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Geographic and dynamic heterogeneity of public pharmaceutical expenditure

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Health Economics Papers
2007:2

University of Southern Denmark

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Abstract

A regression model for per capita public pharmaceutical expenditure, based on aggregate data from fifty Spanish provinces is analyzed. In contrast to previous practice, the effects of determinants on pharmaceutical expenditure are allowed to be heterogeneous by years and provinces using temporally and geographically expanded coefficients. Considerable parametric heterogeneity over time as well as across provinces is found, even when residual dynamic heterogeneity and interdependency as well as residual spatial spillover is controlled for. Thus, the need for further evidence and development of modeling practice when analyzing large area behavior using small area data is demonstrated.

Key Words: pharmaceutical expenditure; spatial expansion; varying coefficients; Seemingly Unrelated Regression; spatial autocorrelation

JEL Classifications: I11, L65, R15, C21, C23

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1. Introduction

During the last decade, the public pharmaceutical expenditure in Spain has grown at a rate superior to the total public health care expenditure (Darbá, 2003a, Darbá, 2003b). Thus, the public pharmaceutical expenditure makes up an increasing proportion of the total public health care expenditure. Pharmaceutical expenditure made up 16.8 percent in 1991 and had in 2002 increased to make up 23 percent of the total health care expenditure (Lopez-Casasnovas *et al.*, 2005). This growth is found not only in Spain, but is a general feature of the European Union countries (Ess *et al.*, 2003); however, with the Spanish pharmaceutical expenditure as a share of public health care expenditure exceeding EU averages (Lopez-Casasnovas, 2005). It is thus crucial to analyze the causes of this growth differential in order to focus on a rational use of medicine.

The regulation of the pharmaceutical market in Spain is shared between national regulatory bodies and the regional authorities. There are notable differences in health resources supply and health care expenditure across regions (Lopez-Casasnovas *et al.*, 2005) and there is evidence of regional variation in prescription rates and expenditure per prescription resulting in regional heterogeneity in pharmaceutical expenditure and in the pharmaceutical expenditure as a share of the total regional health care expenditure (Costa-Font and Puig-Junoy, 2004).

The studies on pharmaceutical expenditure from the regional perspective are very scant though it is possible to find a few works dealing with the analysis of regional health care expenditure (see e.g. Kitchener *et al.*, 2003, Levaggi and Zanola, 2003, Lopez-Casasnovas and Saez, 2001, Moscone and Knapp, 2005). Despite the ample body of evidence of variations in use of procedures in the literature on small-area variation (Folland *et al.*, 2003, Ham, 1988, Joines *et al.*, 2003, Wennberg and Gittelsohn, 1973, Westert *et al.*, 2004), few studies have examined the geographical variability in use of pharmaceuticals (see e.g. Dubois *et al.*, 2002, Metge *et al.*, 1999, Morgan, 2005). The causes of variation discussed in the literature are the prevalence of diseases, mixed opinions of the effectiveness of surgery, practice style, health supply resource and differing patient preferences.

Only a few studies of small-area variation have considered spatial variation in medical practice. Westert *et al.* (2004) studied spatial disparities in hospital discharges (measured by coefficients of variations) and found these disparities to be approximately unchanged during the 1980'es and 1990'es. Joines *et al.* (2003) found that hospitalization rates for low back problems varied significantly across the counties of

North Carolina. They further found that counties with similar rates clustered geographically and concluded that spatial effects are important and should be considered in small area studies. Moscone and Knapp (2005) explored the spatial patterns of mental health expenditure and established – similar to Joines et al. – the importance of controlling for spatial spillover. Moscone and Knapp's study found a positive significant spatial effect suggesting that adjacent local authorities mimic the behaviour of their neighbours and tend to have similar mental health expenditure.

The present study focuses on the provincial variations in the determination of public pharmaceutical expenditure in Spain and aims to contribute to the literature on small-area variation and determination of health care expenditure. Specifically, we suggest an integration of three modeling features. First, parametric heterogeneity is captured by specifying the model effects as functions of a time trend and geographical coordinates of the provinces. Second, in order to obtain efficient results, a Seemingly Unrelated Regression (SUR) framework is applied to capture inter-temporal residual correlation and time-varying residual variances. Finally, residual spatial spillover is controlled for by specifying spatially autocorrelated (SAC) residuals. It is concluded that the effects of determinants vary substantially across time as well as across provinces, and that potentially misleading conclusions regarding effects of key determinants like GDP and health system characteristics may occur if simpler specifications are applied.

