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**Quaderno N. 07-01**

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# Characteristics of demand for antibiotics in primary care: an almost ideal demand system approach

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April 2007

## Abstract

We model demand for different classes of antibiotics used for respiratory infections in outpatient care using a linear approximate almost ideal demand system approach. We compute elasticities to socioeconomic determinants of consumption and own- and cross- price elasticities between different groups of antibiotics. We find significant elasticities between newer/more expensive generations and older/less expensive generations of antibiotics. The larger use of more expensive antibiotics is also associated with the self-dispensing status of practices, *ceteris paribus*.

JEL classification: I0; C3; C43

Keywords: Antibiotic use; Demand equations; Demand elasticities; Almost Ideal Model; Self-dispensing

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\*Department of Economics, University of Lugano; Swiss Federal Institute of Technology, Zurich, Switzerland. Support from the Swiss National Science Foundation is acknowledged. We are grateful to Dr. Enos Bernasconi and Dr. Marco Bissig from the Cantonal Hospital of Lugano for invaluable advice on the selection of antibiotic categories. Any mistake is clearly our fault.

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# 1 Introduction

Antibiotics differ from other pharmaceutical products in many peculiar aspects (Ellison and Hellerstein, 1999). Because of their pharmacological characteristics, they are generally prescribed by doctors. Consequently, patients' preferences for specific therapeutical components may be of little relevance. On the other hand, such aspects as the price may play an important role if consumers bear directly a substantial share of the cost of drugs.

In primary care, doctors may face a first tradeoff between prescribing or delaying an antibiotic therapy under uncertainty on the nature of patient's infection (viral or bacterial). Although the antibiotic therapy is not effective against common viral infections, expected cost savings (time and troubles) in the case of bacterial infections may overcome the expected social loss from bacterial resistance. From the economic point of view, bacterial resistance accounts for relevant external effects. First, several antibiotic therapies can be prescribed before finding the effective one, hence leading to income loss or even premature deaths. Second, the reduced effectiveness of drugs increase social costs to produce new generations of pharmaceutical components.

A second tradeoff is observed between prescribing broad spectrum or narrow spectrum antibiotics. Although the intensive use of broad spectrum components reduces uncertainty in the outcome of the treatment, this may generate higher levels of bacterial resistance. It has been argued that the persistent use of one type of antibiotics may be sub-optimal for the society. The literature suggests that the negative externality of resistance can be reduced by changing the type of antibiotic used (Ellison and Hellerstein 1999; Laxminarayan and Weitzman, 2002; Rowthorn and Brown, 2003), since the same type of bacteria may be susceptible to more than one antibiotic component.<sup>1</sup>

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<sup>1</sup>Increasing rates of *Streptococcus pneumoniae* strains resistant to penicillin has led to the use of macrolides. However, the clinical effectiveness of the latter category has began to decrease as well (Alvarez-Elcoros and Enzler, 1999). The analysis by Ednie et al. (1996) suggests that in areas where penicillin-resistant strains are common, the empirical antibiotherapy using macrolides should then be changed.

Regional heterogeneity in the mix of antibiotics used has been recently observed within countries (Filippini et al., 2006; Kern et al., 2006). This may indicate that some antibiotic components are preferred by local physicians, which raises the issue of optimal use at local level. The increase of resistant organisms force physicians to face an effectiveness constraint in substituting away some types of antibiotics with newer and more effective ones.<sup>2</sup> However, substantial local differences in the mix of antibiotics can hardly be explained only by levels of bacterial resistance and, consequently, the internalization in doctors' decisions. There is no evidence that bacterial resistance significantly varies at local level but the availability of detailed information on its impact and the spread of local guidelines is quite poor. More plausibly, in our view, doctors differ in attitudes towards the same type of antibiotics and their strategies can be influenced by patients' characteristics, antibiotic price and economic incentives.

The current paper focuses on factors affecting the local mix of main antibiotics categories. The analysis suggests that policy instruments, such as locally differentiated taxes on antibacterials affected by resistance problems, may induce a better use of antibiotics.

The demand for specific antibiotic classes has been investigated in studies by Ellison et al. (1997) and Chaudhuri et al. (2003). The focus is on the structure of the demand for two segments of the market: cephalosporins and quinolones. Demand is modelled in two stages: a substance is firstly chosen among a set of substances and a brand/generic version of the product is chosen afterwards. The approach is suitable for the analysis of specific categories of antibiotics since substances constitute close therapeutic substitutes and may be similar in terms of the impact of bacterial resistance. The models rely, however, on the hypothesis that physicians' decisions within a given antibiotic category do not depend on the availability of alternative categories and are firstly based on specific names of substances. We argue that this is not the most realistic scenario and may rather reflect the chemist's view. Instead,

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<sup>2</sup>The resistance-induced antibiotic substitution has been recently addressed by Howard (2004) among others.

doctors seem to be more concerned with the effectiveness of a broad category of antibiotics compared to another one. Moreover, their choices are likely to be affected by perceived resistance for specific antibiotic categories. Doctors may then choose among a limited (broad) set of antibiotic categories classified according to the common practice and shared beliefs regarding their effectiveness.

