47] Indicator variables for therapeutic category are also included in the regression (not reported in Table 5). The estimated price elasticities are: –1.29 for the US, with no significant differences in Canada and Germany, and –0.91 for the UK. The estimated elasticities are significantly smaller in countries with strict regulation: Japan (–0.76), France (–0.67) and Italy (–0.36). This is further evidence consistent with the hypothesis that regulation undermines competition.

These elasticity estimates are larger (in absolute value) than most prior estimates, and several factors may contribute to this. First, several previous studies (for example, Leibowitz et al., 1985) are based on

47 The structural model assumes that the firm sets price, given product characteristics, regulatory and competitive factors, and that quantity depends on price and therapeutic category. The estimation therefore uses two stage least squares, in which price is estimated in the first stage equation using the specification in Table 4 with full interaction.

aggregate expenditures, hence are expected to show less elastic demand than the measures here which also reflect between-drug substitution. Second, most prior studies estimate demand response to out-of-pocket price to consumers, whereas our manufacturer level prices are only roughly proportional to consumer prices, depending on proportionality of distribution margins, taxes and co-payment rates. Rough proportionality between these manufacturer-level prices and out-of-pocket prices to consumers may hold approximately for the US at this time and some consumers in Canada, but not for the other countries. Thus if price sensitivity were driven solely by consumer co-payments, then small or zero quantity elasticities with respect to these manufacturer prices might be expected. Third, to the extent that demand decisions reflect physician incentives, through indicative drug budgets, prescription monitoring by third party payers etc., the full price is the relevant measure, not the consumer's co-payment. Fourth, in countries with regulatory systems that require price reductions if volume exceeds target levels, this imposes a spurious inverse relation between quantity and price that would bias up (in absolute value) the estimate of the price elasticity due to competition.[48] Sorting out the contributions of these factors to the observed elasticities with respect to manufacturer price is an important topic for future research.

48 France applied a total revenue constraint 'envelope globale' to certain products. The UK Pharmaceutical Price Regulation Scheme (PPRS) profit constraint implies a portfolio revenue constraint for each firm, given its capital base. For Italy (the Emilia Romagna region) for 1989-1993, Anessi (1997) estimates own price elasticities for individual cardiovascular products with respect to out-of-pocket prices to be –0.26 to –0.36.

8 CONCLUSIONS

The conventional view, that drug prices are much higher in the US than in other countries, has been based on biased studies that use small, unrepresentative samples and inappropriate methods. The indexes here use accepted price index methods applied to comprehensive data for all matching compounds, including generics and licensed products as well as brand originators. These indexes show smaller cross-national differences in the average cost of drug therapy, at manufacturer prices, than implied by previous studies. With these comprehensive data and appropriate methods, the UK has among the lowest prices of the seven countries in 1992, even ignoring the unmeasured pharmacy discounts, and the lowest per capita volumes.

However, this analysis has also demonstrated the sensitivity of cross-national price comparisons to the methods used, including sample selection, weights, unit of measure, and index. Base-weighted (Laspeyres) indexes consistently exceed comparison-weighted (Paasche) indexes, by up to 50 percentage points, due to dispersion of relative prices and quantity across products, regardless of the country used as base. Thus selecting appropriate weights poses a major challenge for multilateral price comparisons that are of interest in the EU. The safe conclusion is that results will be systematically biased if the comparison is based on a sample that is unrepresentative with respect to either age of molecules, extent of globalization or generics, which should be included, appropriately weighted. Restricting the sample to products available in all countries entails severe reduction and bias in the sample.

This study has also demonstrated that generic competition significantly reduces average prices in the US, the UK, Germany and Canada where the structure of reimbursement encourages generic competition. For the strictly regulated markets of France, Italy and Japan, prices are positively related to the number of generic competitors, plausibly so because generic equivalents in these markets are predominantly licensed co-marketers, not price competitive true generics. Incentives for generic entry are weak where the structure of reimbursement and pharmacy regulation make demand insensitive to price

and where regulated originator prices are very low by the time of patent expiry. The competitive pharmacy environment tends to reduce prices in the US and Canada, relative to other countries, due to larger average pack size and greater volume discounts on large packs. Failure to find similar effects in the UK, which has a similar competitive pharmacy environment, may reflect the inability of these data to capture pharmacy discounts. Thus the estimates here do not show the full effects of generic competition in the UK, including volume discounts. In Germany, France and Italy, which have the most heavily regulated retail pharmacy including unit pack dispensing requirements, there appear to be significant foregone savings due to smaller pack sizes and less volume discounting.

