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Abstract

Because of evidence of causal association between antibiotic use and bacterial resistance, the implementation of national policies has emerged as a interesting tool for controlling and reversing bacterial resistance. The aim of this study is to assess the impact of public policies on antibiotic use in Europe using a differences-in-differences approach. Comparable data on systemic administered antibiotics in 21 European countries are available for a 11-years panel between 1997 and 2007. Data on national campaigns are drawn from the public health literature. We estimate an econometric model of antibiotic consumption with country fixed effects and control for the main socioeconomic and epidemiological factors. Lagged values and the instrumental variables approach are applied to address endogeneity aspects of the prevalence of infections and the adoption of national campaigns. We find evidence that public campaigns significantly reduce the use of antimicrobials in the community by 1.4 to 3.7 defined daily doses per $1,000$ inhabitants. This roughly represents an impact between 7.2% and 18.5% on the mean level of antibiotic use in Europe between 1997 and 2007. The effect is robust across different measurement methods. Further research is needed to investigate the effectiveness of policy interventions targeting different social groups such as general practitioners or patients.

Keywords: Antibiotic use, public policies, national campaigns, difference-in-difference.

JEL classification: I18; C21; C54

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1 Introduction

The overuse of antibiotics is the main force driving the increase of bacterial resistance, which represents a major threat to public health. Antimicrobials may lose effectiveness since they are frequently prescribed for viral infections (Park *et al.*, 2005) or can be sold without an official medical prescription (Llor and Cots, 2009; Vaandnen *et al.*, 2006). Large volumes of antimicrobials are also used in agriculture and veterinary medicine, and in many consumer products where benefits are often unclear (Tan *et al.*, 2002). As illustrated in Figure 1, differences across European countries in antibiotic prescribing practices measured in defined daily doses per 1,000 inhabitants (DID) partially mirror differences in the levels of bacterial resistance captured by the rate of penicillin-non-susceptible *Streptococcus pneumoniae* isolates (PNSP).

Efforts to reduce bacterial resistance through a control of antibiotic use include the limitation of prescriptions, surveillance, and a more careful use of antibiotics in agriculture and food-producing animals. More recently, public authorities have taken an interest in encouraging appropriate consumption of antibiotics in the community (Hawkings *et al.*, 2008; Sabuncu *et al.* 2009). Cost-effectiveness studies on antibiotic treatments are now developed to consider the influence of bacterial resistance (Sabes-Figuera *et al.*, 2008). Because the association between antibiotic use and bacterial resistance may cross regional borders within countries, the implementation of national policies towards antibiotic consumption has emerged as an important tool for controlling and reversing bacterial resistance. However, the effects of these policies are still unclear.

Several studies describe and review national policies towards antibiotic consumpion in specific countries. Goossens *et al.* (2006), for instance, consider policies towards the efficient use of antibiotics in Belgium and France. However, the literature lacks studies providing empirical evidence on the impact of national policies across Europe. Huttner *et al.* (2010) summarize the characteristics of public campaigns in high-income countries but fail to provide sufficient statistical evidence on their impact. An econometric approach is used by Masiero *et al.* (2010) to investigate socioeconomic determinants of antibiotic use across Europe. The authors do not account for the effects of public policies towards the consumption of antimicrobials.

The aim of this study is to assess the impact of public education campaigns on antibiotic use in Europe by means of a differences-in-differences approach, a largely used empirical methodology on the effects of various treatments (Bertrand *et al.*, 2004). We draw information on national campaigns from the public health literature and use data publicly available on antibiotic consumption and socioeconomic determinants for an 11-years period (1997-2007). We control for unobserved individual heterogeneity by means of fixed-effects estimations and address endogeneity aspects of infections and policies with lagged and instrumental variables methods.

The paper is organized as follows. In section 2 we review the literature on policies towards the use of antibiotics and provide a brief overview of public interventions implemented in the European countries. In section 3 we propose an econometric model of antibiotic consumption where the impact of national campaigns is assessed after controlling for the main determinants of consumption. Data are described in section 4. Estimation results and discussion of main findings are presented in section 5. Section 6 concludes.

2 Public policies toward antibiotic consumption

Antimicrobial agents represent a scarce resource since their effectiveness decreases with consumption because of bacterial resistance. Different interventions may act as an effective way to tackle the problem. These can be characterized according to the type of intervention, the geographical area involved, the targeted agents, the instruments used and their message.

