

**Implication of external price referencing and parallel trade on  
pharmaceutical expenditure:  
indirect evidence from lower-income European countries**

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**Running title:** Converging trends of pharmaceutical expenditure in Europe

**Key messages:**

- External price referencing and parallel trade result in lower pharmaceutical prices in higher-income countries and higher prices in lower-income countries, which implies that pharmaceutical expenditure grows more rapidly in the latter than in the former group.
- Using hierarchical linear models on country-level panel data we show that – after controlling for compounding factors – the annual growth rate of pharmaceutical expenditure was 2.1 percentage points larger in the lower- than in the higher-income European countries between 2000 and 2008.
- This trend difference became non-significant after the onset of the global economic crisis, most probably due to disproportionately more pharmaceutical cost-containment measures in lower-income countries compared to higher-income ones.

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## **Abstract**

External Price Referencing (EPR) is applied more and more frequently worldwide by payers to control pharmaceutical prices. Together with the parallel trade of pharmaceuticals, EPR may result in lower pharmaceutical prices in higher-income countries and higher prices in lower-income countries, which implies that pharmaceutical expenditure grows more rapidly in the latter than in the former group. Our objective was to assess this hypothesis. We used hierarchical linear models on country-level panel data to show that – after controlling for compounding factors such as GDP, proportion of old-age population or life expectancy – the annual growth rate of pharmaceutical expenditure was 2.1 percentage points larger in the lower- than in the higher-income members of the European Union between 2000 and 2008. This difference in trends became non-significant (0.6 percentage points) after the onset of the global economic crisis. There was no significant difference between lower- and higher-income countries in the growth rate of non-pharmaceutical health expenditure in either period. Our results indirectly support the presence of price convergence of pharmaceuticals among European countries, and EPR and parallel trade may provide reasonable explanation to the observed trend difference of pharmaceutical expenditure in the two groups of countries between 2000 and 2008. This higher growth rate of pharmaceutical expenditure put extra burden on public health care budgets in lower-income countries and resulted in disproportionately more cost-containment measures compared to higher-income countries after 2008. It remains to be seen whether disappearance of the difference in trend growth rates due to special health policy interventions in countries with economic difficulties is temporary or permanent.

## Introduction

In the European Union lower-income member states tend to spend less on health care both in absolute terms and as a percentage of GDP than their higher-income counterparts. However, as the price of medicines is less different across European countries compared to the costs of non-pharmaceutical health care services and the salary of health care professionals, lower-income countries spend more on pharmaceuticals as a proportion of total health care spending or as a proportion of GDP than higher-income ones (Kaló et al. 2012b, see also Table 1 later). The potentially differing *trends* of pharmaceutical expenditure according to income are much less studied, although it may be interesting from the policy perspective of external price referencing (EPR) and the parallel trade of pharmaceuticals.

External Price Referencing (EPR), or international reference pricing, involves the selection of a basket of countries to compare pharmaceutical prices and create a reference price for the country in question (Espin et al. 2011). The purpose of EPR, among others, may be to negotiate or set prices within a country (Kanavos et al. 2010).

It is applied more and more frequently both worldwide and in Europe, by payers who are aiming to control pharmaceutical prices (Carone et al. 2012), and it seems to be an effective tool to reduce pharmaceutical prices (Galizzi et al 2011; Leopold et al. 2012). Regular price revision, referencing lower income countries and mandate of lowest price in the basket of reference countries are potentially important drivers of price reduction over time (Kaló et al. 2015). Countries may also benefit from lower pharmaceutical prices if they delay the pricing decisions of new pharmaceuticals until many other European countries have already concluded on the price.

In the European Union, parallel trade of pharmaceuticals – when some products are legally imported from another country without the authorization of the manufacturer (Bouvy and Vogler 2013) – has similar, although indirect effects. In the lack of EPR and parallel trade, manufacturers may have more

incentives to adjust their prices to local purchasing power (this strategy is often called differential pricing), resulting in the increase of available funds for and global return on investment of pharmaceutical innovation, whilst ensuring lower prices and as a consequence, better access to medicines in lower income countries (Danzon and Towse 2003; Kaló et al. 2013). However, in the presence of EPR and parallel trade, to minimize price erosion, pharmaceutical companies try to implement narrow international price corridor for their most important medicines (Ridley 2005). Manufacturers also apply specific launch sequence by introducing their new products in countries with traditionally high pharmaceutical prices, and reference these prices in other low-price countries (Creativ-Ceuticals 2014; Leopold et al. 2014).

As a testable consequence at the aggregate (country-) level, both EPR and parallel trade may result in lower pharmaceutical prices in higher-income countries and higher prices in lower-income countries, unless each higher-income country removes those countries from their reference basket that do not have comparable GDP per capita (Bouvy and Vogler 2013). In theory, this implies two potential consequences in lower income countries: (1) access to new pharmaceuticals becomes more limited for patients (Ridley 2005); and (2) the pharmaceutical expenditure grows more rapidly compared to higher-income countries. As limited patient access may have negative impact on the popularity of policymakers, they tend to approve increase in pharmaceutical spending, especially before parliamentary elections (Inotai et al. 2014). This may further increase the rate of pharmaceutical expenditure in lower -income countries. In the above theoretical framework, Boehler (2013) simulated pharmaceutical price changes in Europe due to EPR, and concluded that EPR results in narrow price corridor for new pharmaceuticals; there is a race to the bottom by countries to obtain the European floor price; and the European price erosion of new pharmaceuticals in the early period is faster than in later years.

Unfortunately the time-order relationship between EPR, parallel trade and increased pharmaceutical expenditure in lower-income countries is difficult to establish at an aggregate level, as e.g. the

continuously strengthened application of EPR in Europe has to be considered in its continuum instead of a single intervention point. As current research methodologies and limited availability of data on net pharmaceutical prices across Europe prevented us from exploring the causal relationship between EPR, parallel trade and pharmaceutical expenditure, our research considered addressing their implications only indirectly. If pharmaceutical expenditure did not grow faster in lower compared to higher income countries, the implication of EPR and parallel trade on the European price corridor of new pharmaceuticals cannot be as important as presented in several papers (Ridley 2005; Kaló et al. 2013; Creativ-Ceuticals 2014). On the other hand, the presence of a well-measured difference in growth rates of pharmaceutical expenditure yields indirect support to these phenomena.

Therefore our objective in this study was to assess hypothesis (2) above, i.e. whether the growth rate of pharmaceutical expenditure is truly greater in lower-income than in higher-income European countries. We used hierarchical linear models to control for compounding factors such as GDP, proportion of old age population and life expectancy at birth. We investigated the periods before and after the onset of the global economic crisis separately.