We intend to investigate the structure of the demand for antibiotics used for respiratory infections by modelling the decision process of rationale physicians. We are interested in price and income sensibility of different antibiotic categories. Similarly to Ellison et al. (1997) and Chaudhuri et al. (2003), we model antibiotic demand as a multistage budgeting problem but do not separate all specific substances and generic/brand names for each of them. Instead, we consider a wider set of substances, those that can be prescribed for common respiratory infections in outpatient care. Outpatient antibiotics are aggregated in four groups (*classic* penicillins, penicillins amoxi/clav plus 1<sup>st</sup> and 2<sup>nd</sup> generations of cephalosporins, 3<sup>rd</sup> generation of cephalosporins and quinolones, macrolides), according to what are plausible alternatives in the treatment of respiratory infections.<sup>3</sup>

The allocation of antibiotic expenditure across antibiotic groups is analysed using the Almost Ideal Demand System (AIDS) specification proposed by Deaton and Muellbauer (1980). The AIDS model is commonly used to estimate price and income elasticities of the demand for goods when expenditure share data are available.<sup>4</sup> We compute own- and cross- price elasticities between old and new generations of antibiotics and between antibiotics differently affected by bacterial resistance using data from small geographic areas in Switzerland. We also estimate conditional expenditure elasticities and marginal expenditures shares for each group of antibiotics.

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<sup>3</sup>Most of the antibiotics used in outpatient care are for the treatment of respiratory infections (Blasi et al., 2006; Gonzalves et al., 2001). We focus on this category and exclude antibiotics mainly used for other types of infections. Hence, our categories include all plausible therapeutic substitutes.

<sup>4</sup>Ma and al. (2004) estimated the share equations of animal product consumption for Chinese households. Combining the AIDS model and the two-stage Heckman procedure, Lazaridis (2004) focused on the factors affecting the demand for different types of oils and fats in Greece. Boetel and Liu (2003) estimated a meat demand system and investigated the effect of food information on the meat shares consumed.

The structure of the article is as follows. In section 2 we sketch the application of the linear approximate AIDS model to the demand of antibiotics and discuss some testable hypothesis on elasticities. In section 3 we discuss the data and summarize the variables used in the model. Section 4 gives some results and section 5 concludes.

## 2 The model

In this section we present a model of demand for antibiotics in outpatient care based on the AIDS model. We hypothesize that the individual utility derived from the use of antibiotics is weakly separable from quantities of all other types of goods consumed. Consequently, consumers follow a multistage process to allocate their budget to antibacterial products. In the first stage, the total spending is allocated to broad categories of goods, such as health care versus other types of goods or services. The health care spending is then separated in subgroups, such as pharmaceuticals, diagnostic tests and inpatient care. Given the nature of the infection, the budget share for pharmaceuticals is assigned to antibiotics and other types of drugs. Finally, the choice is between different categories of antibiotics according to their therapeutical attributes, the risks of bacterial resistance and the cost of treatment.

The individual expenditure function derived from the consumer theory is aggregated across individuals to obtain the antibiotic expenditure in the local market area.<sup>5</sup> Muellbauer (1975, 1976) showed that exact aggregation is possible within a specific family of preferences. These preferences are known as the price independent generalized logarithmic (PIGLOG) class of preferences. The PIGLOG class can be denoted by the following expenditure function, which is the minimum expenditure necessary to achieve a certain level of utility at any given price

$$\log c(u, p) = (1 - u) \log a(p) + u \log b(p), \tag{1}$$

where  $u$  is the level of utility,  $a(p)$  and  $b(p)$  represent functions of a price vector  $p$ .

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<sup>5</sup>Aggregation theory provides the necessary conditions under which the aggregate demand, i.e. the representation of market demand, can be treated as if it was the outcome of the decisions of a rational representative consumer. See Muellbauer (1975) and Cornes (1992) for a general discussion.

Following Deaton and Muellbauer (1980) we assume

$$\log a(p) = \alpha_0 + \sum_i \alpha_i \log p_i + \frac{1}{2} \sum_i \sum_j \lambda_{ij} \log p_i \log p_j \quad (2)$$

and

$$\log b(p) = \log a(p) + \beta_0 \prod_i p_i^{\beta_i}, \quad (3)$$

where  $\alpha_0, \alpha_i, \beta_0, \beta_i$  and  $\lambda_{ij}$  are constants, and  $i$  and  $j$  are indexes representing different antibiotic categories.