2. The Spanish pharmaceutical market

In Spain, the prices of publicly financed pharmaceuticals are fully or partially controlled, and the price index of the medicines has practically not risen in the last decade. Nevertheless, this does not preclude that new products entering the market are introduced at a sales price higher than that of the already existing ones. Several studies have shown that the replacement of older drugs by newer, more expensive, drugs is the single most important reason for the increase in pharmaceutical expenditure (see e.g. Dubois *et al.*, 2000, Gerdtham and Lundin, 2004, Morgan, 2005), whereas the real price index of existing drugs is decreasing. The second most important reason is that a larger quantity consumed because of increases in the intensity of medication in terms of defined daily doses per patient. Similar results are found in analysis of the increasing pharmaceutical expenditure in Spain (Darbá, 2003b, Rovira *et al.*, 2001).

The Spanish national health system is a decentralized system in which the regulation of the pharmaceutical market is shared between national regulatory bodies and the regional authorities – called Autonomous Communities (AC) – however, most of the key regulatory bodies are run centrally at national level to reduce diversity and maintain overall control (Costa-Font and Puig-Junoy, 2004); see Figure 1 for a map of provinces by AC.

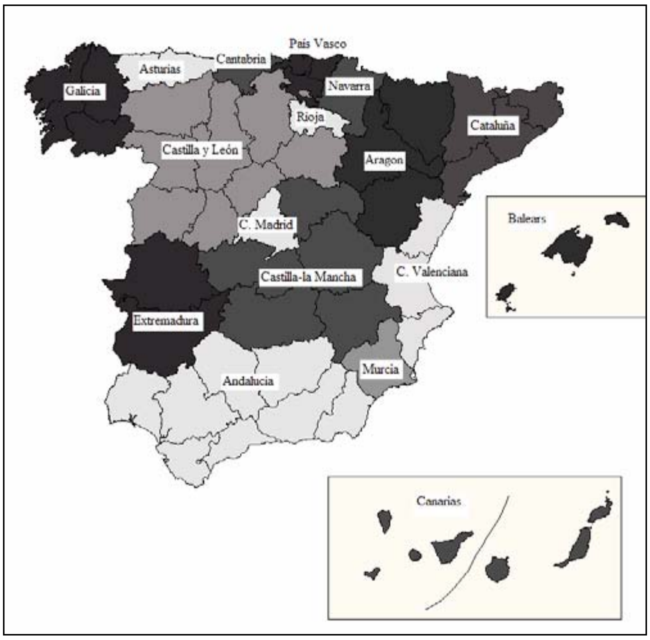

Figure 1. Provinces by ACs

Even though cost containment has been a major priority for publicly financed pharmaceuticals this has not resulted in significant savings in public expenditure (Costa-Font and Puig-Junoy, 2004, Darbá, 2003a, Darbá, 2003b). The average price for pharmaceuticals is below EU averages with older drugs priced significantly below the EU average (Puig-Junoy, 2004). The market for generic drugs was small compared to the EU average accounting for 3 percent of the market sales in 2000 and had increased to 6.4 percent by 2003 (Costa-Font and Puig-Junoy, 2004). There seems to be significant regional heterogeneity in the use of generics (Costa-Font and Puig-Junoy, 2004). New drugs are not priced significantly below the EU average and these drugs account for the largest market share (Costa-Font and Puig-Junoy, 2004, Darbá, 2003a, Darbá, 2003b). Different cost containment policies such as negative lists of excluded drugs, regulation of profits, repayments from pharmaceutical companies, reference pricing system and promotion of the use of generic drugs have had little effect on the overall increase in pharmaceutical expenditure. Some of these policies are under the devolved responsibility of the 17 regional health systems. The ACs have gradually become significant actors in the pharmaceutical policy along with the decentralization process starting in the early 1980s until the completion of the devolution process in 2002.

Funding is mainly centrally collected and distributed to the ACs. Until 2001, the regional health care financing was decided in a separate negotiation between the Minister of Health and the corresponding Regional Ministers in the 17 ACs, mainly allocating funds as block grants following the lines of an unadjusted capitation formula (Lopez-Casasnovas *et al.*, 2005). Since 2002 the health care expenditure is allocated as part of the general financing using a capitation formula with some demographic adjustments. Health care expenditure accounts for around 40 percent of the ACs' total funding. The ACs have some possibilities of raising funding by levying higher taxes; however, various centrally funds strive to maintain territorial equity. There are some inter-regional inequalities in health expenditure per capita, but the coefficient of variation in regional health care expenditure per capita is one of the lowest among health care systems for which territorial health care expenditure may be identified (see Lopez-Casasnovas and Saez, 2001).