As for the type of intervention, policies to improve the use of antibiotics can be categorized in four classes according to the list proposed by Quick *et al.* (1991). There are educational interventions which are persuasive and consider training of prescribers by means of seminars, workshops, face to face or supervisory visits, and assorted printed materials aimed at patients or prescribers. Managerial strategies aim at guiding decision-making. They concentrate, for instance, on carrying drug utilization reviews, giving cost information, following standard treatment guidelines to prescribe, and wraping full courses of therapy. Regulatory interventions legally constraint prescribers to control their decision making via instruments such as registering drugs for marketing, licensing prescribers, and limiting prescribing or dispensing. Finally, economic interventions aim at providing financial incentives to institutions, providers and patients. The effects of these strategies crucially depend on the pricing structure, the price setting and the reimbursement mechanism adopted.

Among the educational strategies that promote the appropriate use of antibiotics and that raise the public awareness of bacterial resistance, public campaigns are one of the most widely used. In European countries, national or regional health authorities are in charge of adopting these campaigns, depending on the level of decentralization of the health care systems. Although antibiotic policies can be implemented at national or subnational level, public campaigns are generally implemented within a national strategy to abate resistance to antimicrobials (Huttner *et al.*, 2010). International organizations are sometimes involved. Rudholm (2002) suggests that the problem of resistance is a global one. Consequently, optimal policies should consider the fact that antibiotic resistance can cross country borders and travel far distances. Coast *et al.* (1998) argue that policies aimed at reducing antibiotic use within a country may not work in another country since local epidemiological factors affect the spreading mechanism of antibiotic resistance. González Ortiz and Masiero (2013) suggest that regional policies could blunt the impact of policies in neighbouring regions through the generation of local spillovers.

The majority of public campaigns are addressed to the general public, focusing on parents of young children. Health-care professionals, specifically primary care physicians, are also targeted. The public is targeted by distributing informational material to patients and by displaying posters in waiting rooms and pharmacies. General practitioners receive educational material such as guidelines, information sheets and booklets. Some campaigns combine different instruments such as advertising on television and radio networks, newspapers and public transports, through the internet or using billboards. The use of the internet to spread information about the program is common to almost all campaigns.

Finally, regarding the message of the intervention, most campaigns attempt to inform the public that antibiotics are not needed for treating viral infections. They focus on respiratory tract infections and combine negative and positive messages. The main message is that bacterial resistance is a major public health issue largely caused by the misuse of antibiotics. This encourages people to follow rigorously the antibiotic dosage regime prescribed by the physician.

2.1 Previous studies on the impact of antibiotic policies

The literature on the impact of antibiotic policies is limited to studies using a descriptive and qualitative approach. Goossens *et al.* (2006) analyse national campaigns in two European countries with high antibiotic use, Belgium and France, between 1997 and 2003. To assess the impact of antibiotic policies, the authors compare rates of antibiotic consumption between the two countries and England, where the rates of antibiotic use are lower and persistent. Findings suggest evidence of reduced antibiotic prescribing in both countries. However, these findings cannot be generalized to countries with lower or already declining levels of antibiotic use. Moreover, the study does not control for differences between the two countries related to the impact of infections, the characteristics of prescribers or demographic aspects over the time period considered.

To assess the impact of antibiotic policies in Central and Eastern European countries, Cizman *et al.* (2004) administer a questionnaire to national representatives. The questionnaire includes information about national antimicrobial resistance surveillance, national consumption of antibiotics in the community and in hospitals, and strategies to optimize the use of antimicrobials. The authors identify countries which have restricted the use of some antibiotics for outpatients and inpatients and briefly describe other types of interventions implemented by these countries. Findings show that only few countries have restricted the use of antimicrobials in ambulatory care, as compared to the common practice of restricting the use of antibiotics in hospitals. The authors realize that antibiotic policy interventions are lacking or only apply to specific interventions or problems.

Using an exhaustive search strategy and structured interviews, Huttner *et al.* (2010) classify and examine the characteristics and outcomes of 22 public campaigns for a more rational use of antibiotics implemented at national or regional level in high-income countries between 1990 and 2007. The majority of these campaigns (16) are located in Europe. Looking at data on the consumption of outpatient antibiotics, the authors try to evaluate the effect of the campaigns. The study concludes that probably there is a relationship between a decline in the use of antibiotics and the implementation of public campaigns. However, this conclusion is based on a qualitative analysis rather than on a statistical/econometric analysis. The approach has some shortcomings since most campaigns do not include a control population and trends in consumption before the interventions are not considered. The analysis cannot clarify whether antibiotic consumption would still have increased without the campaign or if the duration of the intervention was too short to observe measurable effects.