In addition, we estimated the income elasticity of pharmaceutical expenditure and compared it to the income elasticity of health care expenditure in general, obtained in this paper or given elsewhere in the literature. It is reasonable to analyze pharmaceutical expenditure separately from other health expenditures since there is a remarkable cross-country variation both in its value and in its ratio to total health care expenditure in Europe (Lambrelli and O'Donnell 2009; OECD 2011). Our paper also contributes to the scant literature of modelling pharmaceutical expenditure in a cross-country panel data setting (e.g. Clemente et al. 2008).

## **Materials and methods**

## *Data*

The analysis was carried out on aggregate data of 21 European countries (Austria, Belgium, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Luxembourg, Netherlands, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom) between 2000 and 2012. The data originated from the OECD (OECD 2014) and Eurostat (European Commission 2014) databases.

We selected variables that may influence health care expenditure in general and pharmaceutical expenditure in particular. According to Ke et al. (2011), health care expenditure is affected by income, demand side (demographic and epidemiological) factors, technological progress and the characteristics of the health system. These variables are also determinants of pharmaceutical expenditure (Clemente et al. 2008; Lambrelli and O'Donnell 2009). In our study we measured income with GDP per capita, demographic factors with the proportion of the population above the age of 65 years, and we proxied technological progress with life expectancy at birth (c.f. Dreger and Reimers 2005). The main dependent variable was the logarithm of pharmaceutical expenditure per capita but to compare our results with other studies we also used the logarithm of non-pharmaceutical health expenditure per capita as dependent variable in alternative equations.

As for monetary variables, euro was chosen as a common measure; national currency values (for Czech Republic, Denmark, Hungary, Poland, Sweden and the United Kingdom) appearing in the databases above were converted to euro on the given annual exchange rate available from public sources (ECB 2014). We chose to measure expenditure items in a common currency instead of national currency or purchasing power adjusted currency because the prices of pharmaceuticals in different countries are compared in euro at the time of introduction.

The data sources did not cover all country-years, resulting in the presence of missing data. Missing data points within years (altogether 16 out of 273 country-year points) were omitted from the analysis.

### *Methods*

Association between potential explanatory variables and pharmaceutical expenditure as the outcome was assessed by performing descriptive statistical analysis. A series of linear regression models were fitted on each of the country-level explanatory variables and the outcome for the year with the most recent and complete recordings. Goodness of fit was evaluated by calculating correlation coefficients and by visual inspection of each fitted univariate model. The variables included in the exploratory analyses were GDP per capita (in euro), proportion of population above the age of 65 years (in per cent) and life expectancy at birth (in years).

To distinguish between higher- and lower-income countries within the European Union, a given country was considered higher-income if its GDP per capita exceeded mean GDP per capita in 2000 of the entire group of countries. Similarly, if the given country's GDP per capita did not exceed the mean GDP per capita in 2000, the country was taken into account in the lower-income group. This group consists of all new EU member states included in the analysis as well as Spain, Portugal and Greece (altogether 9 countries), while the higher-income group includes the other 12 countries. As part of the preliminary analysis, we also examined graphically how the growth of pharmaceutical expenditure between 2000 and 2012 differed in the higher- vs. lower-income group.

The two groups are well separated by income. Italy, the poorest member of the higher-income group, had 35 per cent larger GDP per capita in 2000 than Spain, the richest member of the lower-income group. Meanwhile, nine members of the higher-income group were within the 35 per cent range of Italy and three members of the lower-income group were within the same range of Spain. The two groups were stable between 2000 and 2012: although there was some reordering of

countries within the groups, it remained true in the whole period that each country in the lower-income group had smaller GDP per capita than any country in the higher-income group.

For a more detailed analysis, we used hierarchical linear models (also known as random effects or mixed models) to describe the trends of pharmaceutical (and also of non-pharmaceutical) health spending levels in the higher- and lower-income group of countries, whilst controlling for the effect of multiple control variables and allowing country-specific random intercepts and random slopes (see e.g. Gelman and Hill 2007). More precisely, our main specification was:

$$(1) \quad Y_{it} = \alpha_i + \tau_{it} * t + \mathbf{X}_{it}\boldsymbol{\beta} + \varepsilon_{it}$$

$$(2) \quad \alpha_i = \alpha_0 + v_i$$

$$(3) \quad \tau_{it} = \delta_{Pre} * Pre_t + \delta_{LPre} * Pre_t * L_i + \delta_{Post} * Post_t + \delta_{LPost} * Post_t * L_i + w_i,$$

where  $i$  denotes country and  $t$  denotes year.  $t=0$  stands for year 2008 and hence  $t$  lies in interval  $[-8, +4]$  for years between 2000 and 2012. We chose 2008 as the baseline year because it separates the periods before and after the onset of the global economic crisis. The crisis started in 2007-2008 but EU-wide GDP still increased by 0.5 per cent in 2008 and fell (by 4.4. per cent) only in 2009.

In equation (1) the dependent variable ( $Y_{it}$ ) is the logarithm of pharmaceutical expenditure per capita or of non-pharmaceutical health expenditure per capita, which are modelled with the time trend and with the vector of explanatory variables ( $\mathbf{X}_{it}$ ). The latter contains the logarithm of GDP per capita, the proportion of population above 65 years and life expectancy at birth. As given in equation (3), the time trend depends on whether the country is a higher- or lower-income country (denoted by  $L_i$ , the dummy variable for being in the lower-income group), on whether the year is before or after the onset of the global economic crisis (denoted by the  $Pre_t$  and  $Post_t$  dummies, respectively) and on the interaction of these two variables. Hence in equation (3) the parameters  $\delta_{Pre}$  and  $\delta_{Post}$  measure the growth in the higher-income group pre- and post-crisis, respectively, while the main parameters of interest are  $\delta_{LPre}$  and  $\delta_{LPost}$ , which show the difference in growth

rates between the lower- and higher-income group before and after the onset of the crisis, respectively. The effects of the control variables are measured by the parameter vector  $\beta$ . The latter can be interpreted as an elasticity if both the dependent and the explanatory variable are given on the logarithmic scale.

To model the hierarchical (i.e. panel) structure of the data, the first-level intercept  $\alpha_i$  and time trend  $\tau_{it}$  are allowed to vary by country (i.e. we allow country-specific random intercepts denoted by  $v_i$  and random slopes denoted by  $w_i$  in equations (2)-(3)). Furthermore, we have the idiosyncratic error term  $\varepsilon_{it}$  in equation (1). The three error terms ( $v_i, w_i, \varepsilon_{it}$ ) are jointly normally distributed with variances  $\sigma_v^2, \sigma_w^2$  and  $\sigma_\varepsilon^2$ , respectively. The country-specific error terms are potentially correlated (their correlation coefficient is denoted by  $\lambda$ ) but they are assumed to be independent of  $\varepsilon_{it}$ .