There seems to be significant differences in hospital specialization, physician density and technology and it has been suggested that this diversity can partly explained by differences in particular Gross Domestic Product (GDP) and population structures (Lopez-Casasnovas *et al.*, 2005). The regional inequality in health expenditure is, however, not correlated with inequality in health outcomes (Lopez-Casasnovas *et al.*, 2005). There is evidence of significant regional variation in prescription rates and expenditure per prescription resulting in significant regional heterogeneity in pharmaceutical expenditure as a share of the total regional health care expenditure (Costa-Font and Puig-Junoy, 2004).

3. Methodology

Assuming a cross-section of $N = 50$ provinces, the basic linear regression model specifies

(1) $$y_t = X_t\beta + \upsilon_t, \quad \upsilon_t \sim N(0, \sigma^2 I)$$

where X_t is an *N* by *K* dimensional matrix of explanatory variables, y_t is an *N* dimensional vector of endogenous observations, β is a *K* dimensional vector of coefficient, and υ_t a residual with variance σ^2.

A restrictive assumption of the model (1) is that β is constant over time and across provinces. In order to allow these coefficients to vary across time and provinces, we apply expansions (Casetti, 1997, Jones and Casetti, 1992), i.e. the effect of the *k*'th regressor (*k* = 0 ,.., *K*, with the convention that β_0 is the constant term, i.e. $X_0 = 1$) is specified as

$$(2) \qquad \beta_k = \alpha_{0k} + \alpha_{Tk}T + \alpha_{Hk}H + \alpha_{H^2k}H^2 + \alpha_{Vk}V + \alpha_{V^2k}V^2 + \alpha_{HVk}HV$$

where α_{jk} (*j*=*T*, *H*, H^2, *V*, V^2, *HV*) are coefficients, T is a time trend, and *H* and *V* the horizontal (west to East) and vertical (South to North) coordinates of the geographical midpoints of the regions respectively, The square terms H^2 and V^2 together with the interaction term *HV* is inserted to allow for non-linear and diagonal dispersion of the β coefficients. Inserting (2) in (1) gives the expanded specification

$$(3) \qquad Y_t = \sum_{k=0}^{K} \{ \alpha_{0k} X_{tk} + \alpha_{Tk} (TX_{tk})$$

$$+ \alpha_{Hk}(HX_{tk}) + \alpha_{H^2k}(H^2 X_{tk}) + \alpha_{Vk}(VX_{tk}) + \alpha_{V^2k}(V^2 X_{tk}) + \alpha_{HVk}(HVX_{tk}) \} + \upsilon_t .$$

Operationally, the expanded specification (3) can be estimated by applying multiplicative interaction terms between X_k and the *T*, *H*, *V* and *HV* variables. Next, the β_k coefficients for each province by each time period, say β_{kit}, can be calculated from (2) together with their standard errors, as the β

parameters are simple linear functions of the α parameters. Finally, the average for each time period and the average for each region are readily obtained to serve illustrative and interpretational purposes.

In order to obtain efficient estimation results, the structure of the residuals needs consideration. First, to account for residual spatial spillover, the spatially autocorrelated (SAC) specification (Anselin, 1988) is applied to the residual of (3), i.e.,

(4) $\upsilon_t = \lambda W \upsilon_t + \varepsilon_t$,

where λ is an autocorrelation parameter and W an $N \times N$ contiguity matrix defined by letting w_{ij} equal $\frac{1}{n_i}$ if provinces i and j are neighbours ($i \neq j$) and 0 otherwise, as n_i is the number of neighbours to province i. Intuitively, the product $W\upsilon_t$ defines a variable, which for each province holds the average of υ_t in the neighbouring provinces. Next, when applying pooled data for T periods, the residuals are inter-correlated across time, and the variances for the cross-sections vary over time. Thus, between any two time periods, the residual covariance of ε_t is specified as

(5) $E(\varepsilon_t' \varepsilon_s) = \sigma_{ts}^2, \;\; t, s = 1,..,T$.

The model defined by (3)-(4)-(5) was estimated efficiently by applying the following Maximum Likelihood approach: We did a grid search of the relevant values of λ from -1 to +1. Conditioned on each λ, a Feasible Generalised Least Squares (F-GLS) estimation (Zellner, 1962) were applied to (3) using $(I - \lambda W) y_t$ instead of y_t and $(I - \lambda W) X_t$ instead of X_t to obtain SUR estimates of β. Finally, the set of results which maximized the log likelihood function were selected.

To provide devices for comparison of alternative models, some quantities are applied. One is a pseudo-R-square (R^2), calculated as the square of the correlation between y and its predicted values. A second device, which similar to the R-square measures can be used as a goodness-of-fit measure for comparison of models, is the familiar Akaike Information Criterion (AIC). Finally, Wald tests for the expansions are provided, i.e., for the hypotheses that α_T and/or (α_H, α_{H^2}, α_V, α_{V^2}, α_{HV}) equal 0.