For therapeutic substitutes, successive entrants enter at lower prices, which is consistent with competition subject to first mover advantage. The lack of evidence of competitive effects from the number of therapeutic substitutes appears contrary to expectations. However, these estimates are almost certainly biased by reverse causation (more products in categories with high demand), and by lack of data on promotional expense and discounts (particularly for the US). The main factors that tend to reduce drug prices in most other countries relative to the US are lower prices for older molecules and lower prices for globally-diffused drugs, which is a proxy for therapeutic value. France, Italy and Japan, which have the strictest price regulation, give relatively low prices for globally-diffused products and depress prices most over the product life-cycle.

It might appear from this analysis that regulatory pressure on prices over the product life-cycle achieves roughly the same effect as generic competition in less regulated markets. However, it would be incorrect to conclude that the net effect on social welfare is the same. These findings suggest that regulation of both manufacturer prices and of retail pharmacy undermines competition in the off-patent sector and that the potential budgetary savings from post-patent competition are not fully realised in countries with strict regulatory systems. Moreover, the benefits of competition in retail pharmacy extend

beyond the level of prices for medicines included in this analysis, and may include competition on prices of OTC and consumer products sold through retail pharmacy, if permitted, as well as convenience and other non-price benefits of competition.

This analysis also has implications for the use of international price comparisons to regulate domestic prices. The conclusions depend on the objectives, but in any case there are no simple answers. One possible objective of such external referencing is to achieve an average domestic price level that is comparable to the average price level in the comparator countries. This objective will not be achieved by comparing prices of individual new branded products at launch, on a product-by-product basis, because post-launch price paths diverge due to country-specific regulatory and competitive environments. A theoretically more appropriate comparison would use the discounted present value of expected prices over the molecule life-cycle. Most countries with external referencing use as their benchmark the unweighted median, mean or minimum price in the market basket drawn from the comparator countries. We have shown that such unweighted measures are extremely sensitive to the sample selected, particularly if the comparison is based on a single pack of a single manufacturer. However, although weighting would in theory reduce instability, there are no obvious appropriate weights for such multilateral comparisons of prices of a single product. If different countries apply external referencing to the same products but use different benchmark countries or different weights, then each country's perspective on the same distribution of relative prices will yield a different conclusion about their relative price level.

A second possible regulatory objective is to set price differences across countries to achieve appropriate per capita contributions to the joint costs of pharmaceutical R&D, based on Ramsey pricing principles (Danzon, 1997b). For this objective, the appropriate comparison is the discounted present value of expected revenue per capita over the originator product's life-cycle, which takes into account cross-national differences in per capita quantity as well as price over the life-cycle, for

example, due to different post-patent generic penetration rates across countries.[49] Further research is necessary on both theory and practical empirical measures, if international comparisons are to be used to achieve the desired price levels for consumers and returns for manufacturers.

49 Danzon and Kim (1996).

REFERENCES

Alexander D, Flynn JE and Linkins LA (1994). 'Estimates of the Demand for Ethical Pharmaceutical Drugs across Countries and Time', *Applied Economics,* 26(8), 821-26.

Anessi EP (1997). *The Effect of User Charges on the Utilization of Prescription Medicines in the Italian National Health Service,* unpublished doctoral dissertation, Philadelphia: The Wharton School, University of Pennsylvania.

Baines DL, Tolley KH and Whynes DK (1997). *Prescribing Budgets and Fundholding in General Practice,* London: Office of Health Economics.

Barral PE (1995). *Twenty Years of Pharmaceutical Research Results Throughout the World (1975-1994),* Paris: Fondation Rhone-Poulenc Santé.

Berndt ER, Griliches Z and Rosett JG (1993). 'Auditing the Producer Price Index: Micro Evidence from Prescription Pharmaceutical Preparations', *Journal of Economics and Business Statistics* 11(3): 251-64.

Boston Consulting Group (BCG) (1993). *The Changing Environment for US Pharmaceuticals,* New York: Boston Consulting Group.

