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An empirical analysis of habit and addiction to antibiotics

by

Massimo Filippini, Giuliano Masiero

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An empirical analysis of habit and addiction to antibiotics

M. Filippini * G. Masiero †

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Abstract

Because of bacterial resistance, current antibiotic consumption is reinforced by past use, and future utility is lower. The purpose of this article is to provide evidence on habit and addictive behavior toward antibiotics by exploring variations in the average consumption of antibiotics across 20 Italian regions. Using a balanced panel dataset (2000-2009), we estimate myopic and rational addiction models in which antibiotic consumption depends upon demographic and socioeconomic characteristics of the population, the supply of health care in the community, antibiotic price, and the "capital stock" of endogenous bacterial resistance measured by past and future consumption. Our empirical evidence shows that past antibiotic consumption stimulates current consumption and is also consistent with the rational addiction hypothesis. The low price elasticity of antibiotic demand suggests that policy measures targeted at antibiotic co-payments may not be effective in controlling antibiotic consumption. There is scope for other policy interventions, such as incentives and information campaigns targeted at doctors.

Keywords: Antibiotic consumption, bacterial resistance, dynamic model, rational addiction.

JEL classification: C21, C23, I1

*Department of Economics, University of Lugano; ETH, Zurich, Switzerland.

†Department of Economics and Technology Management, University of Bergamo, Italy; Department of Economics, University of Lugano, Switzerland. Corresponding author. Tel.: +41 058 666 4731; fax: +41 058 666 4733. E-mail address: giuliano.masiero@usi.ch.

1 Introduction

Antibiotic misuse increases the threat of bacterial resistance, which in turn reduces antibiotic effectiveness over time (Elbasha, 2003; Laxminarayan and Brown, 2001). It has been suggested that efforts to restrict antibiotic use in outpatients have not been very successful since no central agent, such as a hospital administrator or infection control committee, can enforce an antibiotic policy (Harbarth and Samore, 2005). Understanding of the dynamics of antibiotic consumption may help shape appropriate measures of public intervention to optimize the use of antimicrobials. The empirical literature is lacking in this respect.

Recent theoretical studies on the economics of antibiotics suggest that consumers make inter-temporal decisions. To some extent, antibiotics are similar to addictive goods since individuals may develop dependence or experience persistent attitudes toward consumption. Also, current antibiotic consumption may be affected by past consumption because of endogenous bacterial resistance. Static empirical models of antibiotic demand do not consider the process of adjustment toward optimal levels of antibiotic consumption.

The mechanism of transmission of antimicrobial resistance is described by the basic SIS epidemiological model, which is used, for instance, in recent theoretical studies by Herrmann and Gaudet, 2009 and Wilen and Msangi, 2003. The SIS model assumes that the population is partitioned into infected individuals and individuals in good health. Uninfected individuals can become infected through contact with the infected population and individuals can be infected by a drug-resistant strain or a drug-susceptible strain. The transmission of drug-resistant strains to healthy individuals depends on the number and the speed of contacts among individuals. Some individuals infected with a drug-resistant strain naturally recover, but the rate of recovery for those treated with antibiotics remains unchanged.

In this paper, we propose a dynamic approach to investigate antibiotic use in outpatient care that hypothesizes that antibiotic consumption is affected by antibiotic inefficacy, i.e., the stock of bacterial resistance to antimicrobials. The level of inefficacy represents a bad that is indirectly measurable by means of past and future antibiotic use.

Individuals may be myopic in the sense that the effect of present antibiotic consumption on future consumption is not taken into account in their consumption choices. In this case, past consumption is presumed to affect present consumption only through the reduced level of antibiotic effectiveness. Conversely, patients may be aware of future implications of antibiotic use in terms of reduced antibiotic effectiveness. The plausibility of this assumption is also supported by the trust patients place in their doctors, whose superior knowledge of the implications of antibiotic treatment drives patients' decisions. This may imply that addiction to antibiotics is rational. If consumers' perceived benefits from antibiotic prescriptions outweigh the small uncertain costs associated with increased resistance (Brown and Layton, 1996), rational agents may not restrain from increasing consumption over time.

To investigate consumers' behavior, we explore myopic and rational models of habit and addiction to antibiotics. This represents the main novelty of our analysis and provides a significant contribution to the existing empirical literature on antibiotic consumption. We focus on variations in the average consumption of antibiotics across 20 Italian regions using a balanced panel between 2000 and 2009. Estimations are carried out by means of suitable approaches for short dynamic panels.