We also fitted other models. In one specification, to examine the potential sensitivity of the results to the classification of countries into two groups, we measured economic development on a continuous scale and allowed the time trend to depend explicitly on initial (year 2000) logarithmic GDP per capita. More precisely, we estimated equation (3') instead of (3):

$$(3') \quad \tau_{it} = \delta_{0,Pre} * Pre_t + \delta_{1,Pre} * Pre_t * Z_i + \delta_{0,Post} * Post_t + \delta_{1,Post} * Post_t * Z_i + w_i,$$

where  $Z_i$  denotes year 2000 logarithmic GDP per capita of country  $i$  relative to the average. That is,  $\delta_{0,Pre}$  and  $\delta_{0,Post}$  show the average pre- and post-crisis trends, respectively, while  $\delta_{1,Pre}$  and  $\delta_{1,Post}$  indicate the effect of a one per cent larger GDP per capita on the expenditure trends.

In another specification we only allowed country-specific intercepts but not country-specific time trends, while in yet another model we allowed the idiosyncratic error term to follow an autoregressive process as in Baltagi and Wu (1999). Finally, we also estimated a simplified version of model (1)-(3) where the pre- and post-crisis periods are not treated separately, i.e.  $\delta_{Pre} = \delta_{Post}$  and  $\delta_{LPre} = \delta_{LPost}$ . In this specification  $\delta_{Pre} = \delta_{Post}$  measures the growth of the dependent variable in the higher-income group and  $\delta_{LPre} = \delta_{LPost}$  shows the difference in growth rates between the

lower- and higher-income group, averaged for the whole period between 2000 and 2012 and after controlling for the explanatory variables.

Data analysis was carried out by using the R statistical software, its lme4 package (Bates et al. 2014) and the Stata statistical software.

## **Results and Discussion**

Table 1 shows descriptive statistics of the dependent and explanatory variables in the higher- and lower-income European countries between 2000 and 2012. Both pharmaceutical and non-pharmaceutical health expenditure per capita were much lower in the lower-income group than in the higher-income group but there was a substantial variation (with the highest expenditure values in the lower-income group well exceeding the lowest expenditure values in the higher-income group). On average, the ratio of pharmaceutical to total health expenditure was 24 per cent in the lower-income and 14 per cent in the higher-income group, but again, the variations were large. Among the explanatory variables, the biggest difference between the two groups is observed in GDP per capita but life expectancy at birth was also markedly larger in higher-income countries than in lower-income ones.

(Table 1 about here)

Figure 1 shows the time trends of pharmaceutical expenditure in the higher- and lower-income countries, suggesting smaller initial expenditure but a larger growth rate of expenditure in the lower-income than in the higher-income group between 2000 and 2008. The difference in trends disappeared after the onset of the economic crisis: both groups of countries experienced stagnating (or even slightly decreasing) pharmaceutical expenditure in nominal terms between 2009 and 2012.

(Figure 1 about here)

Based on descriptive statistical methods, there is an associative relationship between pharmaceutical expenditure and the three explanatory variables examined in this paper (Figure 2). We obtained the following correlation coefficients with the logarithm of pharmaceutical expenditure in 2008: 0.757 (logarithm of GDP per capita), 0.157 (the proportion of population above the age of 65) and 0.806 (life expectancy at birth). The bottom right panel of Figure 2 also shows that pharmaceutical expenditure is positively correlated with non-pharmaceutical health expenditure, although the relationship is far from deterministic (the correlation coefficient was 0.844 in 2008). Hence our strategy to examine the pharmaceutical expenditure separately from the rest of health expenditure – that is analyzed in more detail in the literature – is justified.

(Figure 2 about here)

Hierarchical linear models make it possible to examine the growth rates of pharmaceutical expenditure in the two groups of countries after controlling for the other explanatory variables. The first column of Table 2 displays the parameter estimates of model (1)-(3) using the logarithm of pharmaceutical expenditure as the dependent variable. After controlling for other compounding factors, the annual growth rate of pharmaceutical expenditure was higher by 2.1 percentage points (with 95% confidence interval [0.4, 3.7]) in the lower-income than in the higher-income group of countries between 2000 and 2008. However, this statistically significant and substantial trend difference disappeared after 2008. The results of model (1)-(3') in the second column of Table 2 show that an e.g. 10 per cent larger initial GDP per capita was associated with a 0.14 percentage point lower annual growth rate of pharmaceutical expenditure between 2000 and 2008 (with 95% confidence interval [-0.25, -0.02]). Again, the trend difference by GDP per capita disappeared after 2008. Similar results (not shown here) were obtained when not the GDP per capita itself but the estimated potential GDP per capita (which intends to capture the pure economic performance of the countries in the absence of demand-side fluctuations) was used in the analysis.

The two other models used for robustness check and not reported in Table 2 (i.e. the random effects model without random slopes and the random effects model with autoregressive error terms) gave similar results: the trend difference was about 2.4 percentage points before the onset of the crisis and not significant after that.

Meanwhile, even after controlling for other factors, the growth rate of pharmaceutical expenditure was much higher before 2008 than after it, so the flattened expenditure curves in Figure 1 cannot be fully explained by the changes in GDP per capita during the crisis. The GDP-adjusted trend growth rate was around 3.6 per cent on average, 2.7 per cent in the higher-income and 4.7 per cent in the lower-income countries until 2008. After 2008 the average growth rate was not significantly different from zero (-0.8 per cent) at the 5 per cent level, and there was no significant trend difference between the higher and lower-income countries.

We also fitted models without separating the two sub-periods (they are not reported in Table 2). In this case no statistically significant trend difference was observed between the pharmaceutical expenditure of the higher- and lower-income countries.

(Table 2 about here)

The country-specific intercepts of the hierarchical linear model (equation (2) in model (1)-(3)) give information about the relative level of pharmaceutical expenditure of countries in 2008 after controlling for GDP per capita, proportion of old-age population and life expectancy. According to Table 3, Greece was characterized by the largest intercept, i.e. the largest expenditure compared to countries with similar income and other explanatory variables (c.f. Lambrelli and O'Donnell 2011, who analyzed failed attempts to control pharmaceutical expenditure in Greece). Table 3 also displays the country-specific time trends before and after the onset of the economic crisis (calculated from equation (3)). After controlling for the other explanatory variables, the model estimates a remarkably high (i.e. higher than 5 per cent) pre-crisis trend growth rate of

pharmaceutical expenditure for Estonia, Greece, Hungary, Ireland and the Slovak Republic (Greece having the largest slope). The vast majority of these countries belong to the lower-income group. Country-specific trend growth rates were generally negative or close to zero after 2008, with two exceptions (Greece and Ireland, both having trend growth rates above 2 per cent even in this period).