Bureau Européen des Unions de Consommateurs (BEUC) (1989a). *Drug Prices and Drug Legislation in Europe,* Brussels: Belgian Consumers' Association, March 1989.

Bureau Européen des Unions de Consommateurs (BEUC) (1989b). Testimony before the US Senate Special Committee on Aging. Oral testimony, November 16, 1989, Brussels: Belgian Consumers' Association.

Burstall ML (1991). 'Europe after 1992: Implications for Pharmaceuticals', *Health Affairs,* Fall, 157-171.

Caves RE, Whinston MD and Hurwitz MA (1991). 'Patent Expiration, Entry, and Competition in the US Pharmaceutical Industry', *Brookings Papers on Economic Activity: Microeconomics,* 1-66.

Danzon PM (1996). 'Defined Daily Doses for Pharmaceuticals', Working Paper, Philadelphia: University of Pennsylvania, The Wharton School.

Danzon PM (1997a). *Price Regulation in the Pharmaceutical Industry: National vs. Global Interests,* Washington, DC: The American Enterprise Institute Press.

Danzon PM (1997b). 'Price Discrimination for Pharmaceuticals: Welfare Effects in the US and the EU' *International Journal of the Economics of Business,* 4(3): 301-322.

Danzon PM (1997c). *Trade and Price Differentials for Pharmaceuticals: Policy Options,* London: Office of Health Economics.

Danzon PM (1998). 'Competition in the Off-Patent Sector: the US Experience', *Pharma Pricing Review,* 3 (3): 46-50.

Danzon PM and Chao L-W (2000a). 'Cross-National Price Differences for Pharmaceuticals: How Large and Why?' *Journal of Health Economics,* 19(2): 141-290.

Danzon PM and Chao L-W (2000b). 'Does Regulation Drive out Competition in Markets for Pharmaceuticals?' *Journal of Law and Economics* (forthcoming).

Danzon PM and Kim JD (1996). 'Price Indexes for Pharmaceuticals: How Accurate are International Comparisons?' Working Paper, Philadelphia: University of Pennsylvania, The Wharton School.

Danzon PM and Kim JD (1998). 'International Price Comparisons for Pharmaceuticals: Measurement and Policy Issues', *Pharmacoeconomics,* 14, Suppl.1: 115-128.

Danzon PM and Liu H (1998). 'Reference Pricing and Physician Drug Budgets: the German Experience in Controlling Pharmaceutical Expenditures', Working Paper, Philadelphia: University of Pennsylvania, The Wharton School.

Department of Health (DOH) (1992, 1993). *Pharmacist Discount Enquiry,* London: Department of Health.

Department of Health (DOH) (1997). *Pharmaceutical Price Regulation Scheme: Second Report to Parliament,* London: Department of Health.

Dranove D and Meltzer D (1994), 'Do Important Drugs Reach the Market Sooner?' *Rand Journal of Economics,* 25(3), 402-23.

Ellison SF, Cockburn I, Griliches Z and Hausman J (1997). 'Characteristics of Demand for Pharmaceutical Products: an Examination of Four Cephalosporins.' *Rand Journal of Economics,* 28(3):426-446.

European Commission (1998). 'Commission Communication on the Single Market in Pharmaceuticals', Brussels: European Commission Directorate General III COM (1998) 588.

Grabowski HG and Vernon JM (1992). 'Brand Loyalty, Entry and Price Competition in Pharmaceuticals after the 1984 Act', *Journal of Law and Economics,* 35(2), 331-50.

Grabowski HG and Vernon JM (1996). 'Prospects for Returns to Pharmaceutical R&D under Health Care Reform', in Helms RB (ed.), *Competitive Strategies in the Pharmaceutical Industry,* Washington, DC: The American Enterprise Institute Press, 194-207.

Griliches Z and Cockburn I (1994). 'Generics and New Goods in Pharmaceutical Price Indexes', *American Economic Review,* 84(5), 1213-32.

Hillman AL, Pauly MV, Escarce JJ, Ripley K, Gaynor M, Clouse J and Ross R (1999). 'Financial Incentives and Drug Spending in Managed Care', *Health Affairs,* 18(2): 189-200.

Ikegami N, Ikeda S and Kawai H (1998). 'Why Medical Care Costs in Japan Have Increased Despite Declining Prices for Pharmaceuticals', *Pharmacoeconomics,* 14, Suppl. 1: 97-105.