4. Data

TABLE 1. Data applied for the study

Variable	Description	Source	Mean	Std. D.
EXP	Pharmaceutical Expenditure per capita	MSC, Inst. of Sanitary Information	164.899	31.710
GDP	GDP per capita	INE, National Statistical Inst.	9241.57	1766.14
PHARM	Pharmacists per 1000 inhabitants	INE, Social Indicators, 2004	1.206	0.225
BEDS	Hospital beds per 1000 inhabitants	MSC, National Hospital Catalogue	0.004	0.001
MED	Medical doctors per 1000 inhabitants	INE, Social Indicators, 2004	4.183	0.739
FEM	Population proportion of females	INE, National Statistical Inst.	0.506	0.006
FOREIGN	Population proportion of foreigners	INE, National Statistical Inst.	0.018	0.019
OLD	Population proportion over 65 years	INE, National Statistical Inst.	0.185	0.042
CHILD	Population proportion from 0 to 4 years	INE, National Statistical Inst.	0.090	0.016

Data for 50 Spanish provinces were collected. These provinces correspond with the NUT-3 level of aggregation according to EUROSTAT (excluding the autonomous cities of Ceuta and Melilla). The provinces are assembled in 17 Autonomous Communities (AC). The ACs correspond with the NUT-2 level of aggregation according to EUROSTAT and they present a higher degree of heterogeneity than the provinces. Regarding the decentralisation process, 7 of the ACs got independent responsibilities during the 1980s and 1990s, while the last 10 got responsibility for health care regulation in 2002. Until then these 10 ACs were centrally regulated.

The data were collected annually from 1996 to 2003 from two sources, The National Statistical Institute (INE) and the Ministry of Health and Consumption (MSC). The dependent variable is Public Pharmaceutical Expenditure (EXP) per capita. This variable includes the expenditure on extra-hospital drugs managed by the administration, but does not take private purchase into account. To capture influence of wealth, Gross Domestic Product per capita (GDP) is included as an explanatory variable.

Further, to capture influence of health care system, the variables number of pharmacists per 1000 inhabitants (PHARM), number of hospital beds per 1000 inhabitants (BEDS), and number of medical doctors per 1000 inhabitants (MED) are included. Finally, to capture influence of population structure, population proportions of females (FEM), foreigners (FOREIGN), people over 65 years (OLD), and 0-4 year old children (CHILD) are included. Table 1 presents the data applied, including means and standard deviations (average over eight years).

The variables describing the population control for socio-demographic risk factors and are considered to be proxies for need, whereas GDP controls for ability to pay. The variables describing the health care system do not solely reflect supply factors but are a result of interactions between demand and supply factors. Some health system variables may be considered to be substitutes of utilization of pharmaceuticals while others are complementary. A priori, one would expect the number of pharmacists to be complementary whereas we have no unambiguous a priori hypothesis for hospital beds and medical doctors.

Figure 2 shows the distribution of variables (average over eight years) by provinces. Spatial patterns are predominant, though not of a unique nature. For the expenditure, a clear indication of spatial spillover is seen. Comparing the maps in Figure 2 to the map of ACs in Figure 1, this spillover seems to be of an intra- as well as a supra-AC nature. Further, there seems to be some tendencies to North/West-South/East contrasts. With respect to GDP, medical doctors, hospital beds and, to some extent, pharmacists a clear North-South contrast is evident. This is also the case for some of the population characteristics, especially elderly, children and to some extent females, while foreigners seem to cluster especially over the East coast provinces.