Our findings support the hypothesis of habit to antibiotic consumption and reject the myopic model in favor of the rational addiction model. Since short- and long-run price elasticity estimates are found to be relatively low, we suggest that increasing copayments may not be a valid instrument to reduce antibiotic consumption and control bacterial resistance. There is scope for other policy measures based on incentives for physicians and information campaigns targeting doctors and patients.

The remainder of the paper is organized as follows. Section 2 provides an overview of aspects of antibiotic demand and discusses models of habit and addiction to antibiotics. In Section 3 we derive our empirical model of demand for antibiotics and discuss the estimation approach. Section 4 presents the results and Section 5 concludes.

2 The dynamics of antibiotic consumption

2.1 Physician versus patient

The Italian healthcare system is based upon a national health service (SSN) mainly financed by general taxation and characterized by universal access to health care for the entire population and asymmetric decentralization of health care provision to the 20 regions. The regions allocate financial resources to the local health authorities (LHAs) within their territories. Patients are registered with GP practices within their province of residence. Antibiotics are prescribed by general practitioners (GPs) operating within the LHA and by pediatricians and specialists.

Antibiotic consumption requires a doctor's consultation, but usually patients do not pay for visits. Patients directly pay a small fraction of the full cost of drugs (copayment). The copayment - "ticket" - includes both a cost-sharing scheme and a reference pricing scheme. According to these, patients are required to contribute to the cost of antibiotics either by a fixed amount per prescription or by a proportional-to-final price amount, or by paying the difference between the final price and the reference price. The reference price is set for drugs that contain the same active ingredient, identical pharmaceutical dosage and package size.

2.2 Information and incentives

Antibiotic treatment cures patients affected by common bacterial infections and significantly reduces recovery time.[1] Antibiotics also have external benefits since they are similar to preventive care. In this sense, the use of antibiotics may contribute to reducing the spread of bacterial infections to other individuals, which increases future social benefits from consumption.

Although direct monetary costs of antibiotic treatment (copayment) are relatively low, antibiotic consumption is characterized by non-monetary and external costs. Current antibiotic use may increase the stock of bacterial resistance, which

[1] A recent survey by the European Commission (2010) indicates that the majority of the Italian population (51%) thinks that antibiotics are effective against common infections, such as colds or flu, which are not cured by antibiotics.

in turn reduces the effectiveness of antibiotics over time (Elbasha, 2003).

Although patients appear to be poorly informed about future costs and benefits of antibiotic consumption, doctors' advice may recognize the full price of addictive antibiotic consumption. The full cost of antibiotic treatment, which includes the monetary price as well as the future cost of reduced effectiveness due to past consumption, could then be weighed against the benefits of antibiotic consumption.

2.3 Alternative models of antibiotics demand

2.3.1 Static models

Static models of antibiotic consumption ignore the link between consumers' preferences in different time periods. They assume that a change in current consumption affects consumers' utility in the current period only and that consumers do not respond to changes in past consumption. Consequently, consumption in different periods is fully separable. This implies that individuals instantaneously adjust to the optimal level of consumption while also taking bacterial resistance into account.

Consider a simple model in which utility depends on the consumption of a composite good, c_t, the consumption of antibiotics, a_t, and the level of bacterial resistance, R_t. Individuals maximize the following utility function:

$$U_t = u(c_t, a_t; R_t), \tag{1}$$

under the usual budget constraint.

Static models of antibiotic demand exploit cross-sectional data. Usually, data on bacterial resistance are unavailable. Filippini et al. (2006) propose an econometric model in which antibiotic use across 26 Swiss cantons varies according to the socioeconomic and demographic characteristics of the population, the incidence of infections, the local supply of health care, and antibiotic price. Findings suggest that antibiotic consumption is significantly related to per capita income, antibiotic price, the density of medical pactices, and demographic, cultural, and educational factors. Kern et al. (2006) investigate variations in antibiotic prescriptions across 23 areas in 16 German states in relation to age, population density,

income, unemployment, and aspects of local health care supply. Regional patterns of use are similar for children and adults, although lower levels of consumption for children are observed in southern regions. The study does not find any significant association between antibiotic consumption and population density, the percentage of elderly people, income, unemployment, gross domestic product, and aspects of local healthcare supply. Matuz et al. (2005) explore regional variations in antibiotic consumption in ambulatory care in Hungary. The authors do not find any significant relationship between antibiotic consumption and the average monthly net income or the demographic structure of the population. Conversely, a significant association is observed between antibiotic consumption and the proportion of individuals receiving free access to selected medicines from the public health system without quantity limits and the proportion of individuals regularly receiving social assistance. Finally, Filippini et al. (2009) estimate an econometric model of the demand for antibiotics using data from 240 small areas in Switzerland. The results suggest a positive relationship between antibiotic consumption and income, the proportion of children between 0 and 14 years of age, and the density of pharmacies and physicians. On the other hand, antibiotic price and the proportion of individuals over 74 years of age show a significant negative impact on antibiotic use.