In conclusion, evidence presented in empirical studies on the impact of antibiotic policies is currently weak, mainly based on descriptive statistics and graphical analysis. In the following section, we will use an econometric approach to provide more convincing evidence of the association between the adoption of antibiotic policies and antibiotic consumption rates.

3 The empirical approach

To investigate the effects of national campaigns for a more rational use of antibiotics, we estimate a model of outpatient antibiotic consumption using a panel data set for a sample of 21 European countries over the period 1997-2007. The model serves as a reduced form that considers both demand- and supply-side factors. In our simple frame, individuals are assumed to follow doctors' prescriptions and to be compliant with the antibiotic therapy. The consumption of outpatient antibiotics is assumed to depend upon sociodemographic characteristics of the population, individuals' health status, antibiotic price, the characteristics of health care supply and the adoption of national campaigns to improve the use of antibiotics.

Antibiotic prescribing practices vary widely across European countries. Mean figures of defined daily doses per 1,000 inhabitants for 21 countries collected by the European Surveillance of Antimicrobial Consumption (ESAC) project between 1997 and 2007 show that France, Greece, and Luxembourg, among others, exhibit significantly higher values of antibiotic use than Austria, Denmark, and the Netherlands (Figure 2).[1] Some of these contries implemented policy interventions to reduce an-

[1] Data are reliable and exhibit a good degree of comparability since the ESAC network screens for detection bias in sample and census data, bias by over-the counter sales and parallel trade, errors

tibiotic consumption during the period considered; other countries did not adopt any type of policy. Table **??** provides a summary of the adoption of national campaigns to improve antibiotic use in Europe. We refer the reader to section 4 for details about the construction of this table.

Since we have information on antibiotic consumption before and after a policy instrument has been introduced, we are able to estimate the effect of policy interventions using a differences-in-differences (DD) approach (Bertrand *et al.*, 2004). The general idea of this approach is to compare the outcome, in our case the *per capita* consumption of antibiotics, of two groups of countries before and after the introduction of a campaign. One group, denoted the "control", is composed of countries that did not introduce any policy instrument to reduce antibiotic consumption. The other group, the "treatment", includes all countries that have adopted some policy measures. Looking at differences in the outcomes observed between the two groups after the introduction of a policy, we can then estimate the impact of antibiotic policy interventions. The typical DD estimation with panel data with more than two periods considers countries and years fixed effects. Therefore, our DD estimation takes into account unobserved time-invariant variables.

Our empirical approach draws from Giavazzi and Tabellini (2005), who apply a DD technique to a large sample of countries to investigate the impact of economic and political liberalizations on economic performance, macroeconomic policy and structural policies. We estimate the following model in the whole sample of treated and control countries:

$$DID_{it} = \beta_0 + \beta_1 POLICY_{it} + x_{it} + \omega_i + \nu_t + \varepsilon_{it}, \tag{1}$$

where DID_{it} denotes defined daily doses of antibiotic consumption per 1,000 inhabitants in country i at time t; $POLICY_{it}$ is a dummy variable which assumes a value equal to 1 in the year of policy implementation and in the following years, and 0 otherwise. x_{it} is a set of other covariates which includes the *per capita* national income (Y_{it}), the physicians' density (DPH_{it}), the percentage of the population below 14 years of age, between 15 and 24, 25 and 64, 65 and 79, and over 80 ($POP_{1it} \ldots POP_{5it}$), the price level for a defined daily dose of antibiotics (P_{it}), and the popula-

in assigning medicinal product packages to the Anatomical Therapeutic Chemical Classification (ATC), and errors in calculations of defined daily doses (Vander Stichele *et al.*, 2004).

tion health status measured by the impact of infectious diseases (INF_{it}). ω_i captures the country-level fixed effects, which are assumed constant over time; and ν_t is the year-specific fixed effect, which is assumed constant across countries. Finally, ε_{it} is an unobserved error term with Z distribution.

By including both time and country fixed effects in Equation (1), we are able to disentangle the impact of public campaigns *per se* from other determinants related to country characteristics or time effects. The main coefficient of interest is β_1 which measures the effect of public campaigns on antibiotic consumption. A negative and significant coefficient would suggest that antibiotic policies were effective in reducing antibiotic consumption over the period 1997-2007.

To correctly identify the impact of antibiotic policy interventions, the econometric model has to satisfy some assumptions. First, we need to exclude the presence of unobserved variables affecting antibiotic consumption that move systematically over time in a different way between the two groups of countries. In our analysis, the assumption sounds reasonable because all countries belong to Europe and, therefore, the general trend in antibiotic consumption is expected to be similar. Moreover, the possibility of unobserved heterogeneity should be negligible given that our regressions include all main socioeconomic determinants of differences in antibiotic use across countries (x_{it}).