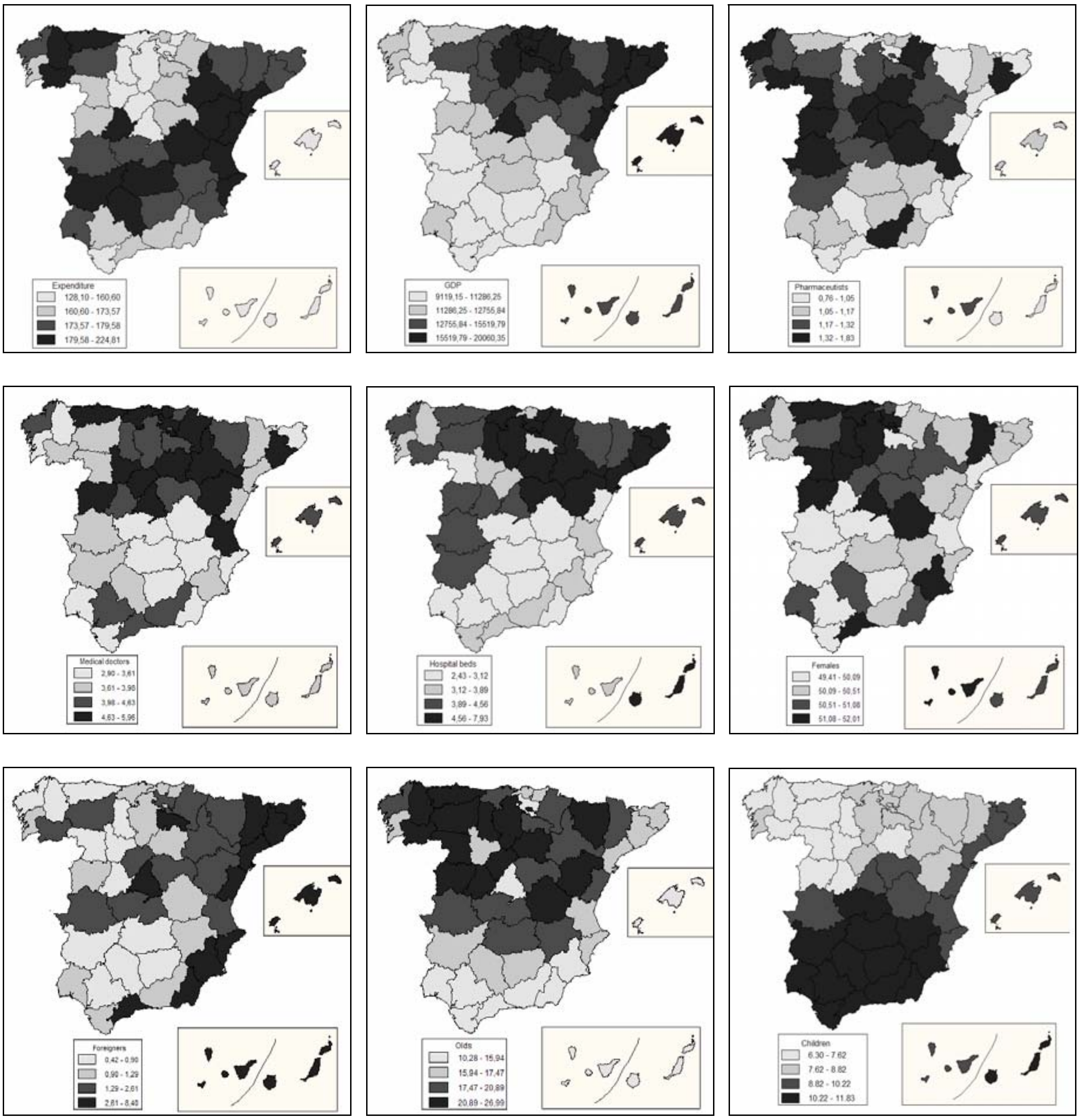

Figure 2. Variables (averaged over eight years) by provinces

5. Results

TABLE 2. SUR model								
	[1] Unexp.	[2] Time and space expanded						
	α_0	α_0	α_T	α_H	α_{HH}	α_V	α_{VV}	α_{HV}
Constant	5.349*** (0.546)	3.945*** (0.664)	-0.048 (0.065)	0.190 (0.202)	-0.062 (0.039)	0.821*** (0.227)	0.276*** (0.083)	-0.140* (0.075)
GDP	0.038 (0.025)	0.117*** (0.032)	-0.005 (0.005)	-0.010 (0.007)	-0.008*** (0.002)	-0.021*** (0.008)	0.001 (0.003)	0.006** (0.002)
PHARM	0.097*** (0.023)	-0.132*** (0.028)	0.002 (0.003)	0.001 (0.010)	0.001 (0.003)	0.033*** (0.010)	0.016*** (0.004)	-0.009** (0.004)
BEDS	0.014* (0.008)	0.018 (0.016)	-0.002 (0.002)	-0.010*** (0.003)	0.001 (0.001)	0.021*** (0.005)	-0.006*** (0.002)	0.007*** (0.002)
MED	0.002 (0.023)	0.088*** (0.030)	-0.008* (0.004)	-0.025*** (0.008)	0.005* (0.002)	-0.053*** (0.009)	-0.020*** (0.004)	0.004 (0.004)
FEM	-0.147 (0.535)	0.130 (0.694)	-0.086* (0.050)	0.365* (0.205)	-0.224*** (0.047)	0.816*** (0.241)	0.438*** (0.091)	-0.104 (0.080)
FOREIGN	-0.005 (0.005)	-0.016*** (0.005)	-0.001 (0.001)	0.004*** (0.001)	-0.001* (0.0004)	0.002 (0.002)	0.001 (0.001)	0.001 (0.001)
OLD	0.131*** (0.048)	0.164*** (0.060)	0.001 (0.005)	-0.011 (0.020)	0.007* (0.004)	-0.004 (0.027)	-0.003 (0.008)	-0.010 (0.008)
CHILD	-0.022 (0.026)	0.096* (0.051)	-0.026*** (0.009)	0.021* (0.012)	-0.013*** (0.003)	0.015 (0.011)	0.016*** (0.005)	-0.001 (0.004)
λ	0.906*** (0.013)	0.758*** (0.041)						
LogL	1367.66	1468.37						
AIC	-2643.32	-2736.74						
R^2	0.125	0.798						
Nondiag. test		97.36***						
Wald test			108.40***	93.02***				
Wald test			201.42***					
Note. Standard errors in parentheses. Significance indicated at 1% (***), 5% (**) and 10% (*) levels.								