Substituting for  $\log a(p)$  and  $\log b(p)$  in (1) we can write the cost function as

$$\log c(u, p) = \alpha_0 + \sum_i \alpha_i \ln p_i + \frac{1}{2} \sum_i \sum_j \lambda_{ij} \log p_i \log p_j + \beta_0 u \prod_i p_i^{\beta_i}, \quad (4)$$

which is linearly homogeneous in prices, provided that the following restrictions on the parameters hold

$$\sum_i \alpha_i = 1, \quad \sum_i \lambda_{ij} = \sum_j \lambda_{ij} = 0, \quad \sum_i \beta_i = 0. \quad (5)$$

By applying the Shephard's lemma<sup>6</sup> and substituting afterwards the indirect utility function<sup>7</sup> derived from (2) we then obtain the expenditure share of the  $i^{\text{th}}$  group of antibiotic substances

$$w_i = \alpha_i + \sum_j \gamma_{ij} \log p_j + \beta_i \log(x/P), \quad (6)$$

where  $x$  is the total expenditure for antibiotics in outpatient care<sup>8</sup>,  $P$  is a price index defined by

$$\log P = \alpha_0 + \sum_i \alpha_i \log p_i + \frac{1}{2} \sum_i \sum_j \gamma_{ij} \log p_i \log p_j \quad (7)$$

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<sup>6</sup>Demand functions in budget share form are derived from a natural logarithmic differentiation of the expenditure function with respect to prices.

<sup>7</sup>Total expenditure  $x$  is equal to  $c(u, p)$  for a utility maximising consumer. Hence,  $c(u, p)$  can be inverted to give  $u(p, x)$ , the indirect utility function.

<sup>8</sup>We define  $x = \sum_i p_i q_i$  as the total expenditure on antibiotics for respiratory infections in outpatient care, where  $p_i$  and  $q_i$  represent the price and the quantity for the  $i^{\text{th}}$  group of antibiotics by the representative consumer.

and

$$\gamma_{ij} = \frac{1}{2}(\lambda_{ij} + \lambda_{ji}). \quad (8)$$

The following restrictions are implied by (5) and (8)

$$\sum_i \gamma_{ij} = \sum_j \gamma_{ij} = 0, \gamma_{ij} = \gamma_{ji} \quad \forall i, j \quad (i \neq j). \quad (9)$$

Provided that (5), (8) and (9) hold, the equation (6) defines a system of demand functions. These are homogeneous of degree zero in prices and total expenditure and satisfy the Slutsky symmetry. The total expenditure is then given by  $\sum w_i = 1$ .

The interpretation of the demand share summarized by (6) is straightforward. Without any change in relative prices and expenditures, i.e. the second and the third terms of the right-hand side of the equation, the budget shares of different groups of antibiotics are constant. Changes in relative prices affect the demand share through the terms  $\gamma_{ij}$ . These capture the effect on the  $i^{th}$  budget share from a one percent increase in the price of the  $j^{th}$  category of goods, with  $x/P$  held constant. Changes in real expenditure are taken into account by the parameter  $\beta_i$ , which is assumed equal to zero.

The share equation also underlines some basic properties of the demand function. Other things being equal, the expenditure share of each group of commodities is inversely associated with its own price and is positively related to the price of other goods. The expected sign of  $\gamma_{ii}$  is then negative. On the other side,  $\gamma_{ij}$  should exhibit a positive sign for any  $i \neq j$  if goods are close substitutes.

The demand for antibiotics may also be affected by variables other than price that account for expenditure shifts. For instance, the incidence of infections may imply seasonal trends in the per capita consumption. Socioeconomic characteristics of the population and aspects of health care supply may also affect antibiotic use. However, these aspects may be of little relevance in the demand share of different classes of antibiotics, unless they shape preferences for specific antibiotic categories.

It has been suggested that patients' age significantly affects the route of administration of antibiotics for lower respiratory tract infections (Mazzaglia et al., 1999) and



the type of antibiotic used (Pendergrast and Marrie, 1999). Moreover, physicians may have an incentive to prescribe the newer and more expensive antibiotics, i.e. those with a broader spectrum of activity which apparently reduce risks for patients. Our model can be easily modified to account for expenditure shifts determined by the structure of the population and cultural differences. We also control for practice status, i.e. whether or not a practice is allowed to directly dispense drugs to the patients, since this might have an impact on the choice of specific antibiotics. Other variables, such as the density of doctors, are neglected in this approach.<sup>9</sup>

Following Ray (1980) and Pollack and Wales (1992), we include the additional determinants in the model by a log-linear scaling procedure. Cultural and regulatory differences (self-dispensing) across regions are taken into account by dummy variables.

From (6) the AIDS model can then be extended to analyse aggregate data on antibiotic consumption across small geographic areas. Assuming separability in quantities consumed for different types of goods, we can write

$$w_i = \alpha_i + \sum_j \gamma_{ij} \log p_j + \beta_i \log(x/P) + \sum_{k=1}^S \nu_{ik} V_k + \sum_{l=1}^L \phi_{il} R_l + \sum_{t=1}^T \rho_{it} DT_t + u_i, \quad (10)$$

where  $\rho_{it}$ ,  $\phi_{il}$  and  $\nu_{ik}$  are new parameters and the index  $i = 1, 2, 3, 4$  denote four groups of antibiotic substances used for respiratory infections summarized in table 1 and discussed in section 3.  $V_k$  is a set of variables that capture demographic and cultural characteristics of the population,  $R_l$  ( $l = 1, \dots, 23$ ) are practice regulation dummy, and  $DT_t$  ( $t = 1, \dots, 4$ ) are time dummies. The random term  $u_i$  is normally and indentially distributed with variance  $\sigma_\varepsilon^2$ . The expenditure share function is linearly homogeneous in all the explanatory variables provided that the new parameters,  $\rho_{it}$ ,  $\phi_{il}$  and  $\nu_{ik}$ , satisfy the following condition

$$\sum_i \rho_{it} = \sum_i \phi_{il} = \sum_i \nu_{ik} = 0, \quad (11)$$

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<sup>9</sup>Determinants of the per capita aggregate demand for antibiotics in outpatient care have been investigated in a previous study (Filippini et al., 2006).

