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Abstract

We hypothesize that parallel trade of heavily regulated medicines is a form of ‘regulatory arbitrage’ that does not necessarily produce equivalent welfare effects as more ‘common’ forms of arbitrage. This paper empirically documents the latter hypothesis drawing upon a unique dataset that contains source country records of parallel imported medicines to the Netherlands. Hence, it allows estimating precise price differences with each source country/product. The data is from one therapeutic group (statins) that accounts for 5% of the market at the time of study and it faced no generic competition. Hence allows identifying a clean effect of PT determinants. Our findings reveal that parallel imports flows are determined by medicines distribution chain regulation, in addition to product price differences in line with the hypothesis of ‘regulatory arbitrage’.

JEL-Code: I180, L510.

Keywords: parallel trade, parallel imports, regulatory arbitrage, pharmaceuticals, supply chain.

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1. Introduction

In the European Union, medicines are regulated products subject to both single market (e.g., regional exhaustion of property rights) and country specific health care regulations (e.g., medicines pricing and distribution regulation). This gives rise to parallel trade (PT), a phenomenon that takes place when a patented product is diverted from the official distribution chain (the distribution channel chosen by the originator) to another one in another European member state where it competes with the official distribution chain as a parallel distributor.

PT is a legal activity because although medicines are products under protection of intellectual property rights (IPR) such rights are subject to European-wide (as opposed to country wide) legal exhaustion after first sale in an existing European member state. Hence, IPR do not confer legitimate control of the product to the originator company upon sale in one-member state country. As a result, if price differences arise across countries, a parallel distribution chain may well be developed in higher price countries in response. A number of decisions adopted by the European Court of Justice have further encouraged distributors to engage in parallel trade (Barfield and Groombridge, 1998). However, this paper does not attempt to examine the effects of parallel trade legislation, nor offer a state of the art of European parallel trade policy. Instead, we attempt to contribute to the literature by examining the extent to which parallel trade (PT) is indeed, explained by distribution chain regulations (statutory margins) rather than other factors including price differences which would drive more 'common arbitrage' (Malueg and Schwartz, 1994; Richardson 2002, Jelovac and Borodoy, 2005 and Peccorino, 2002).

The consolidation of a single European market has unveiled several opportunities for different types of arbitrage. Typically, 'common arbitrage' takes place when an agent profits from product price difference across markets, which typically gives rise to some form of price equalisation between

markets, namely a common price. However, when prices differences result from heterogeneous competitive conditions created from country specific statutory margins (regulatory arbitrage), price equalisation is not guaranteed[1]. Such regulatory arbitrage results from institutional environments including country specific lobbying and pressure group capacities (Grossman and Lai, 2006). Parallel distributors tend to be either distributors or agents that purchase on behalf of authorized distributors, therefore changes in the wholesale price and competitive conditions in the distribution chain are likely to determine the profitability of the parallel trade business[2].

This article argues that Medicines parallel trade falls, at least partially, in this second category, and hence, welfare effects are different from those of common arbitrage. This paper adds to the literature by taking advantage of a unique dataset that contains information on the source country of PT flows (the Netherlands, is the only country where the country of origin could be identified in the IMS database at the time of the analysis). Thus, we can compute for each therapeutic group the exact price difference between the product at source and the price at the point of distribution. In addition, by identifying the destination and source countries we can match for for each product/country the statutory distribution margins (that are added to the price[3], which provides a conservative estimate of the potential gain from PT given the potential presence of rebates and discounts which are not observed. We use data on parallel imports for cholesterol drugs from the 8 countries in Europe (Belgium, France, Germany, Greece, Italy, Portugal, Spain, and the UK) which distributed 95% of all observable parallel imported statins to the Netherlands across 24 quarters (1997-2002).

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[1] The term here is not specific to the pharmaceutical industry regulation. Typically, in other industries, that term is applied when a bank changes its charter from a state bank to a national bank to take advantage of different regulatory treatment, or when a firm changes its country of headquarters to take advantage of different tax regimes

[2] Parallel imports may well be the effect of second degree price discrimination, for example resulting from discounts given by parallel distributors to pharmacists in importing countries (Anderson and Ginsburgh, 1999).

[3] This paper fills this gap by using a unique dataset, which contains a rich set of controls for the regulation of the distribution chain. This is especially important given that identifying bilateral trade flows allows us to ascertain the magnitude of the effect of economic arbitrage (price differences between country of origin and destination) *vis a vis* distribution chain regulatory differences.

Some prior studies on parallel trade have analysed country-specific flows, but for the most part have either not taken into account the presence of generic drug penetration, or the origin of PT flows. Furthermore, previous literature remains inconclusive about the capacity of parallel trade to increase the country's welfare (Mauleg and Schwartz, 1994, Richardson, 2002). In other words, the normative implications for welfare of increasing parallel trade are ambiguous and extremely dependent on the benefits of a unitary price as compared to price discrimination equilibrium. Furthermore, previous empirical studies are limited by the wide therapeutic heterogeneity and the presence of generic competitors in addition to parallel traded products. Hence, we rely on data from one single therapeutic group before it exhibited generic entry and we use data for a rich set of controls that measure the competition of the distribution chain and its reimbursement.

Unlike previous empirical studies, we use a flexible augmented gravity model specification that includes information on the heterogeneity of the supply chain regulation (more specifically retail and wholesale regulation incentives the on proliferation of parallel trade). We can distinguish distribution chain regulation effects from price regulation effects because they are determined by government regulation and, unlike a typical model, there is no reasons that one regulation impact on the other as market chain distribution is general for all products whilst price regulation is product specific. Proprietary data are used and we perform several specifications that range from pooled regression to panel data analysis to capture part of the unobserved heterogeneity in measuring specific parallel import determinants. We estimate parallel-traded sales in the Netherlands for a given drug from a given country in a given quarter. Parallel-traded sales are a function of relative product price and wholesale regulation, the exchange rate (which is a variable separate from relative price), distance, and three different transformations of GDP (difference in GDP per capita, sum of GDP, relative GDP).