Leibowitz A, Manning W and Newhouse JP (1985). 'The Demand for Prescription Drugs as a Function of Cost-Sharing', *Social Science and Medicine,* 21(10): 1063-1069.

OECD (1993). *PPP-GK Results, PPP-GK Results 1990,* Washington D.C.: OECD.

Pharma Pricing Review (1998) 4 (1).

Reekie WD (1996). *Medicines Prices and Innovations,* London: Institute of Economic Affairs, Health and Welfare Unit.

Reekie WD (1997). 'Cartels, Spontaneous Price Discrimination and International Pharmacy Retailing', *International Journal of the Economics of Business,* 4 (3): 279-286.

REMIT Consultants (1991), *Cost Containment in the European Pharmaceutical Market: New Approaches,* London.

Scherer FM (1997). 'How US Antitrust Can Go Astray: the Brand Name Prescription Drug Litigation', *International Journal of the Economics of Business,* 4 (3): 239-256.

Schoffski O (1996). 'Consequences of Implementing a Drug Budget for Office-Based Physicians in Germany', *PharmacoEconomics,* 10(2): 37-47.

Thomas LG (1996). 'Industrial Policy and International Competitiveness in the Pharmaceutical Industry', in Helms RB (ed.), *Competitive Strategies in the Pharmaceutical Industry,* Washington, DC: The American Enterprise Institute Press, 107-129.

Towse A and Leighton T (1999). 'The Changing Nature of NCE Pricing of Second and Subsequent Entrants', in Sussex J and Marchant N (eds.), *Risk and Return in the Pharmaceutical Industry,* London: Office of Health Economics.

Ulrich V and Wille E (1996). 'Health Care Reform and Expenditure on Drugs: The German Situation', *PharmacoEconomics,* 10 Suppl. 2: 81-88.

US Congressional Budget Office (CBO) (1996). 'How the Medicaid Rebate on Prescription Drugs Affects Pricing in the Pharmaceutical Industry', January 1996.

US General Accounting Office (GAO) (1992). 'Prescription Drugs: Companies Typically Charge More in the United States than in Canada', Washington DC: GAO/HRD-92-110.

US General Accounting Office (GAO) (1994a). 'Prescription Drugs: Companies Typically Charge More in the United States than in the United Kingdom', Washington DC: GAO/HEHS-94-29.

US General Accounting Office (GAO) (1994b). 'Medicaid: Changes in Best Price for Outpatient Drugs Purchased by HMOs and Hospitals', Washington DC: GAO/HEHS-94-194FS.

US Government Printing Office (1993). *Health Security Act,* HR 3600 IH/S 1757.

US House of Representatives (1999) (H.R. 644). Prescription Drug Fairness for Seniors Act of 1999.

US House of Representatives, Committee on Government Reform and Oversight. (1998). Minority Staff Report, 'Prescription Drug Pricing in the United States: Drug Companies Profit at the Expense of Older Americans.' September 25, 1998.

Verband Forschender Arzneimittelhersteller EV (VFA) (1997). *Statistics '97: the Pharmaceutical Industry in Germany,* Bonn.

Wardell WM and Lasagna L (1975). *Regulation and Drug Development,* Washington, DC: American Enterprise Institute Press.

APPENDIX: BIAS IN PREVIOUS STUDIES OF PRICE DIFFERENCES

Comparison with GAO

Table A1 illustrates the contribution of samples and methods to the difference between our estimates and those in GAO (1992, 1994a), to the extent possible with our data. The GAO US-Canada comparison (GAO, 1992) reported the ratio of US price to Canadian price for a market basket consisting of one pack for each of 121 branded products. The GAO US-UK comparison (GAO, 1994a) used one pack for each of 77 products and reported a Paasche index for the UK, applying US weights to US/UK price relatives, which is essentially the reciprocal of the Laspeyres index with US as base. The sample in our IMS data only has 85 of the GAO's sample of 121 drugs for Canada, and 56 of the GAO's 77 drugs for the UK.[50] Our measure of price is a weighted average price per standard unit for all forms/strengths/pack sizes for each product, whereas the GAO US-Canada study used the price per pack and the GAO US-UK study used price per pill based on a single pack.