and  $P$  is approximated by the Stone's geometric price index

$$\log P = \sum_i w_i \log(p_i), \quad (12)$$

where  $w_i$  is the share of the  $i^{\text{th}}$  group of antibiotics.<sup>10</sup>

## 2.1 Expenditure and price elasticities

We are interested in studying the response of the demand for different antibiotic groups to changes in price and expenditure. We calculate elasticities at the sample mean of expenditure shares.

Using (6) and (12) we derive the uncompensated (Marshallian) own-price elasticities ( $\varepsilon_{ii}$ ) and cross-price elasticities ( $\varepsilon_{ij}$ ) as<sup>11</sup>

$$\varepsilon_{ii} = -1 + \frac{\gamma_{ii}}{w_i} - \beta_i, \quad (13)$$

$$\varepsilon_{ij} = \frac{\gamma_{ij}}{w_i} - \beta_i \frac{w_j}{w_i}, \quad i \neq j. \quad (14)$$

Using the Slutsky equation, we then obtain the expenditure elasticity for the  $i^{\text{th}}$  antibiotic category given by

$$\eta_i = 1 + \frac{\beta_i}{w_i}. \quad (15)$$

A positive value suggests that good  $i$  is normal.

The income compensated or net (Hicksian) own-price elasticities ( $\delta_{ii}$ ) and cross-price elasticities ( $\delta_{ij}$ ) are obtained by applying the Slutsky decomposition to (15) and using the price index in (12). These can be written as

$$\delta_{ii} = -1 + \frac{\gamma_{ii}}{w_i} + w_i, \quad (16)$$

$$\delta_{ij} = \frac{\gamma_{ij}}{w_i} + w_j, \quad i \neq j. \quad (17)$$

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<sup>10</sup>To avoid simultaneity problems we used the median values of the expenditure shares to calculate the Stone price index defined by equation (12).

<sup>11</sup>See Alston et al. (1994) and Chalfant (1987) for details.

Consumer theory suggests that compensated own-price elasticities are negative for normal goods. Moreover, if (14) and (17) are positive the two groups of antibiotics are cross substitutes, otherwise they are complements.

Using again the Slutsky equation, it is possible to derive a relationship between the compensated cross-price elasticities and expenditure elasticities:  $\varepsilon_{ij} = w_j\sigma_{ij} - w_j\eta_i$ , where  $\sigma_{ij}$  are the partial elasticities of substitution, known also as the Allen elasticities of substitution

$$\sigma_{ij} = 1 + \frac{\gamma_{ij}}{w_i w_j} \quad i \neq j \quad (18)$$

The sign of  $\sigma_{ij}$  determines whether the goods  $i$  and  $j$  are complements or substitutes. If  $\sigma_{ij}$  is positive (negative) the two goods are substitutes (complements).

### 3 Data and variables

Our data cover 240 contiguous market areas representing the whole Swiss territory. The areas exhibit a good degree of internal homogeneity in terms of population density and providers of health care. Aggregate data on outpatient antibiotic sales of different classes of antibiotics were provided by IHA-IMS Health Market Research<sup>12</sup>. The dataset is detailed at product/brand name and data are available quarterly for 2002. Since we focus on respiratory infections, we limited our analysis to the antibiotics mainly used in the treatment of these diseases. We aggregated active substances according to the antibiotic class and the generation. Consequently, we kept 66% of the original dataset in terms of sales. We excluded antibiotics with a parenteral route of administration. Four groups were finally identified (*classic* penicillins, penicillins amoxi/clav plus 1<sup>st</sup> and 2<sup>nd</sup> generation of cephalosporins, 3<sup>rd</sup> generation of cephalosporins and quinolones, macrolides) using the relevant literature on antibiotic treatments and suggestions by experts. These groups are summarized in table 1.

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<sup>12</sup>Data on antibiotic sales derive from transactions between wholesalers and pharmacies and physicians.

Antibiotic group	Description
1 Penicillins (classic)	Penicillin V, amoxicillin, ampicillin
2 Penicillins (amoxi/clav) and 1 <sup>st</sup> – 2 <sup>nd</sup> generation cephalosporins	Clavucanic acid/amoxicillin, cefaclor, cefixime, cefadroxil, cefetamet pivoxil, cefprozil, cefuroxime axetil
3 3 <sup>rd</sup> generation cephalosporins and quinolones	Ceftibuten, cefpodoxime proxetil, moxifloxacin, levofloxacin
4 Macrolides	Erytromycin, clarithromycin, roxithromycin, azithromycin

Table 1: Antibiotic categories used in the treatment of respiratory infections.