One further assumption is that the decision to introduce a public campaign is independent of the level of antibiotic consumption in a country, i.e. policies are exogenous. This assumption is also plausible because the pressure to promote information campaigns does not depend directly on antibiotic consumption. It probably depends on the increasing levels of antibiotic resistance. We are clearly aware that antibiotic resistance is partially caused by the consumption of antibiotics, which may then indirectly influence the adoption of antibiotic policies.

Potential endogeneity problems may lead to biased results in the estimation of Equation (1). Since public campaigns may be driven by high levels of antibiotic use in a country, we check the robustness of our initial results (Model 1) by endogenizing the policy variable using an instrumental variable approach (Model 2). Unfortunately, as we will discuss later, the limited number of instruments reduces the number of observations. The population density, women employment rate, the production of milk and pig meat, the use of fertilizers, and the size of the country are used as instruments for policies. These variables also indirectly measure the level of bacterial resistance within a country. In contrast to bacterial resistance, they are poorly correlated with antibiotic use. Consequently, we believe they can reasonably be used as appropriate instruments for policies.

Another explanatory variable is potentially endogenous in our model: the population health status which is captured by mortality for infectious diseases. Infections are potentially endogenous since a low level of antibiotic use may favour poorer health conditions in the population, e.g. an increased spreading of severe infections. To tackle this problem, we estimate our models using the lagged mortality rate for infectious diseases (INF_{it} instead of INF_{it-1}). This is a simple instrumental variable approach, though pretty efficacious.

One last issue is that the DD estimation results can be affected by positive serial correlation (see Bertrand *et al.*, 2004). To cope with this problem, we report standards errors clustered by country.

4 Data

The consumption rate of antibiotics is available for 21 European countries between 1997 and 2007. This is collected by the European Surveillance of Antimicrobial Consumption (ESAC) project. The consumption rate is most commonly expressed as the number of defined daily doses (DDD) per 1,000 inhabitants per day (DID). The DDD is a technical unit based on the assumed average maintenance dose per day for a drug used for its main indication in adults. Antibiotic use is standardized using the ATC/DDD index for international drug consumption studies (WHO, 2011).

Annual data available on the determinants of outpatient antibiotic use are summarised in Table **??**. These include socioeconomic characteristics of the population (income and demographic structure), supply-side factors (density of doctors), price of antibiotics, and the incidence of bacterial infections measured by the rate of mortality.[2] We use the mortality rate for infectious diseases as a proxy for the incidence

[2]Information on mortality for infectious diseases and price of pharmaceuticals are not available for all countries or years. This reduces the total number of observations in our final regressions.

of infections since morbidity indicators are less complete and reliable.

Data are obtained from a variety of sources. Information on the *per capita* income (measured in US dollars in purchasing power parity), the density of physicians, and the incidence of infections are extracted from publications by the OECD (2010). The demographic structure of the population is derived from Eurostat tables (Eurostat, 2010).

We derive price levels for antibiotics by combining information from two indicators: the comparative price level index (PLI) and the harmonized annual average price index (HICP) for pharmaceutical products. The PLI indicates the price level of each country compared to the average price level of the 25 EU countries in 2005. The HICP includes information on price trends for pharmaceuticals for each country during 2000 and 2005, where 2005=100. These indices are provided by Eurostat (2010).

As for public campaigns, data collection is cumbersome and may result in incomplete data. Moreover, little information is available in scientific journals. For our purpose, we draw the information on campaign characteristics from the recent review by Huttner *et al.* (2010). The authors identify public campaigns implemented at national level in high income countries between 1990 and 2007. Using information from this study, we generate a dummy variable ($POLICY_1$) which takes a value equal to 1 in the year of implementation of the campaign, and 0 in the pre-campaign and post-campaign years (see Table 2). Alternatively, we consider a different policy indicator ($POLICY_2$). This is a dummy variable which takes the value 1 in the years of campaign adoption and in the years post-campaign, and 0 in years before the campaign is adopted. It is worth noticing that the construction of these indicators is facilitated since the characteristics of the campaigns are rather similar.

Information on instruments for policies (population density, size of country, women employment rate, production of milk and pig meat, the use of fertilizers) are also obtained from the Eurostat statistics (Eurostat, 2010).