Our results report evidence that medicines' parallel trade (imports) is an economic activity driven by relative prices consistently with common arbitrage. However, we find that the difference in

the regulation of Medicines distribution margins exerts an effect on trade flows. The latter is consistent with the hypothesis of regulatory arbitrage. The remainder of the paper is as follows. Section 2 provides some background and the theoretical underpinnings of parallel trade and arbitrage in the context of a gravity model. Section 3 presents the methodology, data sources and the approach followed by the analysis, while section 4 presents results and discusses policy implications. Finally, section 5 outlines the main conclusions.

2. Background

2.1. Conceptual considerations

Although parallel trade is defined as a specific form of arbitrage, predictions of arbitrage theory do not seem to be backed by empirical evidence (Kanavos and Costa-Font, 2005). One explanation lies in the creation of some accommodative market equilibrium by drug companies (Ganslandt and Maskus, 2004). Alternative explanations rest on the incentives resulting from country-specific regulations affecting both the probability of undertaking parallel trade and the emergence of long-lasting price differences across countries. In the pharmaceuticals sector, regulatory interventions take place at national level which affect both the product price and the distribution margins (Kanavos and Costa-Font, 2005), as PT takes place primarily at the product distribution level. Therefore, prices do not fully reflect differences in purchasing power across countries as in other products. Hence, medicine flows across countries might be highly correlated with countries regulation.

For arbitrage to take place, the market size of the source country needs should suffice to carry on the activity without leading to major shortages in the country. Hence, the larger a particular market, the more attractive it is for both pharmaceutical manufacturers and parallel distributors to undertake production and trade respectively.

Medicines are funded in most European countries, by a single payer (national health insurance or social insurance system) who negotiates rates and purchases drugs on behalf of the health care system. Statutory margins in the distribution of medicines are common practice across Europe, so that the most widely used model of distribution has to be that the manufacturer sells to the wholesaler and the latter to a retailer (pharmacy). However, there are some exemptions only relating to the structure of the distribution chain itself, namely, some countries allow a degree of vertical integration between wholesalers and retailers, whereas others allow some horizontal integration amongst wholesalers or retailers. Maintaining vertical restraints implies substantial transaction and information costs and, as a result, weak distribution control, combined with a fragmented wholesaler structure, leads to wholesalers in low-price countries channeling part of their stocks to high-price countries.

Assuming that payers regulate prices of pharmaceuticals (Peccorino, 2002) then, *ceteris paribus*, the larger the country market, size the higher the potential bargaining power of the payer. Manufacturers may follow a dual strategy in this case: they can either *deter* parallel imports by setting a sufficiently low (high) price in a high (low) price country such that it would make it unprofitable to perform parallel imports; or, alternatively, they can *accommodate* parallel trade simply by allowing parallel distribution to take place without necessarily taking action on prices. When arbitrage is unlimited then deterrence is more profitable than accommodation. Conversely, accommodation emerges when the potential volume of arbitrage is small and trade costs are relatively high (Ganslandt and Maskus, 2004)[4].

2.3 An empirical gravity specification

[4] Given that the distribution of medicines is heavily regulated across European countries, parallel imports might well result from the lack of total vertical control in the pharmaceutical distribution chain by the manufacturer.

Parallel imports can be specified by using a gravity specification widely used as a baseline model for estimating the impact of a variety of policy issues related to regional trading groups, currency unions and various trade distortions (Bougheas, Demetriades and Morgenroth, 1999; De Grauwe and Skudelny 2000; Glink and Rose 2002). A reduced form of gravity model could be specified, incorporating both demand and supply factors along with trade barriers such as distance, economic mass and other common preference factors. Hence, flow of goods between two locations is *positively* related to their size (or income levels) and *negatively* related to the distance between them, after controlling for a number of other factors which might affect trade through the gravity model (price differences, differences in the competitive pressures of certain regulatory frameworks as promoting parallel trade and the size of the market as an indication of the potential demand and thus profits from parallel trade)[5].. Rather than structurally estimating the parameter of the gravity model, we aim at testing the significance of those parameter that are typically associated with driving both common and regulatory arbitrage.

We assume parallel distributors aim at maximising an expected profit function (Kanavos and Costa-Font, 2005), and hence are more likely to source products to high price high distribution margin countries compared to countries of origin. Given that the relevant price for parallel imported medicines is the wholesale price prevailing in any of the countries in question, the extent of parallel import penetration depends, among other things, on a number of parameters related to drug distributors. The first is the nature of competition prevailing in the wholesale distribution business and the number of wholesalers. The second relates to the economic rents that result from wholesaling, in terms of margins/mark-ups accruing to each wholesale distributor as part of the product's retail price, which in most European countries, are fixed by government regulation.

[5] A structural gravity model could arise from a CES preferences and increasing returns to scale. In that context, distance can be related to transport costs and operates like a relative price, with a coefficient (elasticity) of unity in most cases. GDP (market size) variables are there to account for importer demand and exporter capacity and both should have positive coefficients

Therefore, our research question is whether parallel trade is any different from common arbitrage? Are parallel imports determined by the difference in wholesale margins across countries?

Our empirical strategy has been to estimate first a naïve pooled cross-sectional specification (OLS)to then expand by testing and taking into account the endogeneous determination of parallel imports and prices (2SLS). Finally, we employ a panel data techniques offer more robust specification that controls for potential unobservables correlation between observations for the same country (2SGLS). The specification defined here raises a number of econometric issues: namely, the extent of inclusion of specific fixed effects, given that gravity models do not typically allow for them. The second challenge lies in the limited variability in the regulation of Medicines margins across time. Hence our preferred specification will be a random effects (2SGLS). Specifically, we explore both the pool and panel data model specification possibilities. An augmented logarithmic version of the traditional gravity equation includes geographic controls as follows:

$$\ln M_{ijt} = \beta_o + \beta_1 \ln\left(\frac{p_i}{p_j}\right)_t + \beta_2 \tau_{ij} + \beta_3 \ln(GDP_i + GDP_j)_t + \beta_4 \xi_{ijt} + \beta_5 \left|\ln\left(\frac{GDP_{it}}{N_{it}}\right) - \ln\left(\frac{GDP_{jt}}{N_{jt}}\right)\right| + \beta_6 \ln(Q_i + Q_j)_t + \beta_7 \ln\left(1 - \left(\frac{GDP_{it}}{GDP_{it} + GDP_{jt}}\right)^2 - \left(\frac{GDP_{jt}}{GDP_{it} + GDP_{jt}}\right)^2\right) + \beta_8 X_{ijt} + \varepsilon_{ijt} \quad (1)$$

where *i* and *j* denote the country of origin or export countries and destination country respectively. The error term ε_{ij} captures any other random shocks and unobserved events that may affect bilateral trade between the two countries. Gravity-specific determinants include distance (τ_{ij}), the bilateral sum of GDP $(GDP_{it} + GDP_{jt})$ of the two trading countries, the difference between GDP per capita of the two trading countries $\left[\ln\left(\frac{GDP_{it}}{N_{it}}\right) - \ln\left(\frac{GDP_{jt}}{N_{jt}}\right)\right]$, the relative country size

$\left(1 - \left(\frac{GDP_{it}}{GDP_{it} + GDP_{jt}}\right)^2 - \left(\frac{GDP_{jt}}{GDP_{it} + GDP_{jt}}\right)^2\right)$ and the exchange rate (ξ_{ij}). Given that parallel trade is

theoretically conceptualised as a specific type of arbitrage (Ganslandt and Maskus, 2004), it is arguably driven by the existence of a difference in relative prices between the two countries $\left(\frac{p_{it}}{p_{jt}}\right)$ and a volume effect in the form of total drugs from the specific therapeutic group of interest $(Q_i + Q_j)$. Finally, a number of key determinants are included in X_{ij}. These refer to the relative margins of wholesalers in country *i* with respect to country *j*. Finally, β denotes the vector of coefficients for each variable and ε_{ij} measures the set of other influences on bilateral parallel imports which are part of the error term. The two main variables of interest (treatment variables) are picked up by coefficients β_1 and β_8. The other variables refer to control for either the gravity specification, economic controls which influence trade such as exchange rate and relative income, and finally controls for the demand and size of the market as defined in Table 2.

[Insert Table 2 about here]

3. Data and Empirical Strategy

We used data from the Intercontinental Medical Statistics (IMS) database which contain quarterly data on import sales and units over the 1997-2002 period for a set of products that fall in the therapeutic product category of statins and exhibit parallel trade during the study period. The latter results in a total sample size of 768 observations. However, the presence of some missing observations meant we were left with a final full sample of 625. The data exhibit a three-way panel structure, 4 products 8 exporters to the Netherlands, in 24 quarters. Data for each product were made available at dispensation level. IMS collect data on prices and sales for a number of countries, including the Netherlands, and for the selected product group, statins, on a product-by-product (e.g.

simvastatin, pravastatin, etc) and product presentation basis (e.g. simvastatin, 20mg, 28 tablets). The accuracy of the database's sources has been validated externally (IMS, 2002). Data on wholesale margin and regulation was obtained from publicly available sources for each country department of health. Rather than relying in different therapeutic groups which are subject to different degree of competition and the presence of generic competitors, we instead rely on a single therapeutic group (statins) which accounts for a significant proportion of total retail sales of prescription only medicines in European countries (5.7% in 2002) (**Figure 1**).

Statins are products that lower levels of LDL ("bad") cholesterol by 30-50%, and have been popularly prescribed to (primary and secondary) prevent coronary heart disease (CHD), including myocardial infarction (MI), and their use has been increasing over time, making them, in turn, desirable targets for parallel trade (Kanavos *et al*, 2006). All products within the group were protected by a patent during the study period, therefore, the effect of parallel trade could be isolated from other effects, such as competition from generic equivalents, and studied without having to account for the competition effect due to generic penetration which may be significant (Frank and Salkever, 1991; Grabowski and Vernon, 1992; Ganslandt and Maskus, 2004).

Table 1 illustrates evidence on the variability of margins and competition in the product distribution of each country. The information on the number of competitors the source country is important as it will influence the price in such countries, but it is unlikely to affect the quantity of PT through any other source but though its effect on process. This is important for our instrumentation strategy below. Overall, the suggest marked differences in the regulation of prices and the wholesaling competitive conditions across European countries. We find that in France, wholesaler margins are the lowest in the period of analysis, and other southern European countries also follow

suit. Southern European countries exhibit a significantly higher fragmentation in their wholesaling and retailing practices compared to other European countries.

[Insert Table 1 about here]

An important feature to note is that we have examined parallel import flows of statins into the Netherlands because for that country alone were in a position to identify with precision the source country but only for the Netherlands[6]. Specifically, we were able to identify with precision the price and quantity differences at any point in time between each exporting country and the Netherlands, and estimate the impact of arbitrage in the Dutch market for each of the products within the statins group.

We hypothesize that price differences are consistent with the arbitrage nature of parallel trade, as well as statutory margins the drug distribution system consistent with the hypothesis of 'regulatory arbitrage'. Kanavos and Costa-Font (2005) already find that some of the gains from parallel trade are invisible because of the incentive structures of different stakeholders that play a key role in the distribution of medicines in general and parallel imported medicines in particular, most notably parallel distributors and pharmacies. Some of these gains include informal rebates which we do not observe, which we are assume are a proportion of the price at source country.

[Insert Figure 1 about here]

Our gravity model specifications first reproduce the results of a pooled cross-section specification purely for comparative purposes which is the followed by a panel data approach by including country-pair "individual" effects. Hence, the pooled (cross-section) specification contains a reduced

[6] In this particular case, and for the above study period, the Netherlands parallel imported statins from Belgium, France, Germany, Greece, Italy, Portugal, Spain and the United Kingdom.

form bases on implausible assumptions (e.g., the presence of unobserved heterogeneity resulting from unobserved characteristics related to bilateral trade relationships) , whilst the panel case refers to a random effects approach consistent with the gravity specification whereby some variables are country-specific (e.g. distance). Thus, a country would export different amounts of the same product to two other countries, even if their GDPs are identical and they are equidistant from the exporting country. This is due to potential differences in drug regulation which affect prices and margins and hence gains from PT.