Figure 3 gives a picture about the country-specific hypothetical time trends and about the aggregate time trends in higher- versus lower-income countries of pharmaceutical expenditure by assuming that the explanatory variables (GDP per capita, proportion of population above the age of 65 and life expectancy at birth) were fixed at the given country's average level. These lines differ from those in Figure 1 because the effect of the explanatory variables was controlled for.

(Table 3 about here)

(Figure 3 about here)

For comparison, the third and fourth columns of Table 2 provide estimates from models, in which the dependent variable is the logarithm of non-pharmaceutical health expenditure. In this case there is no statistically significant difference between the time trends of the higher- and lower-income countries in either period (although there is some difference in 2000-2008 if income is measured with GDP per capita on a continuous scale). Hence the difference of time trends observed above between the two groups is a feature of pharmaceutical expenditure not shared by health expenditure in general.

It is also interesting to compare the coefficients of the logarithm of GDP per capita (i.e. the income elasticities) in various models. Table 2 shows that a one per cent increase of GDP per capita increases non-pharmaceutical health expenditure by around 0.90 per cent. This is roughly in line with other estimates in the literature, which generally yield elasticities slightly lower than one (e.g. the elasticity of 0.87 in Baltagi and Moscone 2010). The income elasticity of pharmaceutical

expenditure is slightly less (around 0.6) but note that in this model the effect of GDP is partially captured by a change in trends.

Theory predicts that external price referencing and parallel trade reduce prices of new pharmaceuticals in higher-income countries, and increase drug prices in lower-income ones, hence the growth rate of pharmaceutical expenditure will be higher in the latter compared to the former group. In this paper we fitted various hierarchical linear models on country-level panel data to show that – even after controlling for compounding factors – this trend difference of growth rates was significant in the European Union between 2000 and 2008 but disappeared after the onset of the global economic crisis. Throughout the analysis we measured expenditure items in a common currency (euro) because pharmaceuticals can be regarded as tradeable goods hence their prices can be compared in a common currency – at least at the time of their introduction in a new country. Therefore, for the purpose of the specific examination of pharmaceutical expenditure as opposed to health expenditure in general, the use of purchasing-power-parity-adjusted series (such as e.g. in Clemente et al. 2008) or series in national currency is not justified.

Our results support the presence of narrowing price corridor and the price convergence of pharmaceuticals among European countries because alternative explanations such as volume growth differences or composition effects are unlikely to explain the two percentage point annual difference between the expenditure growths of the two groups in the 2000-2008 period. Although aggregate pharmaceutical consumption by volume is difficult to measure and reliable data sources are rare, sporadic evidence suggests that differences in volume growth cannot be such large. The worldwide Hoebert et al. (2011) study estimates an only two percentage point growth difference in the overall 2000-2008 period in the volume of non-hospital pharmaceutical consumption (which usually constitutes the larger volume in total consumption) between high-income and upper-middle income countries defined more broadly than our classification. Hence we expect a similarly small volume growth difference within the European Union in the given period. It is also possible but

unlikely that a composition effect pushed up aggregate expenditure substantially more in the lower-income than in the higher-income European countries because empirical studies suggest an effect in the opposite direction, i.e. that new medicines tend to be introduced earlier in the higher-income than in the lower-income European countries (Danzon et al. 2005). Hence we can conclude that price convergence lies in most part behind the observed expenditure trend differences, for which EPR and parallel trade provide the most plausible explanations (see also Glynn 2009; Leopold et al. 2012).

Higher growth rate of pharmaceutical expenditure put extra burden on health care budgets in lower-income countries, and resulted in disproportionately more pharmaceutical cost-containment measures compared to higher-income countries after the onset of the global economic crisis (Vogler et al. 2011). Examples include Greece, Portugal, Spain, Ireland, Hungary and the Baltic countries (Vandoros and Stargardt 2013; Garuoliene et al. 2011; Rützel and Pudersell 2011; Behmane and Innus 2011; Kaló et al. 2012a; Leopold et al. 2014). As a consequence the difference in trend growth rates disappeared after 2008. It remains to be seen whether this change due to cost-containment measures in countries with economic difficulties is temporary or permanent. If the EPR hypothesis is correct then the trend difference may return as soon as European economies achieve their normal growth path again.

Finally, it should be noted that there may be competing models for the trend difference of pharmaceutical expenditure in the two groups of countries. For instance, Lago-Penas et al. (2013) separated the long- and short-term effects of GDP on *total* health expenditure by including the potential GDP and the output gap (i.e. the trend and the cycle components of the GDP) as separate explanatory variables. However, pharmaceutical prices and pharmaceutical consumption should depend much less on the cyclical stance of the economy than other components of health expenditure such as the wage of health care employees, so a separate treatment of the potential GDP and output gap (which might partially explain the differing trends in the two groups) is much

less justified for pharmaceutical expenditure than for total health expenditure. Moreover, we did not observe different trend growth rates of non-pharmaceutical health expenditure in the two groups of countries even between 2000 and 2008, which suggests a pharmaceutical-specific explanation for the trend difference – and this again points towards the EPR and parallel trend hypothesis.

## **Conclusion**

Our study is among the first analyses to prove the higher growth rate of pharmaceutical expenditure in lower-income countries, a potential consequence of narrowing European price corridor of pharmaceuticals. As causal relationship between EPR, parallel trade and higher growth rate of pharmaceutical expenditure in lower- vs. higher-income countries could not be established, and we could not control country specific pharmaceutical expenditure for changes in volume or prescription patterns, generalizability of our conclusions is limited. In the future, the examination of product-level data of pharmaceutical consumption from different countries with panel data methods – as was done e.g. in Timur et al. (2011) without focusing on EPR and by Leopold et al. (2012) with descriptive and regression methods – may yield further evidence on the narrowing of the price corridor.

## **References**

- Baltagi B H, Moscone F. 2010. Health care expenditure and income in the OECD reconsidered: Evidence from panel data. *Economic Modelling* **27(4)**: 804-811.
- Baltagi B H, Wu P X. 1999. Unequally spaced panel data regressions with AR(1) disturbances. *Econometric Theory* **15**: 814-823.

Bates D, Maechler M, Bolker B, Walker S. 2014. lme4: Linear mixed-effects models using Eigen and S4. R package version 1.1-5. Downloaded from: <http://cran.r-project.org/package=lme4>

Behmane D, Innus J. 2011. Pharmaceutical policy and the effects of the economic crisis: Latvia. *Eurohealth* **17(1)**: 8-10.

Boehler C. 2013. A new spectre is haunting Europe! International price referencing and its impact on lower income European economies. Poster presented at III. Croatian and III. Adriatic Congress on Pharmacoeconomics and Outcomes Research (The Role of Farmacoeconomics in Developing Countries), Brijuni, Croatia, April 25-27, 2013.