Since almost all countries implemented some policies to increase the public awareness of antibiotic use from 2000, and in order to have a satisfactory control group, we excluded Iceland from the final dataset. Iceland adopted a campaign at the beginning of the period considered (1997 and 1998). The final dataset is an unbalanced panel dataset with 153 observations for Model 1 and 122 observations for Model 2. Since information on instrumental variables for policies is not available for all countries or years, the number of observations in Model 2 is lower. Estimations are performed by means of the statistical software STATA (version 11.1).

5 Results

For the estimation of Equation (1) with panel data, the literature proposes several approaches: the pooled ordinary least-squares model (OLS), the random effects model (RE) and the fixed effects model (FE). As explained in section 3, we are interested in applying a DD methodology. Consequently, we perform some tests to choose the most appropriate estimator among those mentioned above.

Our initial tests indicate that the OLS model can be rejected in favour of the fixed effects model (FE).[3] The Breusch and Pagan lagrangian multiplier test indicates that there are other effects than those captured by the exogenous variables in OLS regressions. The F test that constant terms are homogeneous across regions and time periods is also rejected. Moreover, the Hausman test suggests that the FE approach should be preferred to the random effects approach. For this reason we use a DD estimator where the individual effects are considered as fixed. The parameter estimates reported in Table 3 (Model 1) are those of the FE model. Table 3 also reports the results of the two-stage least squares regression (Model 2) to correct for endogeneity.

As explained in section 3, all regressions include country fixed effects and year dummy variables. The results are stable and no structural differences is observed across the two models. Time dummies do not show any significant increase in the use of outpatient antibiotics *per capita* over time. In both models some coefficients are statistically significant and carry the expected sign. The relatively low number of statistically significant coefficients of socioeconomic variables could be explained, as suggested by Cameron and Trivedi (2005), by the low within variation of these

[3] Preliminary OLS regressions show an R^2 adjusted of 0.59. The goodness of fit slighly increases with the inclusion of temporal dummy variables. The F test is 24.58 (12.51 with time dummies). This suggests that overall regressors have a significant impact on the dependent variable. Moreover, the mean Variance Inflation Factor is lower than 3. Finally, the Shapiro-Wilk test as well as the Jarque-Bera test for normality of errors cannot be rejected using the conventional 95% level of significance.

variables. The number of significant coefficients increases in the two-stage least squares model. Although this is worth of notice, we remind the reader that our main goal is to estimate the coefficient of the policy dummy variable using a DD approach.

5.1 Effects of policies

The effects of antibiotic policies on outpatient antibiotic consumption are reported in Table 3. As explained in section 3, the control group consists of all the countries that did not go through a public campaign to improve antibiotic use during 1997-2007. Thus, when we study the effects of public campaigns, the controls are the countries that never adopted a campaign.

The variable $POLICY_1$ is a dummy variable equal to 1 in the year of adoption of the campaign and 0 afterwards for the treated countries only. Its estimated coefficient captures the average effect of the policy. In line with our expectations, policy coefficients are significant in both models. The dummy variable shows a negative sign, which suggests that the implementation of public campaigns leads to a reduction in the use of antibiotics. One could speculate that individuals informed about the social implications of antibiotic use are more likely to use antibiotics carefully.[4]

Using the estimated coefficients of $POLICY_1$ in Model 1 and Model 2, we observe that the implementation of a public campaign may reduce antibiotic consumption by 1.4 to 3.7 defined daily doses per 1,000 inhabitants. This roughly represents an impact between 7.2% and 18.5% on the mean level of antibiotic use in Europe between 1997 and 2007.

Our results cannot be easily compared with earlier findings in the literature. There is no comparable study we are aware of on the association between outpatient antibiotic use and public campaigns. The few papers that have investigated the correlation between antibiotic policies and antibiotic use either focus on specific countries or do not use quantitative methods, as presented in section 2.

[4]The results above are confirmed if we include the dummy variable $POLICY_2$ which takes the value equal to 1 in the years of campaign adoption as well as in the years post-campaign. This indicator was suggested by the logic that policies need to take some time to show their effects.

5.2 Other effects of covariates

The coefficient on physicians density deserves some comments since it is positive and significant in Model 2. An increase in physicians density by 0.1% increases antibiotic consumption by 3.13 DID. The results might put forward some evidence of supply-induced demand. However, the assumption of a positive relationship between the amount of prescriptions and the number of doctors *per capita* does not necessarily follow. It is known that countries with a greater number of doctors per inhabitant use more antibiotics than countries with a smaller number of doctors per inhabitant (Molstad *et al.*, 2002), and that doctors who spend more time with their patients prescribe fewer antibiotics (Bjerrum *et al.*, 1999).