The dependent variable is the logarithm of real trade of statins in the Netherlands and the logarithm of total trade volume in the country of origin. First, we use the basic specification and consider the impact of core explanatory variables such as GDP, population and distance. Subsequently, in line with recent theoretical developments (Egger, 2002), we include variables measuring the size of trading countries and other barriers that might explain the development of parallel trade such as distance and exchange rates. Cross-section OLS estimates are likely to suffer from substantial heterogeneity bias but we still provide them for comparative reasons. We then estimate two stage least squares (2SLS) and two stage generalised least squares (2SGLS) models to account for the endogenenity if price differences and the panel structure of the data. To instrument price differences, we are able to observe the variability in the competitive conditions in the drug distribution in the source country which we do not expect it would affect the volume of parallel traded product though other mechanisms but prices. Specifically, we use the relative number of wholesalers as an instrument for product price at the wholesale level. Given that prices are regulated, one would not expect they would conflate with direct price regulation in some countries (e.g., some countries might have free drug pricing and regulate heavily the margins of pharmaceutical distributors). Indeed, as discussed elsewhere (Kanavos and Costa-Font, 2005), incentives to purchase parallel imported drugs by wholesalers and pharmacies take place through unobservable discounts which, in the vast majority of cases, remain unaccounted for by health insurance schemes. We test

and confirm the existence of endogeneity in price formation, and confirmed the statistical validity of the instrument with the common F test.

The variables employed in the analysis are presented in **Table 2** and are as follows: (a) (M_{ijt}) is the observed volume of each statin imported into the Netherlands from another EU country; (b) (τ_{ij}), represents the distance between two areas and is defined as the Euclidean distance of latitude and longitude between country capitals; the reason for measuring distance in this way rests on the fact that kilometers are not necessarily a good approximation for distance given alternative and more direct ways of transportation (e.g. air travel); (c) exchange rate (ξ_{ijt}) is an obvious determinant of parallel imports insofar as it impacts price transparency (given that not all countries examined are in the euro area and the period examined corresponds to before the euro was introduced), especially in the context of European integration.; (d) following the predictions of a gravity model, our model includes the bilateral sum of country GDPs (in logs) $\ln(GDP_{it} + GDP_{jt})$, as it is conventional in the literature we measure relative country size (in logs) $\ln\left(1-\left(\frac{GDP_{it}}{GDP_{it}+GDP_{jt}}\right)^2-\left(\frac{GDP_{jt}}{GDP_{it}+GDP_{jt}}\right)^2\right)$, the difference of GDP per capita (in logs) $\left[\ln\left(\frac{GDP_{it}}{N_{it}}\right)-\ln\left(\frac{GDP_{jt}}{N_{jt}}\right)\right]$, and the sum of statins sales in € (in logs) $\ln(Q_{it}+Q_{jt})$ that is the specific therapeutic group in question which has been growing in size during the study period which were included after testing for colinearity in the regression; (e) furthermore, we consider the point of entry of a parallel imported drug or product presentation as a variable to select the sample under consideration. As expected from a model of arbitrage, relative prices between countries (in logs) $\ln\left(\frac{p_{it}}{p_{jt}}\right)$ should be a key determinant, with a negative expected sign. Finally, (g) a set of variables has been added to measure the aggregate number of distributors, which accounts for the degree of competition in the distribution chain in both countries proxied by the

relative number of wholesalers in the Netherlands and the exporting country $\ln\left(\frac{N_{it}}{N_{jt}}\right)$ and the (h) relative wholesaler $\ln\left(\frac{\eta_i}{\eta_j}\right)_t$ and account for possible economic incentives for parallel trade which are exogenous proxies for regulations.

4 Results

4.1 Preliminary evidence

We begin by reporting evidence of trends and stylised facts, which appear to suggest an increase in parallel import penetration to the Netherlands post 1999 (**Figure 2**). Whilst this is initially attributable mainly to a single product (simvastatin), subsequently, other competitor statins increase their share in total statin imports. According to IMS, the market shares of parallel imported statins were about 30% over the study period. These evidence is suggestive that the Netherlands is compared to other European countries one of the most dynamic parallel importers.

Figure 3 reports the patterns of trade from each of the potential countries of origin. The most common country of origin of parallel imported drugs in the Netherlands, at least in the earlier parts of the study period, was France. This is not totally unexpected although France does not have the lowest statin price among exporting countries. Significant exporting activity by France may be due to the fact that France is a large country with a significant capacity to parallel export (Kanavos and Costa-Font, 2005). At the same time, of all the other existing countries that can potentially export, France is, together with Belgium, closest geographically to the Netherlands. Finally, the wholesale margin in France is the lowest of the countries considered (**Table 1**), and this can be interpreted as an incentive for wholesalers to divert part of their stocks to other countries, seeking higher returns.

[Insert Figure 2 about here]

Importantly, the evidence presented in **Figure 3** suggests that although 90% of parallel imported statins into the Netherlands were sourced in France in 1997, Spain's market share has increased significantly since 2000. By 2002 Spanish exports accounted for 40% of all statins parallel imported into the Netherlands.

[Insert Figure 3 and Table 2 about here]

4.2 Econometric specifications

By undertaking the econometric estimation of the gravity equations following the premises of equation (2) we then attempt to ascertain the influence of economic versus regulatory determinants of parallel import entry and penetration. Purely for comparative purposes, **Table 3** provides the estimates of a pooled OLS, two stage least squares (2SLS) and two stage generalised least squares (2SGLS) model which includes equation (2). Given the panel nature of the data, we clustered by country of origin and product. Yet, as the observations are not independent due to the correlation of PT flows both between and within countries, out preferred specification is the GLS one s to account for potential different distributional assumptions. The treatment variables in the specification refer to relative price differences between importing and exporting countries and difference in regulatory margins which influence the wholesalers decision to source other countries through PT. Accordingly, we include as a key covariate the wholesalers' mark-up difference to measure the effect of competitive conditions in the drug distribution system.