Bouvy J, Vogler S. 2013. Background paper 8.3. Pricing and reimbursement policies: impacts on innovation. Priority medicines for Europe and the world “A public health approach to innovation” update on 2004 background paper. *World Health Organization*. Available at: <http://apps.who.int/medicinedocs/documents/s20229en/s20229en.pdf>

Carone G, Schwierz C, Xavier A. 2012. Cost-containment policies in public pharmaceutical spending in the EU. *Economic Papers* **461**, September 2012. Available at: [http://ec.europa.eu/economy\\_finance/publications/economic\\_paper/2012/pdf/ecp\\_461\\_en.pdf](http://ec.europa.eu/economy_finance/publications/economic_paper/2012/pdf/ecp_461_en.pdf)

Clemente J, Marcuello C, Montañés A. 2008. Pharmaceutical expenditure, total health-care expenditure and GDP. *Health Economics* **17(10)**: 1187-1206.

Creativ-Ceuticals 2014. External reference pricing of medicinal products: simulation-based considerations for cross-country coordination. Available at: [http://ec.europa.eu/health/systems\\_performance\\_assessment/docs/erp\\_reimbursement\\_medicinal\\_products\\_en.pdf](http://ec.europa.eu/health/systems_performance_assessment/docs/erp_reimbursement_medicinal_products_en.pdf)

Danzon P M, Towse A. 2003. Differential pricing for pharmaceuticals: reconciling access, R&D and patents. *International Journal of Health Care Finance and Economics* **3(3)**: 183-205.

Danzon P M, Wang Y R, Wang L. 2005. The impact of price regulation on the launch delay of new drugs - evidence from twenty-five major markets in the 1990s. *Health Economics* **14(3)**: 269-292.

Dreger C, Reimers H E. 2005. Health care expenditures in OECD countries: A panel unit root and cointegration analysis. *International Journal of Applied Econometrics and Quantitative Studies* **2(2)**: 5-20.

ECB. 2014. Statistical Data Warehouse. *European Central Bank*, 2014. Available at:

<http://sdw.ecb.europa.eu/browse.do?node=2018779>

Espin J, Rovira J, de Labry A O. 2011. Working Paper 1: External Reference Pricing. WHO/HAI Project on Medicine Prices and Availability, Review Series on Pharmaceutical Pricing Policies and Interventions. World Health Organization and Health Action International. Available at:

<http://www.haiweb.org/medicineprices/05062011/ERP%20final%20May2011.pdf>

European Commission. 2014. Eurostat database, 2014. Available at:

<http://epp.eurostat.ec.europa.eu/portal/page/portal/statistics/themes>

Galizzi MM, Ghislandi S, Miraldo M. 2011. Effects of reference pricing in pharmaceutical markets. *Pharmacoeconomics* **29(1)**: 17-33.

Garuoliene K, Alonderis T, Marcinkevicius M. 2011. Pharmaceutical policy and the effects of the economic crisis: Lithuania. *Eurohealth* **17(1)**: 1-4.

Gelman A, Hill J. 2007. *Data Analysis Using Regression and Multilevel / Hierarchical Models*. 1<sup>st</sup> edn. Cambridge University Press.

Glynn D. 2009. The effects of parallel trade on affordable access to medicines. *Eurohealth*. **15(2)**:1-4.

Inotai A, Petrova G, Vitezic D, Kaló Z. 2014. Benefits of investment into modern medicines in Central-Eastern European countries. *Expert Review of Pharmacoeconomics & Outcomes Research* **14(1)**: 71-79.

- Hoebert J, Laing R, Stephens P. 2011. The world medicines situation 2011. Pharmaceutical consumption. *World Health Organization*. Available at:  
<http://apps.who.int/medicinedocs/documents/s20035en/s20035en.pdf>
- Kaló Z, Alabbadi I, Al Ahdab OG, Alowayesh M, Elmahdawy M, Al-Saggabi AH, Tanzi VL, Al-Badriyeh D, Alsultan HS, Ali FM, Elsis GH, Akhras KS, Vokó Z, Kanavos P. 2015. Implications of external price referencing of pharmaceuticals in Middle East countries. *Expert Review of Pharmacoeconomics & Outcomes Research* **15(6)**: 993-8.
- Kaló Z, Annemans L, Garrison L P. 2013. Differential pricing of new pharmaceuticals in lower income European countries. *Expert Review of Pharmacoeconomics & Outcomes Research* **13(6)**: 735-741.
- Kaló Z, Boncz I, Inotai A. 2012a. Implications of economic crisis on health care decision-making in Hungary: An opportunity to change? *Journal of Health Policy and Outcomes Research* **1**: 20 -26.
- Kaló Z, Inotai A, Merész G. 2012b. International Comparison of Pharmaceutical Expenditure in Middle Income Countries: Methodological Questions. *Value in Health* **15(4)**: A21
- Kanavos P, Nicod E, Espin J, van den Aardweg S. 2010. Short- and long-term effects of value-based pricing vs. external price referencing. *Eminent*, January 2010. Available at:  
[http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/valuebased\\_pharmapricing\\_012010\\_en.pdf](http://ec.europa.eu/enterprise/sectors/healthcare/files/docs/valuebased_pharmapricing_012010_en.pdf)
- Ke X, Saksena P, Holly A. 2011. The determinants of health expenditure: A country-level panel data analysis. *Working Paper of the Results for Development Institute*, World Health Organization. Available at: [http://www.who.int/health\\_financing/documents/report\\_en\\_11\\_deter-he.pdf](http://www.who.int/health_financing/documents/report_en_11_deter-he.pdf)
- Lambrelli D, O'Donnell O. 2008. Why does the utilization of pharmaceuticals vary so much across Europe? Evidence from micro data on older Europeans. *University of York HEDG Working Paper* 09/06.