Although physicians are more informed than patients about drug resistance and are ethically constrained to avoid unnecessary antibiotics, they may overprescribe antimicrobials either to meet patient's expectations or because they fear misdiagnosing bacterial infections (Cizman, 2003). Patients usually regard antibiotics as a valid alternative to anti-inflammatory drugs for colds or flu. They also suffer from poor information in relation to physicians and look for evidence of physician's quality. The physician's willingness to prescribe antibiotics may then appear as a mark of quality (Das and Sohnesen, 2006). Patients may fancy immediate treatment and the physician must decide between prescribing or persuading the patient that a delay is appropriate.

We did not find any significant effect of changes in the average national income. Nevertheless, the coefficient of income is positive in both regressions. Positive income effects for antimicrobials are observed by Baye *et al.* (1997) using US data, Filippini *et al.* (2009a) using aggregated Swiss data at small area level, and in a previous study on European country data with a shorter time period, i.e. 2000-2005, than ours (Masiero *et al.*, 2010). Conversely, negative income effects are found by Filippini *et al.* (2006) using Swiss data at cantonal level. One possibile explanation for the relatively low value of the coefficient of income is that the increasing concern on the effects of bacterial resistance from the 1990s may have reduced income elasticity of outpatient antibiotic expenditure over time. Another explanation is that high-income countries are more likely to substitute away antibiotics for other treatments, *ceteris paribus*.

As expected, antibiotic price has a negative impact on consumption, although this is not significant. Generally, antibiotics are perceived as necessary in the case of presumed bacterial infections. Furthermore, antibiotics are purchased under doctor's prescription and the share of price bore directly by the patient is usually very low. This may imply that individuals are not very responsive to changes in antibiotic prices, although price demand elasticities may also vary according to the type of antibiotic therapy, e.g. newer and more expensive antibiotics are more price elastic than traditional ones (Filippini *et al.*, 2009b).

The coefficients of mortality rate for infectious diseases are not significant. As for demographic covariates, we only observe a significant association between the proportion of individuals aged 65-79 and increasing levels of antimicrobial consumption. This result seems to support the hypothesis that increasing prevalence of chronic health problems as people grow older may determine an increase in the utilization of health care goods and services, including drugs. Di Matteo and Grootendorst (2002) also observe a slighly significant increase in drug expenditure in the population between 64 and 74, although the evidence is not confirmed by the more recent study by Di Matteo (2005).

6 Conclusion

Several studies show that a decrease in the use of antibiotics may reduce levels of bacterial resistance. During the last decade, many European countries undertook public health programs to optimize antibiotic use in the community. Nevertheless, the effectiveness of policies for a rationale use of antibiotics is still unclear. In particular, the influence of public campaigns on antimicrobial usage, and therefore on bacterial resistance, has not been assessed accurately (Huttner *et al.*, 2010).

In this paper, we estimate the impact of antibiotic policies in Europe by means of a differences-in-differences methodology. The approach allowed us to identify the effect of campaigns on antibiotic use by relating differential changes in antibiotic use across countries and over time to changes in the relevant policy variables. The key identification assumption in our analysis is that national policies are likely to affect antibiotic consumption more in countries where levels of bacterial resistance are higher as compared to other countries.

The results provide some evidence that the use of public campaigns represents an effective strategy to reduce the overuse of outpatient antibiotics. Countries that adopt public campaigns succeed in terms of reducing their levels of antibiotic use over time. Further research is necessary to assess the impact of policy interventions on the levels of bacterial resistance through the reduction of antibiotic consumption.