To our knowledge, the only study that utilizes panel data and includes bacterial resistance among explanatory variables is the recent investigation by Masiero et al. (2010) on socioeconomic determinants of antibiotic use in Europe. The population income, demographic structure, density of general practitioners, and their remuneration method appear to be significant determinants of antibiotic consumption. The responsiveness of antibiotic use to changes in bacterial resistance is found to be relatively low, between 0.09 and 0.18. A limitation of this study is that the process of adjustment toward optimal levels of antibiotic consumption is neglected.

2.3.2 Models of myopic addiction

Recent theoretical studies on the economics of antibiotics assume inter-temporal decisions (Laxminarayan and Weitzman, 2002; Herrmann, 2010). Although the

empirical literature is replete with studies on endogenous tastes in the consumption of cigarettes and alcohol (e.g., Chaloupka, 1991; Jones, 1994; Baltagi and Griffin, 2001; Hidayat and Thabrany, 2010), the investigation of the dynamics of antibiotic consumption is lacking.

In a model of addiction to antibiotics as habit formation, greater past consumption of antibiotics increases the desire for present consumption. This represents the so-called reinforcement condition required for addiction, which suggests that individuals who have undergone antibiotic treatment in the past are more likely to consider the use of antibiotics in the current period.[2] However, individuals ignore the future benefits and costs of their decisions and are, therefore, myopic. The hypothesis of myopic behavior in the consumption of antibiotics could be plausible for a number of reasons. Patients and their doctors may not be fully aware of the future harmful consequences of current antibiotic consumption. This is because limited information is available on the levels of antimicrobial resistance, and agents may not be able to evaluate correctly the impact of resistance on future antibiotic efficacy. Patients may not be aware of studies that demonstrate conclusively that prior use of antibiotics increases a person's risk of acquiring a resistance infection (Laxminarayan, 2001).

Assume that past antibiotic consumption is a measure of antibiotics inefficacy, i.e., the stock of bacterial resistance, R_t. The variation in antibiotic efficacy over time, $\Delta R_t/\Delta t$, depends on the consumption of antibiotics and the depreciation rate of the stock of bacterial resistance, ρ, - the rate at which bacteria regress to the susceptibility state in the absence of antibiotic treatment, also called the "fitness cost of resistance" -. The stock of bacterial resistance can then evolve

[2] This may be explained by some physical or psychological effects which persist over time. It may also reflect physicians' attitudes toward antibiotic prescriptions. Under uncertainty on the nature of patients' infection, antibiotic therapy may appear to have been beneficial even though patients' relief was not due to the treatment. General practitioners may prefer antibiotic therapies since they were presumably effective in the past or patients are not willing to wait for recovery.

according to the following relationship:[3]

$$R_t = (1 - \rho)\, R_{t-1} + a_{t-1}. \tag{2}$$

This stock adjustment condition relates the stock of habit to the consumption of antibiotics. Although this stock depends on antibiotic consumption, it is redefined to represent the influence of bacterial resistance.[4]

2.3.3 Rational addiction and time preferences

The main insights of rational addictive behavior are theoretically derived by Becker and Murphy (1988). A sizable empirical literature compares myopic and rational models of addictive behavior (e.g., Luo et al., 2003; Tiezzi, 2005).

In the case of antibiotics, rational individuals are aware that higher levels of antibiotic consumption decrease future utility, given the amount of future consumption (tolerance condition for addiction). Rational consumers weigh current benefit from consumption against the future health consequences in terms of the risk of antibiotic inefficacy and the future costs of purchasing new antibiotics. For instance, since endogenous bacterial resistance reduces antibiotic efficacy over time, individuals know that more therapies have to be considered before finding the one effective in curing the infection.[5]

Following Becker and Murphy (1988), we can extend Eq. 1 to write the lifetime utility function of rational agents with a constant rate of time preference, δ, as:

$$\sum_{t=1}^{\infty} \delta^{t-1} U_t, \tag{3}$$

where $\delta = 1/(1 + r)$ and r is the interest rate.