Most variables reflect the expected coefficient, specifically we divide the variables between picking the effect of price differences (treatment variables) as defined in Table 2 measuring the effect of common and regulatory arbitrage, and controls. The difference refers to those specific of a gravity specification (distance and country mass), trade economic controls such as (income and exchange rates) and those specific of the arbitrage activity (demand for statins proxied by the total market and the country size). Results for the most part are consistent with expectations, monetary barriers to trade – such as exchange rates –reveal the expected negative effect on parallel imports[7]. Similarly, transport costs – measured by distance – reduce parallel import penetration consistently with the prediction of a generalised gravity model, and it influences entry decisions are associated with distance. Some variables such as the combines GDP did not reveal stable results throughout different specifications. As expected, bilateral parallel trade flows increase with the size of the statins market. Finally, and consistent with our theoretical predictions, relative wholesaler mark-ups are associated with import penetration and the entry decision to undertake parallel trade. When we examine entry rather than PT penetration we find consistent estimates. Table A1 reveals the determinants of entry condition on observing some PT in the period of analysis and using the same variables as in the gravity specifications. We find that entry decisions are based on capacity to source and price difference. Finally, the variables are in logs so they can be interpreted as elasticities.

Next, we tested for endogeneity following Wooldridge (2009) suggesting unambiguous evidence of endogeneity. Accordingly, we instrumented the price difference using data on relative pharmacist margins across countries $\ln\left(\frac{\rho_i}{\rho_j}\right)_t$ and the relative number of wholesalers across countries $\ln\left(\frac{\eta_i}{\eta_j}\right)_t$. The theoretical justification for including these variables as instruments lies in the fact that they are strongly associated with the formation of drug public prices given that both pharmacy

[7] This has to do with the fact that in some parallel exporter countries such as Spain and France the introduction of the euro has eliminated the exchange rate variability with the Netherlands

margins (mark-ups) and the least competitive conditions for drug distribution are responsible for the formation of final public prices, whilst they do not appear to be associated (both in prior correlation analysis and in OLS regression models that include this variable as a covariate) with parallel trade volume, given the latter is driven by the nature of incentives at wholesale level. On the other hand, parallel trade strongly is associated with price differences. Therefore, an instrumental variables (IV) estimation should provide a consistent estimate of the coefficients of interest and could well correct for any omitted variable bias (Angrist and Krueger, 2001).

[Table 3 about here]

Table 3 reports the results of a gravity equation specification estimated using OLS, instrumental variables and 2SGLS. Importantly, country- and product-specific effects might be driving the dynamics of parallel trade flows, or more generally, some unobserved heterogeneity might be present which need to be accounted for. This could be corrected using panel data analysis however fixed effects would not be consistent with a model including distance so we rely on random effects. We considered estimating the model using country of origin fixed effects, however two of the most relevant variables could not then be included in the specification, namely distance (given that distance is fixed), and the difference in margins (given that the variability across time is limited which reduced the power of its estimates). Hence, we have decided not to present the estimates.

Table 3 reports the estimates of the gravity equations. Findings indicate that some determinants of common trade do not apply to PT, such as distance and though relative. Indeed, given that trade takes place within Europe, transport costs become negligible. The difference between 2SLS and OLS estimates with regards to the effect of relative prices and wholesale margins was suggestive of the presence of unobservables and confounder effects. However, GLS estimates suggest that in addition to pure price differences (elasticity of 3.4 of a unit difference in relative

prices), the effect of distribution margins remains significant consistently with the hypothesis of regulatory arbitrage. Our preferred specification (3.3) is consistent with expectations with regards to the gravity model specifications (positive effect of combined economic mass (GDP) but no effect of country distance), a higher demand for statins would reduce the volume of PT whilst country size is expected to produce the opposite effects on trade.

An important picture comes out of such a strategy. Consistently with PT as a form of common arbitrage, medicine price difference exerts an effect in explaining parallel trade volume, but a large proportion of PT is driven by changes in the regulation of distribution margins Indeed, differences in wholesale mark-ups are found to increase Medicines parallel import flows in line with the regulatory arbitrage hypothesis. The effect of the difference in wholesale margin compares to that of a change in total volume of statins.

5. Conclusion

This paper is the first to examine medicine parallel imports employing data that includes source country information, and employs a gravity specification common in models of trade to identify PT determinants. The identification of the source country allows to estimate the price difference per product/country alongside differences in statutory margins that arguably are driving both common and regulatory arbitrage rationale of parallel trade. Our data is from the Netherlands (a country that rank among the highest parallel importers) and for one therapeutic group: statins (a therapeutic group subject to patent protection during the period of analysis and not affected by generic entry). This paper studies the influence of price differences and differences in statutory margins in driving parallel trade flows..

We find that medicines parallel trade in Europe is indeed a regulation-induced phenomenon (in addition to a common form of arbitrage) given that the difference in statutory distribution margins significantly explains PT flows. This is consistent with theoretical predictions in other similar settings (Peccorino, 2002). Indeed, PT is an activity that mainly takes place at the distribution level. Hence, changes in the statuary margins across countries provide incentives for the development of parallel distribution channels. However, given that both prices and Medicine distribution channels are regulated, does not lead to price equalisation (Kanavos and Costa-Font, 2015) The latter has important implications for European economic policy and suggests that the traditional beneficial effects that are typically associated with market arbitrage do not necessarily hold in this case. However, our results need to be taken with caution as they rely on only one therapeutic group, and refer to a period where the European Union was restricted to 15 members, one would expect differences in the nature of the activity in a Europe of 28 members as it is today.