- Lambrelli D, O'Donnell O. 2011. The impotence of price controls: failed attempts to constrain pharmaceutical expenditures in Greece. *Health Policy* **101(2)**: 162-171.
- Leopold C, Mantel-Teeuwisse AK, Seyfang L, Vogler S, de Joncheere K, Laing RO, Leufkens H. 2012. Impact of External Price Referencing on Medicine Prices – A Price Comparison Among 14 European Countries. *Southern Medical Review* **5(2)**: 34-41.
- Leopold C, Mantel-Teeuwisse AK, Vogler S, Valkova S, de Joncheere K, Leufkens HG, Wagner AK, Ross-Degnan D, Laing R. 2014 Effect of the economic recession on pharmaceutical policy and medicine sales in eight European countries. *Bulletin of the World Health Organization* **92(9)**: 630-640.
- OECD. 2011. Pharmaceutical expenditure. In: *Health at a Glance 2011: OECD Indicators*. OECD Publishing. Available at: [http://dx.doi.org/10.1787/health\\_glance-2011-63-en](http://dx.doi.org/10.1787/health_glance-2011-63-en)
- OECD. 2014. Stat Extracts 2014. Available at: <http://stats.oecd.org/>
- R Core Team. 2014. R: A language and environment for statistical computing. *R Foundation for Statistical Computing*, Vienna, Austria. URL: <http://www.R-project.org/>.
- Ridley D B. 2005. Price differentiation and transparency in the global pharmaceutical marketplace. *Pharmacoeconomics* **23(7)**: 651-658.
- Rüütel D, Pudersell K. 2011. Pharmaceutical policy and the effects of the economic crisis: Estonia. *Eurohealth* **17(1)**: 5-8.
- Timur A, Picone G, DeSimone J. 2011. Has the European Union achieved a single pharmaceutical market? *International Journal of Health Care Finance and Economics* **11**: 223-244.
- Vandoros S, Stargardt T. 2013. Reforms in the Greek pharmaceutical market during the financial crisis. *Health Policy* **109(1)**: 1-6.
- Vogler S, Zimmermann N, Leopold C, de Joncheere K. 2011. Pharmaceutical policies in European countries in response to the global financial crisis. *Southern Medical Review* **4(2)**: 69–79.

## TABLES

Table 1: Descriptive statistics of the variables in the higher- and lower-income European countries (2000-2012 combined)

	Higher-income countries					Lower-income countries				
	N	Mean	S.D.	Min.	Max.	N	Mean	S.D.	Min.	Max.
Pharmaceutical exp. per capita (euro)	147	411	89	238	614	110	236	105	52	586
Non-pharma health exp. per capita (euro)	147	2535	643	1224	4344	110	772	421	176	1716
Total health exp. per capita (euro)	147	2946	662	1584	4646	110	1007	516	228	2113
Pharmaceutical exp. / GDP (per cent)	147	1.28	0.39	0.45	1.93	110	1.84	0.40	1.11	2.84
Total health exp. per GDP (per cent)	147	8.82	1.68	4.61	11.77	110	7.51	1.41	4.73	10.23
Pharma / total health exp. (per cent)	147	14.4	3.5	6.5	23.3	110	24.8	4.9	16.7	40.2
GDP per capita (1000 euro)	156	34.2	11.5	21.0	80.8	117	12.6	5.0	4.4	23.6
Population above 65 years (per cent)	156	16.1	2.3	10.7	21.0	117	15.5	2.1	11.4	19.8
Life expectancy at birth (years)	156	79.8	1.3	76.6	82.3	117	76.8	2.9	70.9	82.6

Source: own calculations based on OECD, Eurostat and ECB data.

Unweighted averages and standard deviations (S.D.)

N = number of country-year observations

Table 2: Estimation results from hierarchical linear models

Dependent variable		Log pharmaceutical expenditure per capita		Log non-pharmaceutical health expenditure per capita	
		(1)-(3)	(1)-(3')	(1)-(3)	(1)-(3')
<i>Trend equations (2000-2008)</i>					
Trend (2000-2008)	$\delta_{Pre}$	0.0266*** (0.0062)		0.0162*** (0.0055)	
Trend (2000-2008) * lower-income	$\delta_{LPre}$	0.0207** (0.0084)		0.0105 (0.0068)	
Average trend (2000-2008)	$\delta_{0,Pre}$		0.0360*** (0.0062)		0.0214*** (0.0052)
Trend (2000-2008) * Log GDP per capita in 2000	$\delta_{1,Pre}$		-0.0136** (0.0059)		-0.0110** (0.0048)
<i>Trend equations (2008-2012)</i>					
Trend (2008-2012)	$\delta_{Post}$	-0.0120* (0.0072)		0.0157** (0.0063)	
Trend (2008-2012) * lower-income	$\delta_{LPost}$	0.0061 (0.0096)		-0.0096 (0.0082)	
Average trend (2008-2012)	$\delta_{0,Post}$		-0.0078 (0.0064)		0.0125** (0.0055)
Trend (2008-2012) * Log GDP per capita in 2000	$\delta_{1,Post}$		-0.0093 (0.0065)		0.0026 (0.0054)
<i>Control parameters</i>					
Log GDP per capita (euro)	$\beta_{GDP}$	0.588*** (0.061)	0.605*** (0.062)	0.896*** (0.055)	0.893*** (0.055)
Proportion of population above 65 years (per cent)	$\beta_{old\ age}$	-0.0273** (0.0129)	-0.0286** (0.0129)	-0.0128 (0.0112)	-0.0167 (0.0115)
Life expectancy at birth (years)	$\beta_{life\ exp}$	0.0071 (0.0136)	0.0024 (0.0137)	0.0245** (0.0123)	0.0244** (0.0123)
Constant	$\alpha_0$	-0.164 (1.116)	0.0526 (1.144)	-3.361*** (1.008)	-3.261*** (1.013)
<i>Hyperparameters</i>					
Standard deviation of $v$	$\sigma_v$	0.283*** (0.048)	0.288*** (0.049)	0.240*** (0.054)	0.243*** (0.051)
Standard deviation of $w$	$\sigma_w$	0.017*** (0.003)	0.016*** (0.003)	0.013*** (0.002)	0.013*** (0.002)
Standard deviation of $\varepsilon$	$\sigma_\varepsilon$	0.048*** (0.002)	0.048*** (0.002)	0.044*** (0.002)	0.044*** (0.002)
Correlation of $u$ and $v$	$\lambda$	0.327 (0.213)	0.344 (0.204)	-0.138 (0.299)	0.116 (0.297)
<i>Number of observations</i>				257	
<i>Number of countries</i>				21	

Source: own calculations based on OECD, Eurostat and ECB data

Standard errors are reported in parentheses.

\*\*\*  $p < 0.01$ , \*\*  $p < 0.05$ , \*  $p < 0.1$

All models were estimated on the country panel between years 2000 and 2012.