The model for public pharmaceutical expenditure was estimated using a multiplicative Cobb-Douglas type specification, which were linearized by applying log transforms of the variables. A baseline unexpanded model and a model expanded by time and geographical coordinates. To enhance interpretation, the geographical coordinates *H* and *V* were mean-adjusted prior to the estimations. All models are controlled for residual temporal heterogeneity and dependency as well as spatial spillover by applying the integrated SUR and SAC framework.

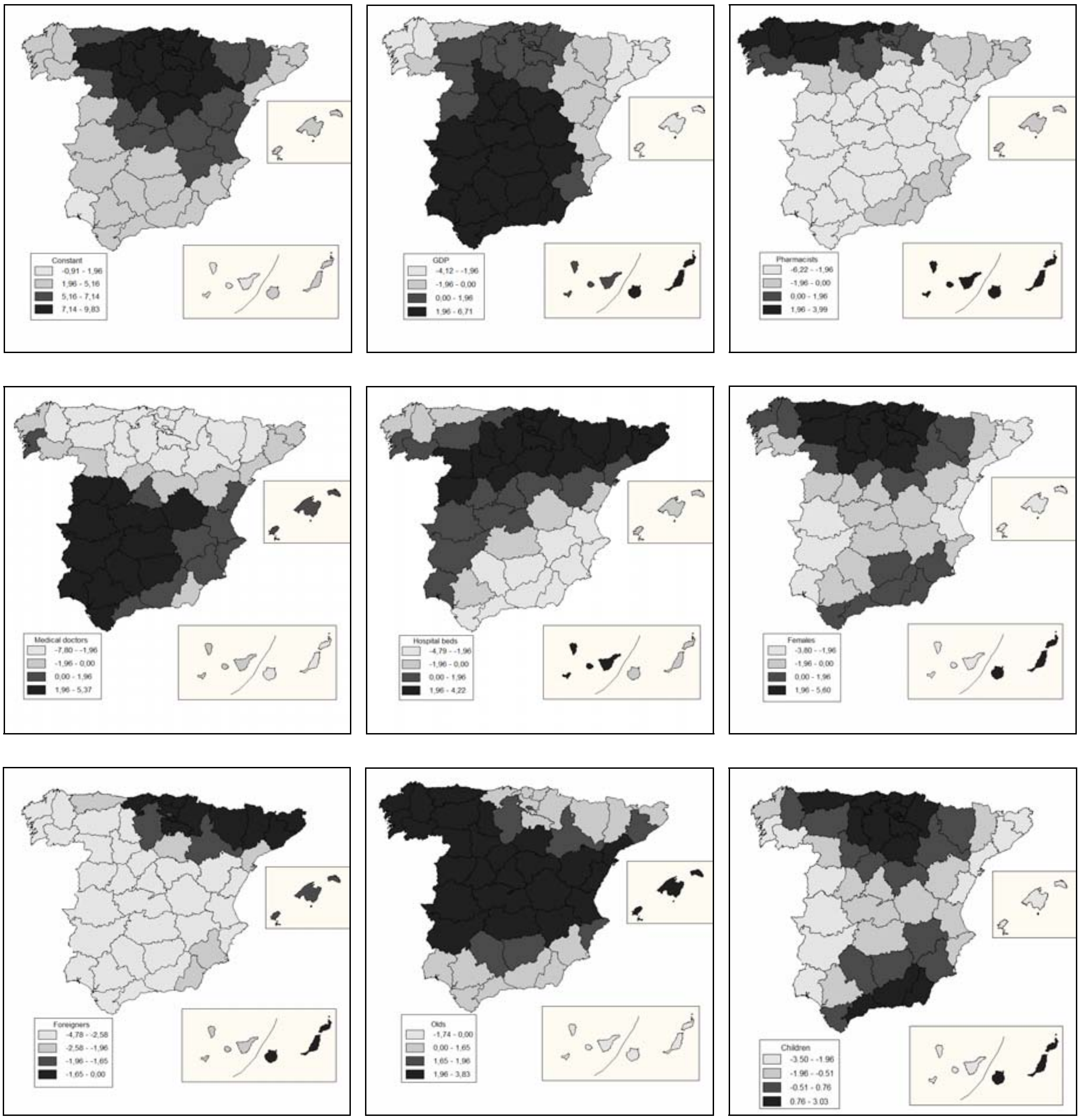

Figure 3. T values of coefficients (averaged over eight years) by provinces

Comparing initially the unexpanded specification [1] and the specification expanded by time [2], the importance of accounting for temporal parametric heterogeneity is evident. The LogL, AIC and R^2 criteria strongly support the expanded specification, and the Wald tests support the full expansion as well as the temporal and geographical parts. Further, one or more expansion coefficients are found to be significant for all variables. Several interpretational differences are obtained across the unexpanded and the expanded specifications. While the unexpanded specification reports GDP to be insignificant, the expanded specification shows GDP to have a baseline positive coefficient, which is exerted to considerable geographic variation. The baseline coefficient refers to the case T=H=V=0, i.e. the effect for 1995 for a province located in the geographical midpoint of Spain. This should not be directly compared to the corresponding coefficient of the unexpanded model [1]. To support interpretation of the geographical pattern, Figure 3 shows the *t* values of the coefficients by provinces (averaged over years). From the figure, it is seen that GDP exerts a significantly positive impact on EXP in the southern provinces, while a significantly negative impact is exerted in the North-Western and North-Eastern provinces.

Likewise, the coefficients for health system characteristics are exerted to considerable geographical variation. The effect of PHARM on EXP is seen to be significantly negative in the middle part of the country and significantly positive in the North-Western provinces. Considering BEDS, the effect is seen to vary from significantly negative in the South-Eastern provinces to significantly positive in a belt of Northern provinces, with an exception of the North-Western Galician and Asturian provinces. Regarding MED, a significantly negative effect is found for the Northern provinces, while a significantly positive effect is reported for the Southern provinces, with an exception of a belt of provinces along the South-Eastern coastal line. The effect of MED is further seen to be exerted to a temporal dispersion, as the time interaction is significantly negative. Considering Figure 4, where the coefficients are shown by years (averaged over provinces) together with 95 percent confidence intervals, the effect of MED is seen to drop from insignificant to significantly negative during the years.