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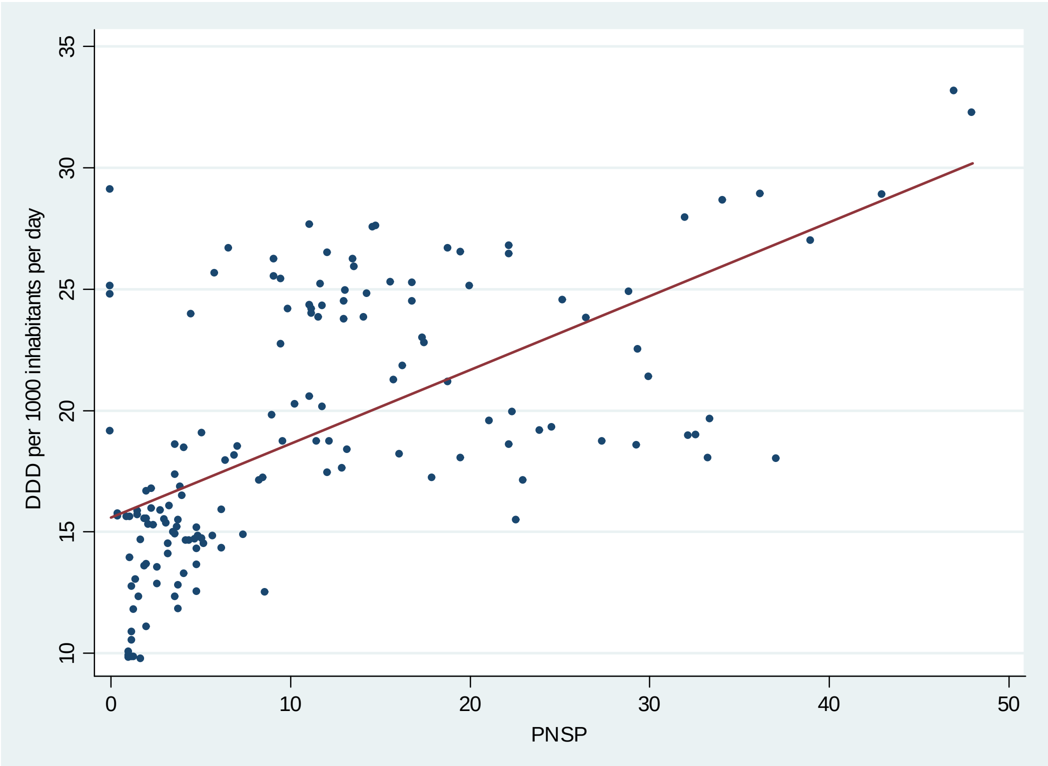

Figure 1: Antibiotic consumption and levels of bacterial resistance in PNSP (rate of penicillin-non-susceptible *Streptococcus pneumoniae* isolates) in 20 European countries between 2000 and 2007. Data source: European Surveillance of Antimicrobial Consumption (ESAC) and European Antimicrobial Resistance Surveillance System (EARSS).

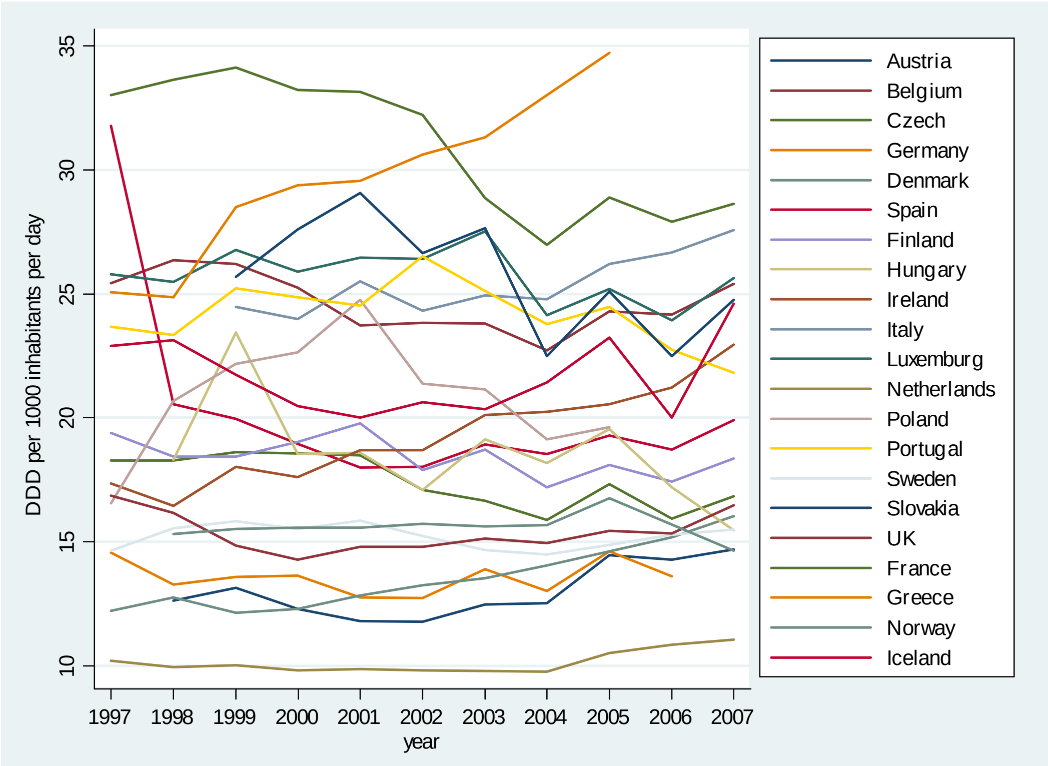

Figure 2: Outpatient antibiotic use in DID (defined daily doses per 1000 inhabitants per day) by country and year (2000-2007). Data source: European Surveillance of Antimicrobial Consumption (ESAC).