Penicillins are among the first discovered antibiotics and have been largely used against streptococcus pneumoniae pathogens, which are a primary cause of respiratory tract infections (Schito et al., 2000). In particular, *classic* penicillins (penicillins V, ampicillin, amoxicillin) are commonly utilized to treat angina from streptococci and only rarely for other types of respiratory infections. The rate of penicillin-resistance streptococcus pneumoniae has substantially increased since the mid-1980s (CDC, 1994).

Newer penicillins (amoxi/clav) can be combined with some cephalosporins since they belong to the same broad classification (beta-lactams). The spectrum of amoxi/clav and 2<sup>nd</sup> generation of cephalosporins are very similar. Observed cross-resistance between cephalosporins and penicillins may imply that patients infected by penicillin-resistant bacteria may be resistant to cephalosporins as well. The 1<sup>st</sup> generation of cephalosporins is currently of very little use.

The 3<sup>rd</sup> generation of cephalosporins has a broader activity spectrum compared to previous generations, which implies that it can be used against a larger variety of bacteria. Consequently, it is suitable for more severe infections. Nevertheless, it is generally used as an alternative to the 2<sup>nd</sup> generation. Practices may significantly vary across the areas since some doctors are more likely than others to preserve the 3<sup>rd</sup> generation for more resistant bacteria.

Similarly, quinolones have a large range of antibacterial activity, which includes multidrug resistant strains responsible for respiratory tract infections. Since this category should also be used with caution and better preserved for more severe cases, we considered it in a group together with the 3<sup>rd</sup> generation of cephalosporins. When the nature of the infection is uncertain and doctors are quite risk averse, 3<sup>rd</sup> generation of cephalosporins and quinolones may be preferred to penicillins and other cephalosporins.

Finally, macrolides are generally known as an alternative to beta-lactams. In some cases, bacterial resistance is more severe than for penicillins. Resistance to macrolides has increased over time among penicillin-resistant pneumococci and penicillin-susceptible strains. The preference for either penicillins or macrolides may then depend upon established local practices and patients preferences.

Average prices of each antibiotic group have been imputed using expenditure data and quantities. Quantities are measured in days of treatment (DOT) and prices are consequently defined in currency units per one day of treatment. A daily dose is standardised by the WHO.

	Min	Mean	SD	Max
Expenditure share				
1	0.018	0.093	0.029	0.233
2	0.149	0.463	0.069	0.704
3	0	0.141	0.056	0.430
4	0.154	0.303	0.073	0.787
Price				
1	0.974	1.589	0.212	2.639
2	2.331	3.340	0.220	4.018
3	4.974	5.935	0.291	7.451
4	3.614	4.787	0.344	6.086

Table 2: Summary statistics of budget shares and prices for different groups of substances.

Table 2 gives some summary statistics of expenditure shares and prices for the four groups of substances. Penicillins (amoxi/clav) and early generations of cephalosporins and macrolides represent the largest shares of the expenditure. Note, however, that

strong differences are observed across the areas. These categories may account for 15% only of the total expenditure. On the other hand, in some areas they are largely used and may reach a share of more than 70%.

Information on the other variables included in the model are also obtained from IHA-IMS (table ??). Demographic variables include the share of the population classified in 5 ranges of age. Note, for instance, that individuals under 26 represent less than 1% of the total population in some areas and more than 20% in others. Similarly, the proportion of people between 60 and 74 largely varies across areas, from 9.5% to almost 25%. Areas located at the border with other European countries represent 12.5% of the total number of areas. French and Italian speaking areas are 43.7% and are generally characterized by a more intensive use of antibiotic per capita. We defined a dummy variable that takes value equal to 1 if the area has a Latin culture (French and Italian) and 0 otherwise. A dummy has also been defined for borderland location. Finally, the impact of self-dispensing practices is captured by a dummy variable that takes value equal to 1 if most practices in the area (> 50%) are self-dispensing practices, and 0 otherwise. Around 23% of the areas exhibit a large proportion of self-dispensing practices.

Variable	Description	Min	Mean	Max
<i>POP</i> <sub>1</sub>	Population under 14/total population	0.088	0.166	0.218
<i>POP</i> <sub>2</sub>	Population between 15 and 25/total population	0.069	0.125	0.185
<i>POP</i> <sub>3</sub>	Population between 26 and 59/total population	0.423	0.495	0.638
<i>POP</i> <sub>4</sub>	Population between 60 and 74/total population	0.095	0.136	0.249
<i>POP</i> <sub>5</sub>	Population over 74/total population	0.034	0.077	0.139
<i>DBOR</i>	Areas with a borderland location		0.125	
<i>DLAT</i>	Areas with a Latin culture		0.437	
<i>SELF</i>	Areas with a rate of self-dispensing practices above 50%		0.233	

Table 3: Variables notation and summary statistics.

## 4 Estimation results

The AIDS model defined by equation (10) is used to investigate the expenditure shares of the four groups of antibiotics for respiratory infections. Independent variables include the prices of different antibiotic categories, consumer expenditure, demographic and cultural aspects of the local demand, seasonal dummies and practice status. All explanatory variables are expressed in natural logarithms, with the exception of dummy variables.