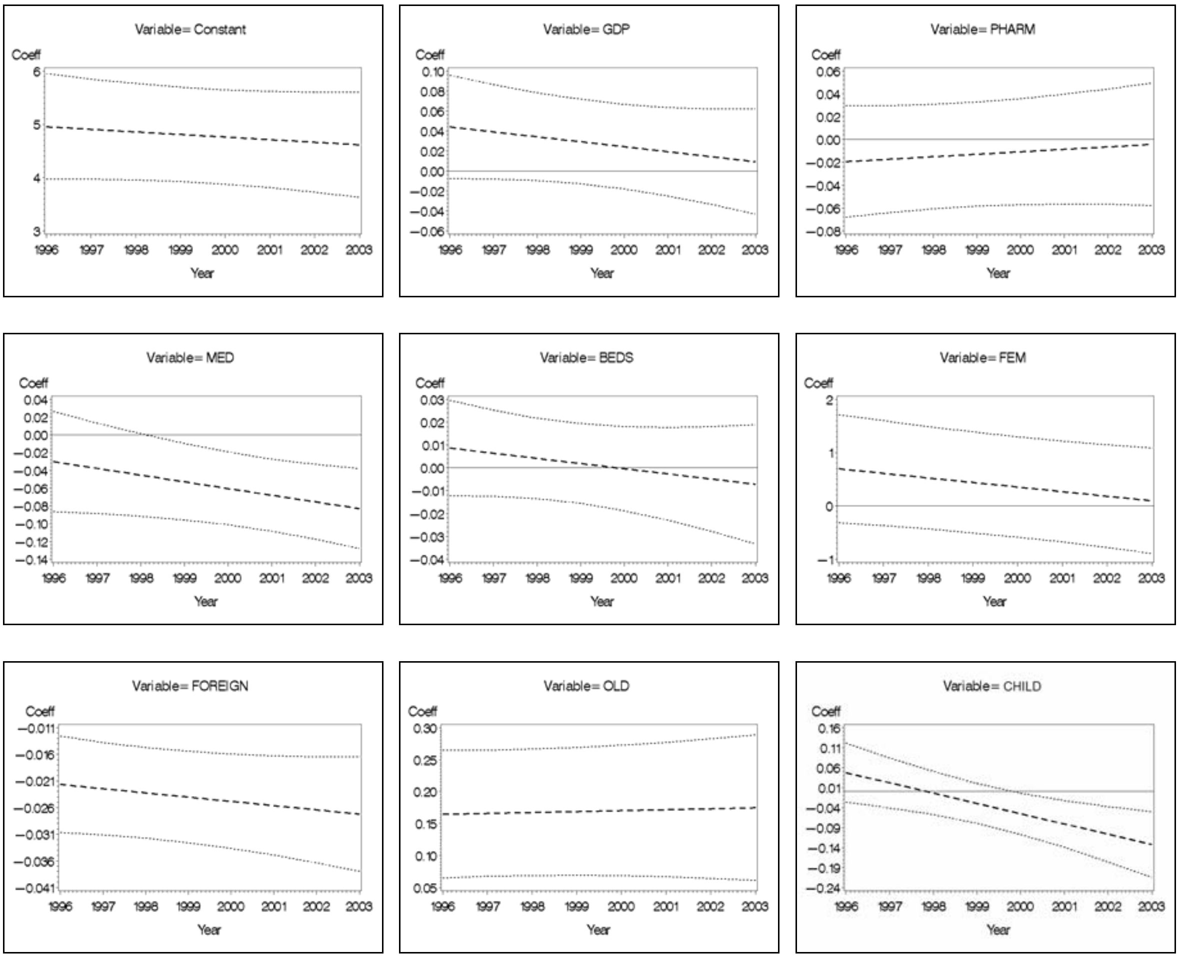

Figure 4. Coefficients (averaged over provinces) by year

Turning to the effects of characteristics of population structure, these are found to exert temporal as well as geographical heterogeneity. The effect of FEM is seen to be significantly negative in provinces in the Eastern and Western part of the country (especially belonging to the Extremadura, Valenciana and Cataluña ACs) and significantly positive in the provinces of the Northern ACs. The effect is further falling over years as indicated by Figure 4. For the case of FOREIGN, the effect is negative throughout the years and in most of the country, with an exception of the North-Eastern provinces where it is insignificant. Considering OLD, the effect is significantly positive throughout years and for most provinces with an exception of the very Southern and some North-Eastern provinces, where it is insignificant. Finally, the effect of CHILD are by and large parallel to that of

FEM, i.e. the effect is falling from significantly positive to significantly negative throughout years, and it is significantly negative for a few Eastern and Western provinces, while it is significantly positive for a few Northern provinces of the Pais Vasco and Navarra ACs.

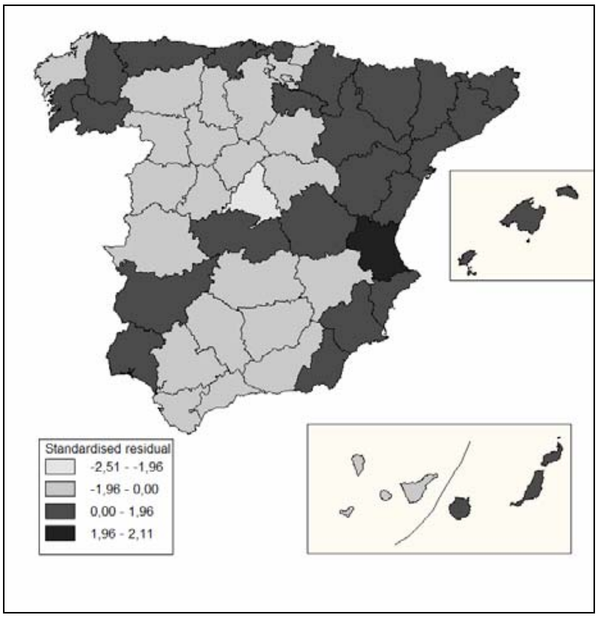

Figure 5. Standardised residuals (averaged over eight years) by provinces

Finally, Figure 5 shows the standardised residuals by provinces (averaged over years). Except for two provinces, the residuals are within a band of plus/minus 1.96. Thus, the geographical variation of the pharmaceutical expenditure seems to be well captured by the model.

6. Conclusions

The present study analyzes determination of public pharmaceutical expenditure and adds to previous knowledge practice by explicitly modeling temporal as well as geographical parametric heterogeneity while controlling for unobserved residual patterns in the forms of spatial spillover as well as temporal heterogeneity and interdependence. The necessity of accounting for heterogeneous effects of determinants is evident, as the effects of all determinants are exerted to substantial geographical and/or temporal variations. Especially, the effects of key determinants like GDP and health system characteristics are shown to be potentially misestimated when parametric heterogeneity is ignored. Thus, the complexity of spatial and temporal heterogeneity and spillover is clearly illustrated, and the need for further evidence and development of modeling practice is demonstrated.

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