Description	Variables	Mean	Std. dev.	Min.	Max.
Outpatient antibiotic consumption	DDDs per 1000 inhab. per day (DID)	19.87	5.83	9.75	34.73
Income per capita	GDP in PPP/pop. (Y)	26802.27	10363.57	8898	71400
Antibiotic price	Comparative price levels for pharmaceutical products (P)	95.23	23.81	36.65	165.58
Demographic structure of population	Pop. under 14/pop. (POP_1)	17.78	2.36	13.90	25.70
	Pop. 15-24/pop. (POP_2)	13.29	1.83	10.20	17.50
	Pop. 25-64/pop. (POP_3)	53.84	1.94	47.90	58.1
	Pop. 65-79/pop. (POP_4)	11.55	1.55	8.2	15.20
	Pop. over 80/pop. (POP_5)	3.54	0.82	1.80	5.40
Density of doctors	Nr./1000 inhab. (DPH)	3.15	0.61	1.90	4.90
Infections	Mortality rate for infectious diseases (INF)	6.77	3.42	2.00	20.10
Population density	Population/km^2	101.93	53.92	2.91	393.90
Country area	km^2	203068	170053	2586	551500
Animal production	Tons of cow's milk/1000	6300.63	7265.99	112.95	28723.91
	Number of pigs/1000	10509.78	15469.91	73.72	81321
Use of fertilizers	Tons/1000	919186	1115849	15852	4988800

Table 1: Variables notation and summary statistics Data sources: ESAC, OECD, Eurostat, and European Observatory of Health Systems and Policies.

Country	Year										
	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Austria											
Belgium				■	■	■			■	■	■
Czech Republic											
Germany				■	■	■	■	■	■	■	■
Denmark											
Spain										■	■
Finland											
Hungary											
Ireland											
Iceland	■	■									
Italy											
Luxemburg								■	■	■	■
The Netherlands											
Poland											
Portugal								■	■	■	■
Sweden											
Slovakia											
United Kingdom											
France						■	■	■	■	■	■
Greece					■	■	■				
Norway								■			

Table 2: The implementation of national campaigns in Europe between 1997 and 2007 (years of campaign implementation are highlighted).

	Model 1 (Fixed effects) Obs. 153			Model 2 (2SLS) Obs. 122		
Variables	Coefficients	St. Err.	p-value	Coefficients	St. Err.	p-value
Constant	13.38773	10.81521	0.231	-12.30656	15.41851	0.425
Y	0.000023	0.000064	0.730	0.000121	0.000118	0.305
INF_{t-1}	-0.024336	0.131526	0.855	0.071602	0.143798	0.619
DPH	2.578951	1.729093	0.152	3.128074	1.356139	0.021
POP_1	-0.162891	0.307134	0.602	0.211355	0.458741	0.645
POP_2	-0.507961	0.327057	0.137	-0.076476	0.317848	0.810
POP_4	1.804238	0.355211	0.000	2.198311	0.480476	0.000
POP_5	-2.185347	1.738107	0.224	-1.936096	1.650253	0.241
P	-0.051554	0.035081	0.158	-0.028272	0.043339	0.514
$POLICY_1$	-1.437221	0.567456	0.020	-3.682141	1.502993	0.014
dt_1	-0.477217	1.849433	0.799	0.280478	1.753773	0.873
dt_2	-1.145775	1.768012	0.525	-0.163466	1.607206	0.919
dt_3	-1.423682	1.604730	0.386	-0.443355	1.413800	0.754
dt_4	-0.928832	1.452470	0.530	0.211679	1.181271	0.858
dt_5	-1.399952	1.2144970	0.263	-0.157246	0.934441	0.866
dt_6	-1.124569	0.919446	0.236	0.039486	0.724095	0.957
dt_7	-1.764281	0.748660	0.029	-0.646103	0.553530	0.243
dt_8	-0.783783	0.632413	0.230	-	-	-
dt_9	-1.305654	0.478819	0.013	-	-	-
σ_u	5.893451	-	-	5.878605	-	-
σ_e	1.139026	-	-	1.234114	-	-
ρ	0.963992	-	-	0.957788	-	-

Table 3: Parameter estimates for differences-in-differences models of antibiotic consumption.

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