Table 3: Estimated country-specific intercepts and time trends of pharmaceutical expenditure after controlling for compounding variables

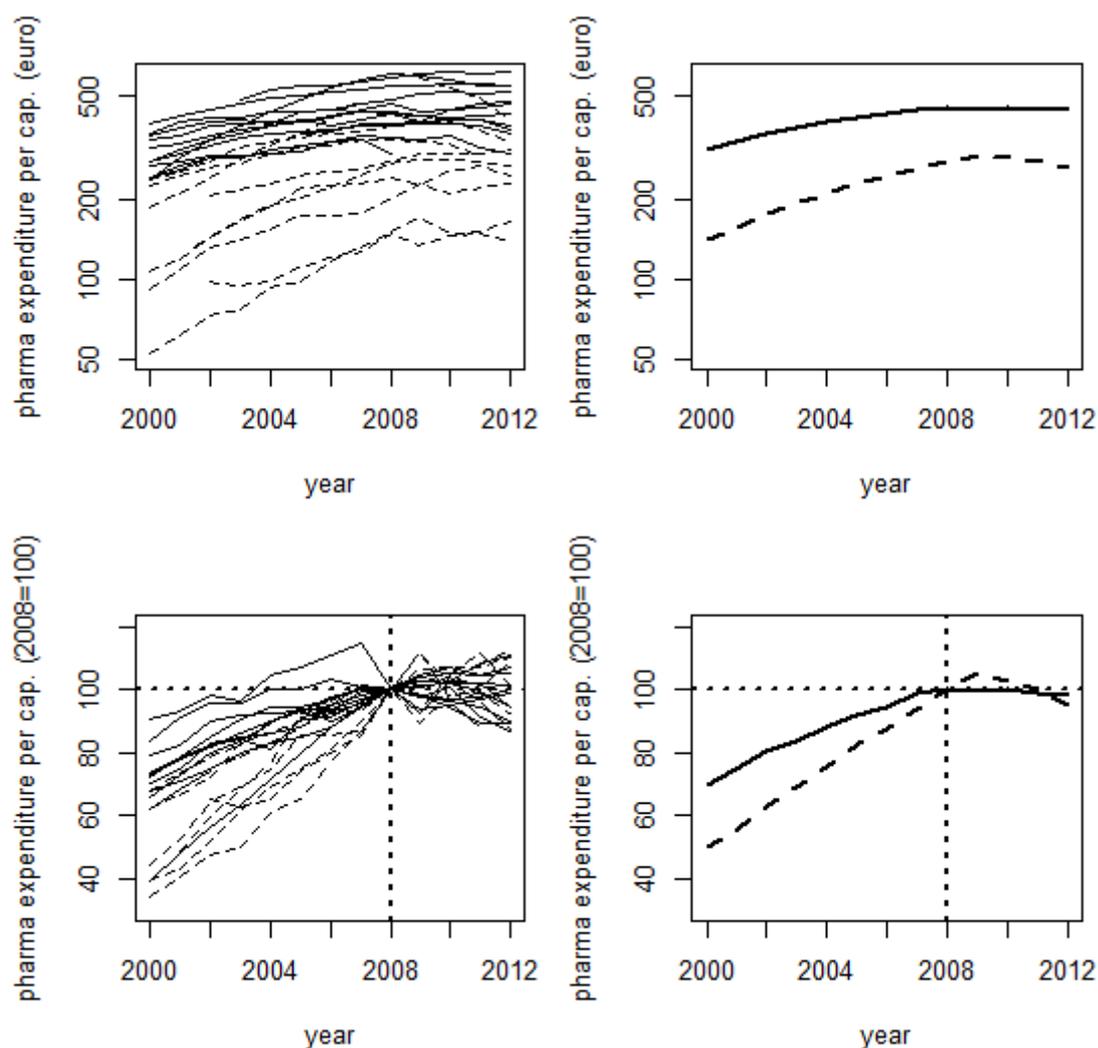
Country	Intercept	Annual time trend	Annual time trend
		2000-2008	2008-2012
	$v_i$	$\tau_{it}$ for $t \leq 2008$	$\tau_{it}$ for $t > 2008$
<i>Higher-income countries</i>			
Austria	0.054	0.030	-0.009
Belgium	0.376	0.026	-0.013
Denmark	-0.378	0.020	-0.019
Finland	-0.009	0.030	-0.009
France	0.313	0.025	-0.014
Germany	0.289	0.040	0.001
Ireland	0.016	0.065	0.027
Italy	0.245	0.009	-0.029
Luxemburg	-0.639	0.005	-0.034
Netherlands	-0.168	0.037	-0.002
Sweden	0.011	0.019	-0.020
United Kingdom	-0.262	0.011	-0.028
Average of higher income countries	-0.013	0.026	-0.012
<i>Lower-income countries</i>			
Czech Republic	-0.189	0.045	-0.008
Estonia	-0.384	0.063	0.009
Greece	0.461	0.081	0.028
Hungary	0.210	0.057	0.003
Poland	-0.363	0.028	-0.026
Portugal	0.226	0.030	-0.024
Slovak Republic	0.050	0.056	0.003
Slovenia	0.023	0.039	-0.014
Spain	0.118	0.031	-0.023
Average of lower income countries	0.017	0.048	-0.006

Source: own calculations based on OECD, Eurostat and ECB data

Results from the hierarchical linear model (equations (2) and (3)) on pharmaceutical expenditure per capita (first column in Table 2)

## FIGURES

Figure 1: Pharmaceutical expenditure per capita in the higher- (solid line) and lower-income (dashed line) group of countries, 2000-2012