In Eq. 3, forward-looking agents are assumed to be time consistent. This means that current preferences regarding future behavior are in accordance with

[3] This simple relationship assumes that the effects on antibiotic efficacy generated by the consumption of other agents are negligible or hidden from consumers. However, bacterial resistance generated by other agents may also represent a constraint. Although bacterial resistance plausibly spreads within regions, i.e., it is a local phenomenon, researchers have hypothesized some global effects (Rudholm, 2002).

[4] See Jones (1999) for an interpretation of stocks of habits in state adjustment models.

[5] Throughout the paper, we assume that individuals make decisions on antibiotic consumption following the advice of their doctors, as suggested above in Section 2.2. We hypothesize that doctors are perfect agents and patients are compliant with the prescribed antibiotic therapy.

this behavior. The assumption has been challenged by Gruber and Köszegi (2001) who extended the analysis to time inconsistency. Antibiotic consumption under time-inconsistent preferences would indicate, for instance, that individuals state that they agree with a more careful use of antibiotics and are aware of costly implications of bacterial resistance. Nevertheless, they are unable to act in accordance with this view and ignore these aspects in their future choices of consumption.[6]

3 Model specification and econometric approach

For our empirical approach, we simplify the dynamic equation 2 and assume that bacterial resistance fully depreciates after one period, i.e. $\rho = 1$. Using (1) and (2), we can then write the lifetime utility function (3) as:

$$\sum_{t=1}^{\infty} \delta^{t-1} u\left(c_t, a_t, a_{t-1}, e_t\right), \tag{4}$$

where e_t represents the impact of unmeasured life-cycle variables on utility.

Following Becker et. al. (1994), we can define the maximization constraint as:

$$a_0 = a^0 \text{ and } \sum_{t=1}^{\infty} \delta^{t-1}\left(c_t + P_t a_t\right) = A^0, \tag{5}$$

where P_t is antibiotic co-payment at period t, a^0 is the initial condition indicating the level of antibiotic consumption at period zero, and A^0 is the present value of wealth.

The first-order conditions to solve the problem above imply that the marginal utility of current antibiotic consumption plus the discounted marginal effect on the next period's utility of current consumption is equal to the marginal utility of wealth multiplied by the current co-payment. Furthermore, the marginal utility of wealth equals the marginal utility of the composite good in each period. Using a quadratic utility function, the solution of the first-order conditions leads to the following first-difference equation:

$$a_t = \theta a_{t-1} + \delta\theta a_{t+1} + \theta_1 P_t + \theta_2 e_t + \theta_3 e_{t+1}. \tag{6}$$

[6] Two extreme kinds of agents, naive and sophisticated, are of interest. Naive agents attach extra value to antibiotic consumption in the current period relative to future periods but are unaware of their future inability to use antibiotics more carefully. Conversely, sophisticated patients realize that they are time-inconsistent.

In this equation, current antibiotic consumption is a function of past and future consumption, co-payment, and unobservable variables. The θ coefficients depend on the parameters of the quadratic utility function. For further details see Baltagi and Griffin (2001). A comprehensive discussion on the interpretation and the derivation of Eq. 6 can be found in Becker et al. (1994).

To empirically investigate the dynamics of antibiotic consumption, we modify the first-difference equation 6, as in Baltagi and Griffin (2002), and write the following equation:

$$\begin{aligned} a_{it} &= \beta_0 + \beta_1 a_{it-1} + \beta_2 a_{it+1} + \beta_3 P_{it} + \beta_4 Y_{it} + \beta_5 POP_{1it} + \beta_6 POP_{3it} \\ &\quad + \beta_7 DPOP_{it} + \beta_8 DPH_{it} + \beta_9 INF_{it} + \beta_{10} IMM_{it} + v_{it}, \end{aligned} \tag{7}$$

where a_{it} is the level of antibiotic use in the ith region ($i = 1, ..., 20$) at time t, measured in defined daily doses per 1000 inhabitants; Y_{it} is real GDP per capita, and POP_{1it} and POP_{3it} denote respectively the percentage of the population below 14 and above 74. $DPOP_{it}$ is population density and DPH_{it} is the density of physician practices. Finally, INF_{it} captures the rate of infectious diseases, IMM_{it} denotes the rate of working permits for foreign workers, and ν_{it} is a disturbance term.