We estimated the model through the Zellner's Iterative Seemingly Unrelated Regression (SUR) procedure with STATA. The set of restrictions led to a singular residual variance/covariance matrix. Consequently, we dropped one share equation from the system. This is the first category, *classic* penicillins, which represents the smallest budget share on average across the four groups. Using the estimated parameters of the share equations of the other three groups and the restrictions applied above, we then obtained the parameters for the dropped category.

Results are reported in Table 4. Each equation has been estimated with 960 observations, since data for 240 areas were quarterly available. The adjusted  $R^2$  is 0.262, 0.369 and 0.387, respectively for group 2 (penicillins amoxi/clav and early generations of cephalosporins), group 3 ( $3^{rd}$  generation of cephalosporins and quinolones) and group 4 (macrolides).

The impact of consumer expenditure on the demand share of group 3 is positive, whereas it is negative for groups 2 and 4. Note, however, that the value is close to zero and the expenditure coefficient is significant at less than 1% for macrolides only. Moreover, the sign of the latter coefficient cannot be a proof of inferior type of goods, since the dependent variable is the budget share rather than quantity. As detailed in table 5 below, income elasticities are all positive, which suggests that different outpatient antibiotic categories are normal goods.

Similarly, price elasticities will be analysed later on in section 4.1. Price coefficients are not very informative at this stage. Most of them are significant at less than 1% with few exceptions, but the demand for amoxi/clav and cephalosporins

	Penicillins (amoxi/clav) and 1 <sup>st</sup> - 2 <sup>nd</sup> generations cephalosporins		3 <sup>rd</sup> generation cephalosporins and quinolones		Macrolides	
Obs.	960		960		960	
R <sup>2</sup>	0.262		0.369		0.387	
	Coeff.	S.E.	Coeff.	S.E.	Coeff.	S.E.
Constant	0.758***	0.073	0.211***	0.056	0.211***	0.071
$P_1$	-0.021**	0.010	0.077***	0.010	-0.050***	0.010
$P_2$	0.248***	0.027	-0.141***	0.018	0.086***	0.022
$P_3$	-0.141***	0.018	0.031	0.023	0.032*	0.019
$P_4$	-0.086***	0.022	0.032*	0.019	0.104***	0.027
$x/P$	-0.000	0.004	0.004	0.003	-0.013***	0.004
$POP_1$	-0.008	0.028	0.035*	0.021	-0.027	0.027
$POP_2$	0.054**	0.027	-0.025	0.020	0.006	0.026
$POP_4$	0.032*	0.018	-0.005	0.014	-0.004	0.018
$POP_5$	0.008	0.010	0.032***	0.007	-0.037***	0.009
$DBOR$	0.010	0.006	-0.005	0.005	-0.015**	0.006
$DLAT$	-0.015**	0.006	0.042***	0.004	-0.025***	0.006
$SELF$	-0.034***	0.006	-0.003	0.005	0.040***	0.006
$DT_1$	-0.039***	0.006	0.020***	0.004	0.024***	0.005
$DT_2$	0.004	0.006	0.012***	0.004	-0.037***	0.005
$DT_3$	0.042***	0.006	-0.007*	0.004	-0.050***	0.005

\* significant at 10%, \*\* significant at 5%, \*\*\* significant at 1%

Table 4: Parameter estimates for the restricted linear approximate AIDS model of antibiotic groups.

I-II (group 2) and the demand for macrolides (group 4) are unexpectedly positively affected by their own prices and negatively related to the price of other categories. However, the result cannot be interpreted as a sign of complementarity rather than substitution with other categories.

The demand share of all of the four antibiotic categories is significantly affected by the structure of the population and cultural aspects. We used the age class 26-59 ( $POP_3$ ) as the baseline category. The signs of  $POP_2$  and  $POP_4$  suggest that a higher proportion of individuals between 15 and 25 years of age and between 60 and 74 in the area has a positive impact on the share of penicillins and cephalosporins I-II (group 2) used. On the other hand, we did not find clear evidence that a higher proportion of children ( $POP_1$ ) negatively affects the share of penicillins and positively affects the



share of macrolides. According to Otters et al. (2004), there has been a decrease in the proportion of narrow-spectrum antibiotics prescribed for children between 1987 and 2001 in the Netherlands. By contrast, the proportion of macrolides increased from 8% to 16%. Similarly, Schindler et al. (2004) showed that macrolides were the most frequently prescribed antibiotics (48.1%) for respiratory infections among children aged between 0 and 6 in Germany.

However, we can show that an increasing proportion of elderly people ( $POP_5$ ) positively affects the antibiotic share of cephalosporins III and quinolones and has a negative impact on the demand share of macrolides (group 4). The result is in accordance with findings by Mazzaglia et al. (1999), who suggested that cephalosporins are the antibiotics most frequently prescribed for lower respiratory tract infections in adults, while macrolides are the less prescribed.

The borderland location seems to reduce the demand share of specific antibiotic categories such as macrolides. Accordingly, areas with a French/Italian culture exhibit a significantly lower consumption of macrolides (group 4), penicillins and cephalosporins I-II (group 2) compared to areas with a German culture. On the other hand, there is a higher consumption share of 3<sup>rd</sup> generation cephalosporins and quinolones. Similar differences are observed at a larger scale across European countries. France and Italy, for instance, use a relatively larger amount of 3<sup>rd</sup> generation cephalosporins compared to other European countries (Coenen et al. 2006).