For the US-Canada comparison, our sub-sample yields estimates similar to the full GAO sample with GAO's index measure: the ratio of US price for the market basket relative to Canadian price (mean of US PSU/mean of Canada PSU) is 1.34 for their full sample of 121 products (column 2 of Table A1a)[51] and 1.31 for our subsample of 85 products (column 3, Table A1a). As a rough indicator of the effect of selecting a single pack, note that this unweighted mean US price/mean Canada price ratio falls from 1.31 to 1.11 when the IMS weighted average price per unit for all forms/strengths/pack sizes (column 4, Table A1a) is substituted for GAO's single pack price (column 3). Column 5, which reports molecule level prices (weighted average over

50 The GAO lists brand name and manufacturer. In our sample, if the same manufacturer could not be matched between two countries, the same brand name product from a sole source producer is substituted, if available. Otherwise, no match was made and the product could not be included.

51 We are unable to explain the difference between our estimate of 1.337 and the 1.32 reported in GAO (1992).

Table A1a **Contribution of sample and index methods to GAO price comparisons – Canada-US price comparisons using GAO list of drugs**

	GAO full sample products (GAO prices)	GAO-IMS matched products (GAO prices)	GAO-IMS matched products (IMS prices)	GAO-IMS matched molecules (IMS prices)	IMS full sample molecules (IMS prices)
Laspeyres price index (US weights)	–	–	0.791	0.753	1.021
Paasche price index (US weights)	–	–	0.768	0.717	0.447
Paasche price index (Canada weights)	–	–	1.263	1.327	0.979
Laspeyres quantity index (US weights)[a]	–	–	0.836	1.127	1.989
Paasche quantity index (Canada weights)[a]	–	–	0.811	1.073	0.871
Population ratio (Canada/US)	–	–	0.103	0.103	0.103
Paasche index/ Laspeyres index	–	–	0.970	0.952	0.438
Mean of US PSU	45.175	53.347	0.725	0.635	1.542
Mean of Canada PSU	33.782	40.634	0.655	0.504	0.957
Mean of (US PSU/ Canada PSU)	1.766	1.766	1.661	1.668	3.183
Mean of (Canada PSU/ US PSU)	0.746	0.770	0.812	0.831	2.709
Mean of (US PSU)/ Mean of (Canada PSU)	1.337	1.313	1.106	1.260	1.611
Median of (US PSU/ Canada PSU)	1.433	1.355	1.282	1.289	1.196
Median of (Canada PSU/ US PSU)	0.698	0.738	0.781	0.776	0.836
N	121	85	88	77	420

Notes:

a Adjusted for population.

PSU= price per standard unit

Table A1b **Contribution of sample and index methods to GAO price comparisons – UK-US price comparisons using GAO list of drugs**

	GAO full sample products (GAO prices)	GAO-IMS matched products (GAO prices)	GAO-IMS matched products (IMS prices)	GAO-IMS matched molecules (IMS prices)	IMS full sample molecules (IMS prices)
Laspeyres price index (US weights)	–	–	0.698	0.740	0.834
Paasche price index (US weights)	–	–	0.616	0.642	0.560
Paasche price index (UK weights)	1.600[b]	–	1.433	1.352	1.199
Laspeyres quantity index (US weights)[a]	–	–	0.836	0.776	0.957
Paasche quantity index (UK weights)[a]	–	–	0.737	0.674	0.642
Population ratio (UK/US)	–	–	0.219	0.219	0.219
Paasche index/ Laspeyres index	–	–	0.882	0.868	0.671
Mean of US PSU	0.859	0.878	0.811	0.773	2.221
Mean of UK PSU	0.448	0.508	0.594	0.603	1.255
Mean of (US PSU/ UK PSU)	3.462	2.750	2.266	1.943	3.421
Mean of (UK PSU/ US PSU)	0.552	0.583	0.738	0.841	1.191
Mean of (US PSU)/ Mean of (UK PSU)	1.915	1.728	1.367	1.281	1.770
Median of (US PSU/ UK PSU)	2.436	2.218	1.906	1.669	1.795
Median of (UK PSU/ US PSU)	0.411	0.452	0.525	0.600	0.557
N	77	56	57	56	377