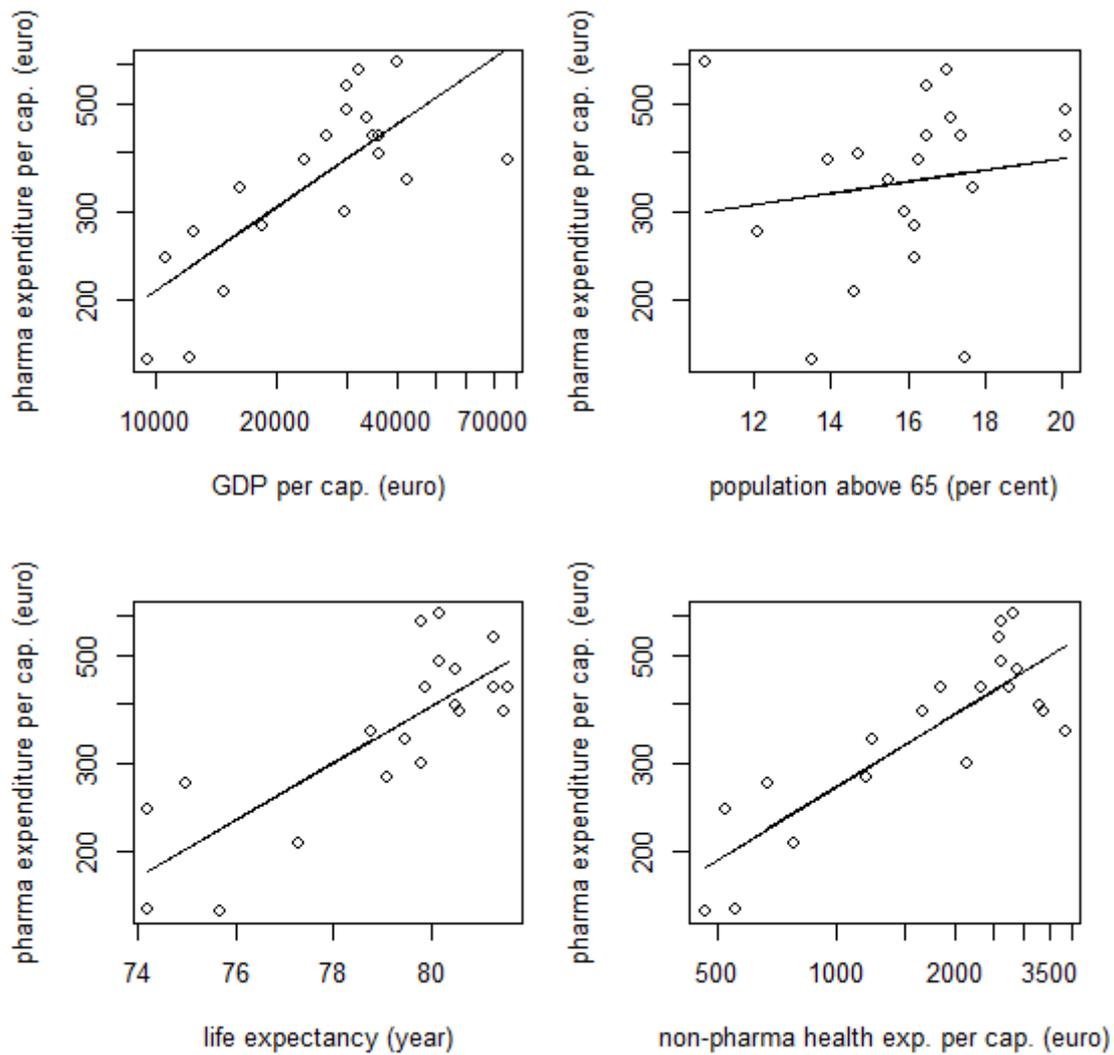
Source: own calculations based on OECD, Eurostat and ECB data

Solid lines indicate higher-income, dashed lines lower-income countries.

Lower panel shows data normalized to 2008=100%. Upper panel uses per capita values on the logarithmic scale.

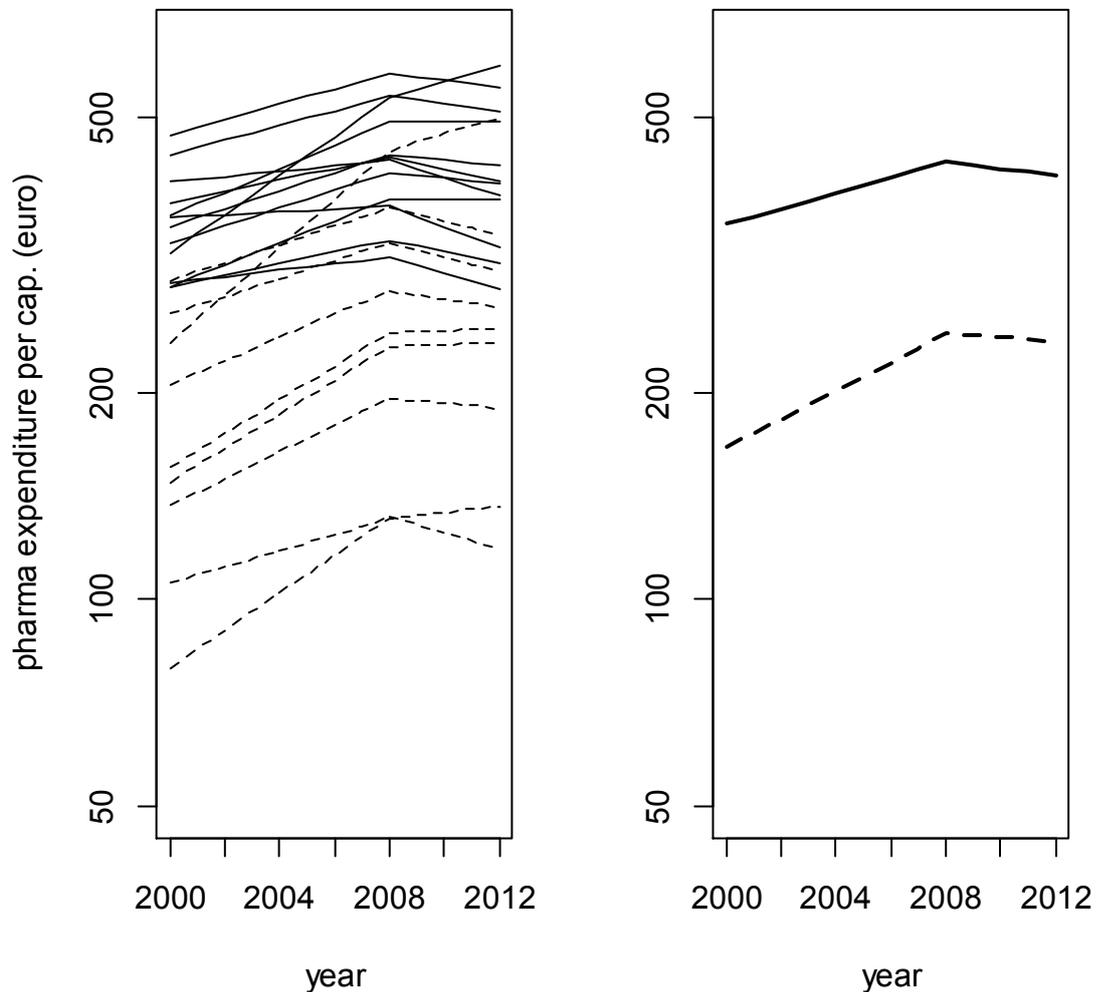
Graphs on the right show group-wise means (of higher- vs. lower-income countries). Group-wise means were calculated after imputation of missing values from the hierarchical linear model (originally 16 values were missing out of the 273 country-year data points).

Figure 2: Relationship of pharmaceutical expenditure per capita and other variables in 2008



Source: own calculations based on OECD, Eurostat and ECB data  
 Logarithmic scales are used for the expenditure variables and GDP. Univariate regression lines are displayed.

Figure 3: Estimated country-specific and average time trends of pharmaceutical expenditure when explanatory variables are fixed at their country-specific averages (solid lines: higher-income, dashed lines: lower-income countries)



Source: own calculations based on OECD, Eurostat and ECB data  
 Results from the hierarchical linear model on pharmaceutical expenditure per capita (first column in Table 2) when the explanatory variables are fixed at each country's average level.  
 Logarithmic scale is used.  
 Solid lines indicate higher-income, dashed lines lower-income countries.  
 The graph on the right shows group-wise means (of higher- vs. lower-income countries).