Self-dispensing practices seem to contribute, at least partially, to a larger use of more expensive antibiotics, *ceteris paribus*. The estimated coefficients indicate that a high proportion of self dispensing-practices is significantly related to a larger demand share of macrolides (group 4). As a consequence, self-dispensing practices are also associated with a lower demand share of penicillins and cephalosporins I-II (group 2), which are less expensive than macrolides on average.

The current literature argues that dispensing doctors have a tendency to prescribe more medicines *per capita* than non dispensing physicians (Trap et al. 2002). The evidence, however, does not directly imply that self-dispensing physicians are more likely to prescribe more expensive antibacterials, *ceteris paribus*. There are

some possible explanations for the behaviour of dispensing doctors. First, it may be that dispensing doctors are more risk averse and, therefore, perceive a lower risk in prescribing newer versions of pharmaceuticals with a broader spectrum. Accordingly, Morton-Jones and Pringle (1993) found that prescribing costs per patient are generally higher for dispensing doctors. Another explanation may derive from Howard’s view that the increasing rate of bacterial resistance could lead general practitioners to substitute away from older and inexpensive drugs to newer and often more expensive antibiotics (Howard, 2004). Our findings suggest that this effect is stronger for self-dispensing doctors who are directly involved in the distribution of drugs. A third reason is related to a profit maximizing behaviour, since doctors get a mark up on directly dispensed drugs or may be influenced by effective marketing strategies set by pharmaceutical companies.

Finally, seasonal effects are highly significant. Note that the share of more expensive antibiotics (group 3 and 4) is higher in winter (1<sup>st</sup> quarter) and lower during the summer (3<sup>rd</sup> quarter). This may be related to doctors’ risk aversion in periods when the incidence of infections is generally higher. Accordingly, patients’ willingness to pay for drugs may raise with the perceived risk of infection. By contrast, less expensive antibiotics, such as penicillins and early generations of cephalosporins, are used less often during the 1<sup>st</sup> quarter and more often in the summer quarter.

## 4.1 Elasticities

Using the estimation results from table 4 and applying the definitions derived in section 2.1, we calculate the own-price, cross-price and expenditure elasticities of the demand for antibiotic categories. The figures are summarized in tables 5 and 6. Some important implications can be straightforwardly derived.

Looking at the expenditure elasticities in table 5, we notice that these are positive for all antibiotic groups. The result suggests that antibiotics are normal goods and is in accordance with Baye et al. (1997), who estimated that anti-infectives have positive income elasticity (1.331). More specifically, Chaudhuri et al. (2003) observed

	Uncompensated price elasticities	Compensated price elasticities	Expenditure elasticities
Classic penicillins	-1.009	-0.906	1.095
Penicillins (amoxi/clav) and 1 <sup>st</sup> - 2 <sup>nd</sup> generation cephalosporins	-0.464	-0.001	1
3 <sup>rd</sup> generation cephalosporins and quinolones	-1	-0.859	1
Macrolides	-0.643	-0.353	0.958

Table 5: Price elasticities and expenditure elasticities evaluated at the sample mean.

positive expenditure elasticities for different types of quinolones, ranging from 0.3 to 2.20. Since our expenditure elasticities are close to one, the consumption share of each group of antibiotics remains constant as the amount spent on other groups changes. The evidence then indicates that antibiotics in outpatient care can be denoted as necessities. As income raises, the need for additional consumption of antibiotics is negligible, *ceteris paribus*.

All uncompensated own-price elasticities have the expected negative sign and vary substantially from -1.009 to -0.464. The comparison with the existing literature is not straightforward, although some similarities might be pointed out. Focusing on anti-infectives, Baye et al. (1997) estimated uncompensated own-price elasticity equal to -0.916. Ellison et al. (1997) found significant and negative uncompensated own-price elasticities for the four types of cephalosporins analysed. Looking at quinolones only, Chaudhuri et al (2003) calculated a relatively high uncompensated own-price elasticity, equal to -2.5 on average and ranging from -0.45 to -5.5.

Our estimates indicate that the demand for 3<sup>rd</sup> generation cephalosporins and quinolones (group 3) and the demand for classic penicillins (group 1) are more price elastic than the demand for penicillins amoxi/clav and 1<sup>st</sup> and 2<sup>nd</sup> genera-

	Classic penicillins	Penicillins (amoxi/clav) and 1 <sup>st</sup> - 2 <sup>nd</sup> gen. cephalosporins	3 <sup>rd</sup> generation cephalosporins and quinolones	Macrolides
Classic penicillins	-	0.509	6.873	-0.076
Penicillins (amoxi/clav) and 1 <sup>st</sup> - 2 <sup>nd</sup> gen. cephalosporins	-	-	-1.158	0.388
3 <sup>rd</sup> generation cephalosporins and quinolones	-	-	-	1.749

Table 6: Allen elasticity of substitution between two groups of antibiotics.