Notes:
a Adjusted for population.
b Reported in GAO reports.
PSU= price per standard unit

all products), shows that adding generics to the GAO sample of products has little effect. However, expanding the sample to include all molecules common to both Canada and the US (column 6, Table A1a) changes the Canada-US Laspeyres index from 0.75 for the GAO sub-sample to 1.02 for the full sample of matching molecules. Thus excluding molecules in which generics predominate is one major source of the bias in the GAO comparison. A second major source of bias results from using as an index the ratio of unweighted mean prices. For our full sample, the ratio of unweighted mean prices (mean of US PSU/mean of Canada PSU) is 1.61, whereas the Laspeyres index (US weights) is only 1.02. The bias from using the mean of the price relatives is larger and even the sign is uncertain: the US appears 218 percent higher than Canada when Canada is the base (mean of US PSU/Canada PSU), whereas Canada appears 171 percent higher than the US when US is the base (mean of Canada PSU/US PSU)!

GAO's UK-based Paasche index cannot be replicated in our sample to check the impact of using only 56 of their 77 products, because GAO (1994a) does not report their weights. However, using the 56 GAO products and IMS average product prices and weights yields a UK-based Paasche index of 1.43, compared to 1.60 reported by GAO (Table A1b). Expanding the sample to include all matching molecules (column 6, Table A1b) reduces this index to 1.20, while the ratio of the unweighted means is 1.77 (mean of US PSU/mean of UK PSU). Again, the unweighted mean price relatives show sign reversal, with the US higher or lower than the UK, depending on the base.

Thus the results for the UK, like those for Canada, show that using a sample focused on leading branded products and using an unweighted index can each lead to bias of at least 20 percentage points. Use of a single pack adds additional, smaller bias. The major source of sampling bias appears to be the selection of molecules in which the branded product has a dominant market share, not the exclusion of generics that are available for those molecules in the sample that have generics. However, exclusion of generics would certainly be a more significant factor for comparisons involving countries with very different generic

shares, such as a comparison between France and the US. The upward bias is exacerbated by the use of unweighted means, as in GAO US-Canada, which give undue weight to relatively high-priced products. Comparisons based on unweighted price relatives (as in Minority Staff, 1998) are even more biased and extremely unstable to the point of reversing sign, depending on which country is the base.

Comparison with BEUC (1989)

For their study of drug prices in the then 12 member states of the European Economic Community (EEC), the Belgian Consumers' Association (BEUC, 1989a) drew a sample of the 25 leading prescription drugs, by sales value, in each state in 1987, to which they added any omitted drugs that were in the top 10 by volume (volume unit unspecified). Drugs were matched across countries if they were produced by the same manufacturers or were the sole source product. Generics were explicitly excluded on the grounds that: (1) prices differ between generic products within a country; and (2) single generic products are rarely in the top 25 in terms of sales. Thus substitutability between generic equivalents was ignored. Prices were imputed for missing products – only 78 of the sample of 125 products (62 percent) were available in nine or more of themember states – and where form/pack size did not match across member states.

Most of the analysis focuses on retail prices. The one comparison of manufacturer prices (retail minus an average distribution percentage) reports an index of the unweighted average price for the market basket relative to the EEC-average of 100. Normalising this index relative to its UK value (since the EEC average includes countries that are not in our sample) yields the following: France 0.58, Italy 0.74, Germany 1.127 (based on BEUC, 1989a, Table X). Thus based on this unweighted average of a small sample of brand-only retail prices, the UK appears relatively costly. As discussed previously, our SU indexes for all matching molecules, including generics, show UK prices either similar to or lower than prices in France and Italy for this

period, with precise estimates depending on the weights and price measure used. BEUC (1989b) extended this study to include the US, based on a sample of the 25 products for which they could find a match. The retail price of this market basket of 25 products (unweighted and excluding VAT) showed the US at 1.28 of the UK index, compared to France 0.58, Italy 0.60 and Germany 1.24. These retail price indexes, which include distribution margins, are not strictly comparable to the manufacturer indexes reported here. Nevertheless, the general conclusion appears to hold, that comparisons based on an unweighted average of branded product prices only, excluding generics, tend to yield upward biased estimates of prices for relatively unregulated countries that have large generic shares, notably the US, Germany and the UK, compared to France and Italy, which have strict price regulation and negligible generic shares.

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