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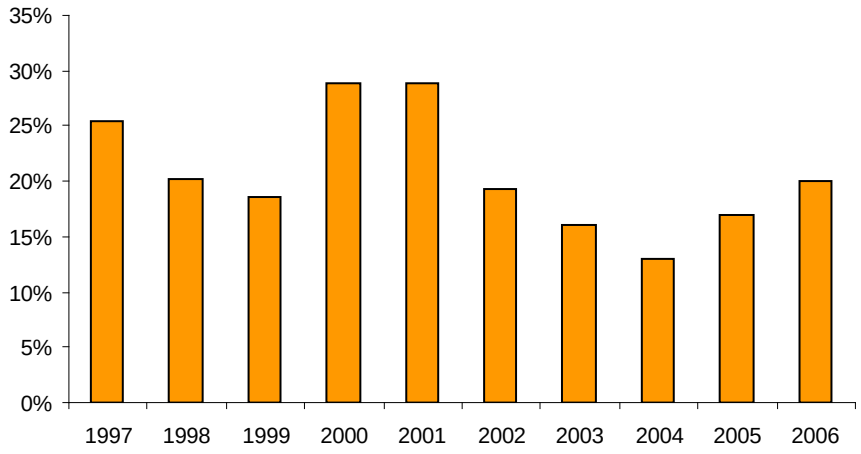
Figure 1

Market share of parallel imported statins in the Netherlands, 1997-2006

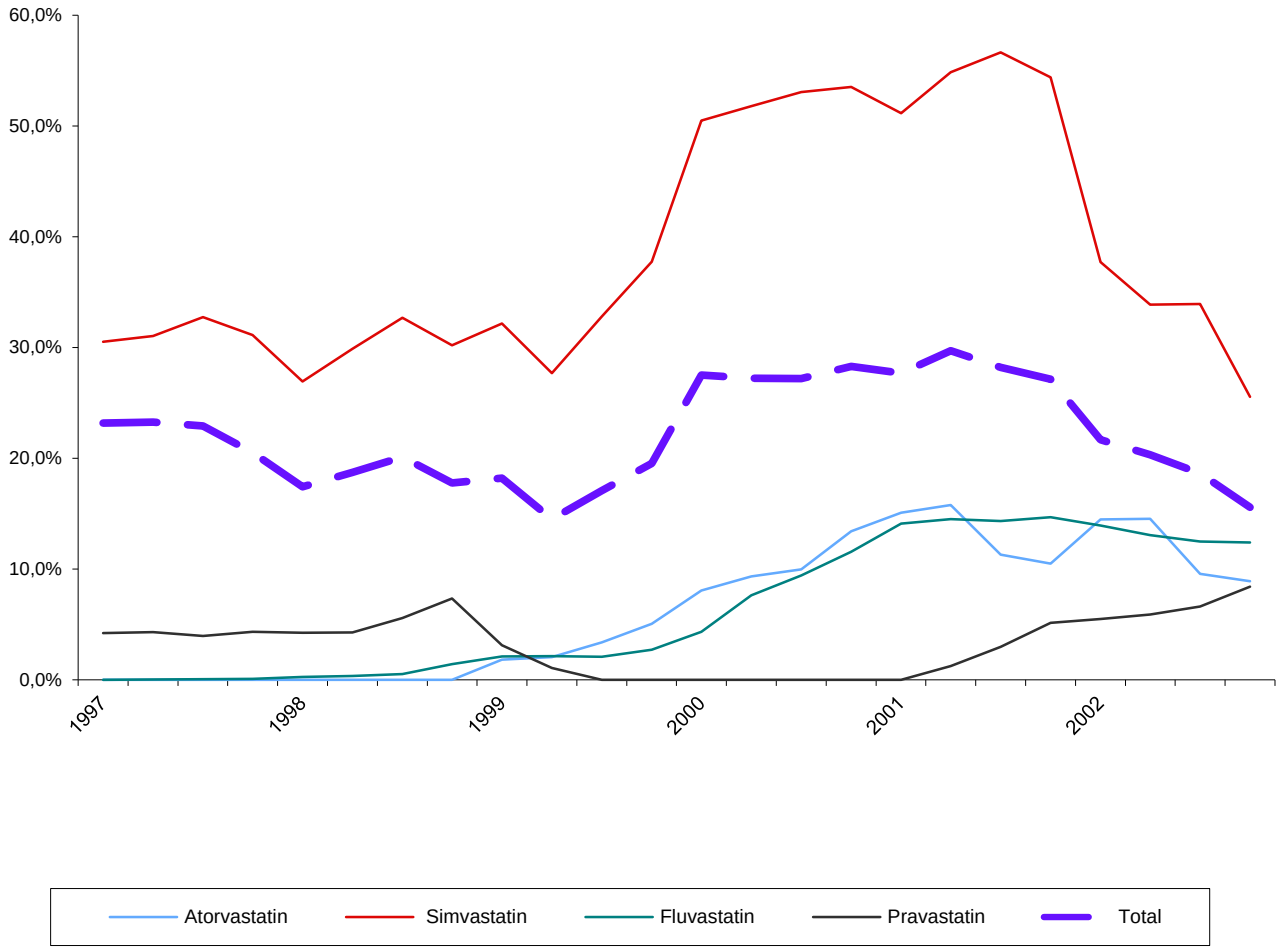


Note: The figure reports the proportion of total parallel trade volume as a proportion of total volume of statins in the Netherlands for the period 1997-2002 (where we observed the origin of parallel trade) and 2003-2006 (where we only observe the the total volume but we could not identify the origin).

Source: The authors from IMS, 2004.