tion cephalosporins (group 2) and the demand for macrolides (group 4). It is worth noticing that the highest own-price elasticities are found for the most expensive antibiotic category (group 3) and the traditional and less frequently used antibiotics (classic penicillins). The rationale may be that doctors and patients are more likely to increase or reduce the consumption of the latest generation of cephalosporins and quinolones when their price changes, since this category of antibiotics is at least partially used to reduce uncertainty on the severity of the infection and the implications in terms of bacterial resistance. On the other hand, they are less likely to leave commonly used antibiotic therapies such as previous generations of cephalosporins, penicillins and macrolides. Classic penicillins represent a traditional antibiotic therapy whose comparative advantage has been substantially undermined by better alternatives. Consequently, they may be quite sensitive to variations in relative prices.

As expected, the Hicksian own-price elasticities are smaller in magnitude compared to the Marshallian elasticities. This suggests that the pure effect of substitution is only partially compensated by the income effect.

Substitution and complementary relationships among antibiotic groups are cap-

tured by the Allen elasticities presented in table 6. Positive values denote that two groups are substitutes. In our case, narrow spectrum antibiotics such as penicillins amoxi/clav and early generations of cephalosporins do not appear to be good substitutes for antibiotics with a larger spectrum such as new cephalosporins and quinolones. The rationale may be that old generations of cephalosporins are not perceived to be effective against severe infections. Moreover, newer generations are generally taken into account to overcome specific problems of bacterial resistance encountered in the use of previous generations.

As a consequence, doctors may prefer to switch to classic penicillins or macrolides rather than to the latest generations of cephalosporins and quinolones when the price of group 2 increases. This hypothesis is in accordance with the positive sign of elasticities of substitution between group 3 and groups 1 and 4.

The Allen's elasticity of substitution confirms that the demand for classic penicillins follows the demand for macrolides when the price of the latter category changes. The result may be associated to a certain degree of persistency in patients' tastes. For instance, doctors argue that children have a preference for macrolides rather than penicillins. This could imply that an increase in the price of macrolides is likely to induce a higher consumption of cephalosporins or newer antibiotic components, thus driving the utilization of classic penicillins downward, *ceteris paribus*.

## 5 Conclusion

The demand for antibiotics has been investigated in the studies by Ellison et al. (1997) and Chaudhuri (2003). The focus is on specific market segments where antibiotic substances constitute very close therapeutic substitutes and are similar in terms of the impact of bacterial resistance. There are, however, arguments for considering a more extended set of drugs.

We propose a model of the demand for antibiotics for respiratory infections prescribed in outpatient care. We aggregate therapeutic components in a reasonable number of categories to define the doctor's plausible choice set. Therapeutic proper-

ties and the risk of bacterial resistance are then simultaneously taken into account. Conversely from previous studies, our linear approximate almost ideal demand system model includes determinants of the demand structure other than price, such as demographic and cultural characteristics of the population and practice self-dispensing status.

The results lead us to the conclusion that the highest demand elasticities are observed for the 3<sup>rd</sup> generation cephalosporins and quinolones, the newer and more expensive antibiotic category, and classic penicillins, the most traditional and cheapest category. We found complementary effects between antibiotics with a relative narrow spectrum (penicillins amoxi/clav and cephalosporins I-II) and antibiotics with a relative large spectrum (3<sup>rd</sup> generation cephalosporins and quinolones), and between classic penicillins and macrolides. On the other hand, demand elasticity suggests a good degree of substitution between the other categories, i.e. different types of penicillins, macrolides and early cephalosporins, 3<sup>rd</sup> generation cephalosporins and macrolides.

As for the impact of population characteristics, we observed that an increasing proportion of elderly people positively affects the proportion of new cephalosporins/quinolones and reduces the proportion of macrolides used. The Latin culture is associated with a more substantial use of new cephalosporins/quinolones and macrolides and a lower proportion of penicillins amoxi/clav and cephalosporins I-II.

We found evidence that self-dispensing practices have a tendency to shift upward the demand share for newer and more expensive antibiotics and to reduce the demand share of traditional and less expensive antibiotics such as penicillins amoxi/clav and cephalosporins I-II.

In our view these results are important because of current policy interest in battling bacterial resistance and promoting a correct use of antibiotics. Our findings help to enlighten the pharmaceutical purchasing process and doctors' behaviour. Health care policy makers could then shape reforms by taking into account the incentives to prescribe different antibiotic substitutes. More effective dissemination of information

on prices and the impact of bacterial resistance to physicians and patients might be an example of measure to improve efficiency in the use of antibiotics.

Moreover, our results suggest that the introduction of a local tax on the antibiotic components that are responsible for higher levels of bacterial resistance may contribute to change the antibiotic mix and, therefore, to improve efficiency in antibiotic consumption. Since overconsumption determines a negative externality for the society, there might be good reasons for supporting this special mechanism of taxation.

Finally, data on the incidence of bacterial resistance at a local level are not easily available. We think that it would be advisable to promote their regular collection and to use them in new studies in order to see what effect they may have on antibiotic prescribing practices, and more generally on the econometric results.

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