Figure 2

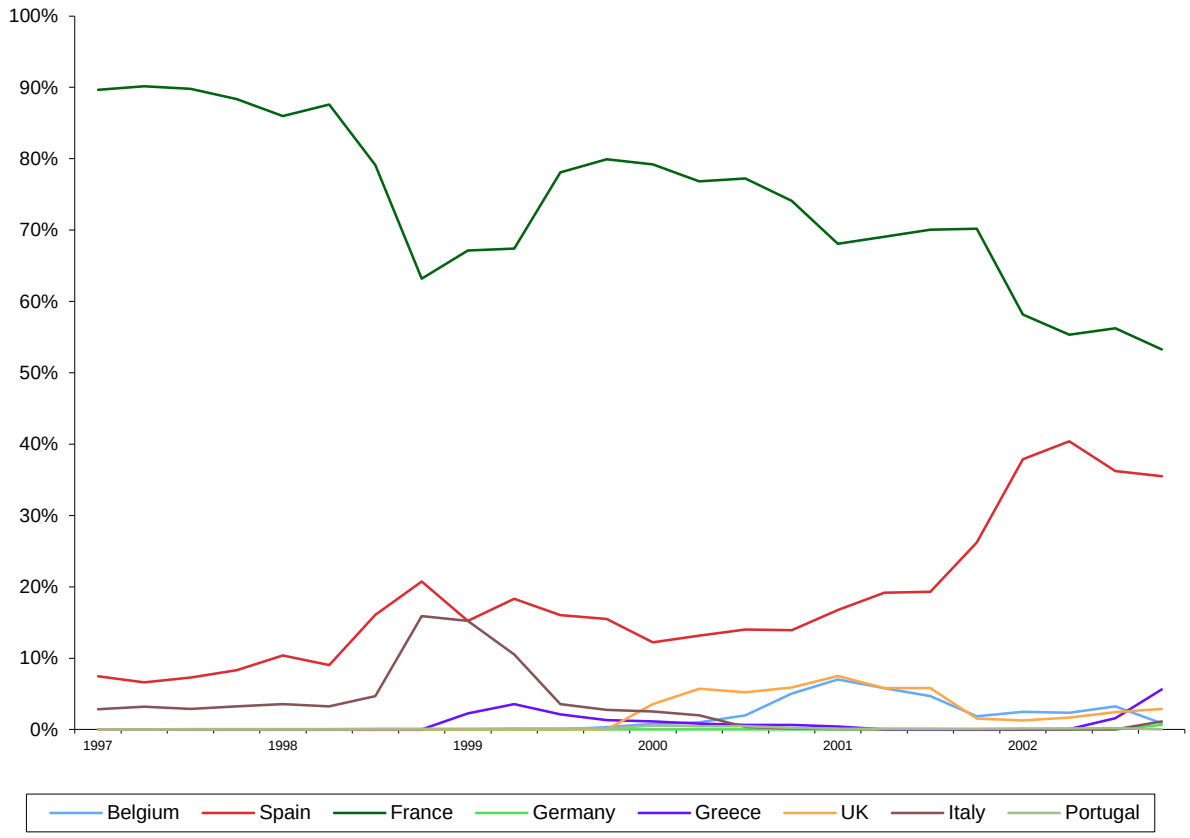
Parallel trade penetration of statins in the Netherlands (parallel imports as a % of total product market), 1997-2002



Note: **This figure reports (for each specific products that ate included in the statins therapeutic group) the penetration of parallel trade defined as the ratio of parallel traded volume and total volume in percentage terms. Source: The authors from IMS, 2004.**

Figure 3

Proportional (%) Origin of parallel imported statins in the Netherlands, 1997-2002



Note: This figure displays for each year of the study 1997-2002 the proportion of parallel trade sales of statins in the Netherlands per country of origin.
Source: The authors from IMS, 2004.

Table 1
Pharmaceutical price structure and distribution chain market structure in selected EU countries, 1997-2002

Country	Ex-Manufacturer[2] (% price)	Number of wholesalers	Wholesaler margin (% price)[3]	Pharmacy density (Population per pharmacy)	Pharmacy margin (% price)[3]
Netherlands	63.4	4	**10.8**	6,100	20.2
Belgium	56.6	13	8.5	5,200	29.2
France	64.8	12[1]	**3.8**	**2,800**	26.2
Germany	51.2	16	7.7	3,900	27.3
Greece	63.1	130	**5.5**	**1,420**	24
Italy	63.8	95[1]	**6.7**	3,700	20.4
Portugal	67.8	18	8.4	4,000	19
Spain	62.7	51	**6.7**	**2,000**	26.8

[1] Excluding regional offices and counting only head offices of the same wholesaler.
[2] Ex-manufacturer price as a proportion of price, assuming price=100.
[3] Margins expressed as a proportion of price, assuming price=100.

Notes: This table provides (for a number of countries of the study which are Medicine parallel exporters in to the Netherlands and the Netherlands) information on the average ex-factory (ex-manufacturer) price, the distribution margin of both distributors and manufacturers in such countries, and the average number of wholesalers and pharmacists in the countries of analysis.

Sources: Paterson *et al*, 2003a; European Association of Pharmaceutical Wholesalers, 2005.

Table 2
Variables and descriptive statistics

Variable	Abbreviation	Description	Mean (s.e)
Dependent variable			
$\ln(M_{ijt})$	lquantity	Bilateral trade flow volumes of statins (logs) [a]	1.513 (2.646)
Entry	Entry	Dummy variable measuring the entry of a new drug in the parallel trade market[a]	0.283 (0.450)
(a) Gravity Model Controls			
$\ln(\tau_{ij})$	Ldist	Euclidean distance of latitude and longitude (in logs) of the country capitals	6.467 (0.941)
$\ln(GDP_{it}+GDP_{jt})$	lG	Bilateral sum of GDPs (logs)[b]	10.782 (0.107)
(b) Trade Specification Controls			
ξ_{ijt}	Ler	Exchange rates in euros (logs)[b]	0.0679 (0.102)
$\left\lvert \ln\left(\frac{GDP_{it}}{N_{it}}\right)-\ln\left(\frac{GDP_{jt}}{N_{jt}}\right)\right\rvert$	labsR	Difference of per capita GDPs (absolute terms and logs)[b] (N=population)	0.949 (0.618)
(c) Demand and Capacity Controls			
$\ln(Q_{it}+Q_{jt})$	lsumst	Sum of total sales of statins (logs)[a]	11.494 (0.608)
$\ln\left(1-\left(\frac{GDP_{it}}{GDP_{it}+GDP_{jt}}\right)^2-\left(\frac{GDP_{jt}}{GDP_{it}+GDP_{jt}}\right)^2\right)$	lS	Relative country size (logs) [b]	-0.711 (0.247)
Treatment variables			
$\ln\left(\frac{p_{it}}{p_{jt}}\right)$	lrelP	Relative price between Netherlands and source country adjusted by defined daily doses (DDD)[a]	-0.359 (0.436)
$\ln\left(\frac{\eta_i}{\eta_j}\right)_t$	lrelMWS	Relative wholesalers' drug margins (logs)[c]	-0.518 (0.296)

Note: This table provides the descriptive statistics of all the variables employed in the study. The two dependent variables refer to the volume of parallel imported Medicines and the probability of entry for each product and time. Our treatment variables include (i) relative official wholesale difference in (regulated) margins between importing and exporting country exclusive of informal rebates ('regulated arbitrage'), and the (ii) product price difference between importing and exporting countries ('common arbitrage'). Finally, we consider a number of controls that can be classified as follows: a) those that derive from a gravity equation of trade such as distance and bilateral sum of GDPs which should decrease and increase respectively the probability of trade. b) Relative country size which explains the capacity of being a parallel exporter without producing major product shortages. c) The size of the statin market which measures the demand for statins overall (sum of total sales of statins). d) Income differences across countries and exchange rates with the euro which would be expected to respectively increase and decrease respectively the volume of trade. Export Country (i), Import County (j) and time (t).

Sources: [a] IMS data 1997-2002.

[b]OECD Economic Outlook data 1997-2002. [c] EFPIA, several years (www.efpia.org).

Table 3
Augmented Gravity Equation Estimates (OLS and 2SLS)
Dependent variable: bilateral parallel trade flows to the Netherlands (in M_{it})

	OLS (3.1)	2SLS (3.2)	2SGLS – RE (3.3)
	coeff (s.e)	coeff (s.e)	coeff (s.e)
lrelMWS	-0.969 (0.719)	-1.754 [c] (0.935)	-1.643 [a] (0.536)
lrelP	-0.501 (0.306)	4.012 [a] (1.059)	3.458 (1.671)
ldist	1.809 [a] (0.263)	5.877 [b] (2.939)	6.564 (4.951)
ler	-1.638 (1.683)	-7.042 [b] (3.068)	-2.225 (9.129)
lG	-11.90 [a] (3.384)	-15.815 [a] (5.027)	12.690 [a] (3.58)
lS	145.798 [a] (18.978)	193.058 [a] (34.457)	77.845 [a] (23.38)
labsR	-4.278 [a] (0.742)	-5.067 [a] (1.091)	-1.176 (1.255)
lsumst	3.164 [a] (0.638)	3.852 [a] (0.896)	-1.798 [b] (0.717)
Intercept	188.991 (40.584)	245.661 [a] (62.091)	-78.49 (37.979)
R^2 (Adjusted)	0.15		
N (Observations	625	610	610
Wald χ^2_8 $(\nabla\beta_i = 0)$		82.33	57.38

*Restricted to molecules where there is some evidence of parallel trade.
Note 1: [a] Denotes significance at 1% level, [b] denotes significance at 5% level, and **estimates contain robust standard errors**

Appendix 1.

Table A1

Entry (Probit)

Dependent variable: 1 refer to the existence of some trade flows to the Netherlands (in M_{it})

	Entry (Probit)	
	coeff	s.e
Ldist	0.999 [a]	(0.148)
lrelP	0.386 [b]	(0.159)
Ler	-0.255	(0.869)
lG	-3.663 [b]	(1.856)
lS	74.108 [a]	(12.383)
labsR	-2.209 [a]	(0.419)
Lsumst	1.223 [a]	(0.347)
lrelMWS	-0.458 [b]	(0.202)
Intercept	72.694	(23.547)
R^2 (Adjusted)		
N (No. of observations)	625	
Pseudo R^2	0.13	
Likelihood Ratio χ_8^2	91.29	

*Restricted to molecules where there is some evidence of parallel trade.

Note : [a] Denotes significance at 1% level, [b] denotes significance at 5% level, estimates contain robust standard errors

Appendix 2: Variable Description

Bilateral trade flow volume **lquantity**

Distance **ldist**

Exchange rate **ler**

Entry **entry**

LabsR . Referes to thedifference of log of GDPpc between export and import country, representing a proxy for country's relative factor endowment. The smaller the difference, the more intra-industry trade and the lower inter-industry trade.

Expected sign: negative

$$R_{ijt} = \left| \log\left(\frac{\text{GDP}_{it}}{N_{it}}\right) - \log\left(\frac{\text{GDP}_{jt}}{N_{jt}}\right) \right|$$

Following Egger 2000

- **lG** is the Bilateral sum of GDP: the larger the overall economic space, the larger trade between these two countries. Expected sign: positive

$$G_{ijt} = \log(\text{GDP}_{it} + \text{GDP}_{jt})$$

- **lS** is the Relative country size: the larger the measure, the more similar the two countries in terms of GDP, and therefore, the more intra-industry trade. Expected sign: positive

$$S_{ijt} = \log\left(1 - \left(\frac{\text{GDP}_{it}}{\text{GDP}_{it} + \text{GDP}_{jt}}\right)^2 - \left(\frac{\text{GDP}_{jt}}{\text{GDP}_{it} + \text{GDP}_{jt}}\right)^2\right)$$

lsumst refers to the Sum of total sales of statins (log). Expected sign: positive

ln(Q_i + Q_j)

The logic of a additive specification would be that the number of sales stand out as a proxy for market size. The larger the size, the more the opportunities to trade (although this is already taken into account with bilateral sum of GDP).

lrelWS refers to the relative number of wholesalers as an IV for price difference. IV

Ln(Ni/Nj)

Expected sign: positive

- We are interested in the relative number of wholesalers between the two countries, since the higher and positive the difference, the more parallel trade will take place.

lrelP is the relative price between Netherlands and source country. *Expected sign: negative.* A high ratio between pi and pj means that pi is much larger than pj, therefore, the higher the price in export country, the lower the parallel trade.

$$\mathbf{Ln(p_i/p_j)}$$

With the price difference, there were problems when doing logs, converting negative price differences in missing values. The relative price gives same info and does not have problems in doing logs.

lrelMWS is the relative price between WS margins in export and import country. *Expected sign: negative*. A high ratio between wholesalers margins export and import country means that wholesalers margin is much larger in export country, therefore, the higher the margin in export country, the lower the parallel trade.

$$\mathbf{ln(\eta_i/\eta_j)}$$

Same logic as price difference.