From Eq. 7 one can obtain the discount rate (δ) as the ratio between the estimated coefficient of a_{t+1} (β_2) and the estimated coefficient of a_{t-1} (β_1). The coefficient β_1 captures the impact of past consumption on current consumption. Consequently, a positive and significant coefficient is consistent with the hypothesis that antibiotic use is a habit or addictive behavior. The coefficient β_2 measures the impact of future consumption on current consumption. A positive and significant coefficient would be consistent with the hypothesis of rational addiction and would support rejecting the hypothesis of myopic addiction.

One can easily limit the focus to myopic consumers by combining Eqs. 1 and 2. Myopic agents maximize current period utility instead of the lifetime utility function (3), under the assumption that current antibiotic consumption is affected by past consumption as hypothesized by (2). A myopic model of addiction can be derived from (7) by dropping the lead term a_{t+1}:

$$
\begin{aligned}
a_{it} &= \beta_0 + \beta_1 a_{it-1} + \beta_2 P_{it} + \beta_3 Y_{it} + \beta_4 POP_{1it} + \beta_5 POP_{3it} \\
&\quad + \beta_6 DPOP_{it} + \beta_7 DPH_{it} + \beta_8 INF_{it} + \beta_9 IMM_{it} + v_{it}. \qquad (8)
\end{aligned}
$$

For the estimation of myopic and rational models of addiction to antibiotics, we have a balanced panel data set for the 20 Italians regions. To account for unobserved heterogeneity, we could use a fixed effects (LSDV) or a random effects (RE) model. However, the estimation of the dynamic panel data models (7)-(8) using LSDV or RE estimators is not appropriate. This is because the inclusion of lagged and lead-dependent variables among regressors violates the strict exogeneity assumption. In fact, lagged and lead variables are correlated with the error term, which leads to biased and inconsistent estimates of LSDV and RE.[7] In the literature, several instrumental variable estimators have been proposed to solve this problem. Anderson and Hsiao (1982) proposed a simple instrumental variable estimator. Arellano and Bond (1991) as well as Blundell and Bond (1998) proposed two different estimators based on the general method of moments (GMM-AB and GMM-BB). A problem with these estimators is that properties do not hold for small panel data (small N and T).[8]

Kiviet (1995) suggested an alternative approach to small panel data sets for the estimation of dynamic models with just a lagged variable, such as model (8), based on the correction of the bias of the LSDV model.

In a Monte Carlo analysis, Judson and Owen (1999) and Kiviet (1995) showed that in typical aggregate dynamic panels characterized by T lower than or equal to 20 and N lower or equal to 50, as in our case, the Anderson-Hsiao and the Kiviet-corrected LSDV (LSDVC) estimators have better properties than the GMM estimator proposed by Arellano and Bond (1991). Despite having a higher average bias, the corrected LSDV estimator turns out to be more efficient than the Anderson-Hsiao. This suggests that the corrected LSDV estimator is an effective approach for small panels ($T \leq 20$), while the Anderson-Hsiao estimator is more appropriate for large panels, as the efficiency of the latter improves with T.

[7] For a discussion of this issue and for a presentation of econometric models for panel data see Baltagi (2001).

[8] For a discussion of this issue, see Harris et al. (2008), p. 269.

An alternative method to solve the endogeneity problem is the fixed-effects two-stage least squares approach (FE2SLS) inspired by the original work of Balestra and Nerlove (1966). This approach is discussed in detail in Baltagi (2001) and applied by Baltagi and Griffin (2002). The approach employs the within transformation and utilizes the exogenous variables and their lags as instruments. Obviously, the effectiveness of the FE2SLS estimator critically depends on the quality of the instruments adopted.

Our panel includes 20 regions for the period $2000 - 2009$. Given the characteristics of the panel, we choose the LSDVC and the FE2SLS estimators for our myopic model of addiction defined by (8).[9]

For the estimation of the dynamic model in (7), the corrected LSDV estimator is not completely appropriate. The reason is that this estimator is valid in the presence of exogenous regressors only. To the extent that one-period forward consumption (a_{it+1}) is endogenous, as discussed in Becker et. al. (1994), the coefficient of this variable is biased. This potential endogeneity problem, caused by lagged and forward consumption, can be solved by the FE2SLS approach, as suggested by Baltagi and Griffin (2002). We consider lagged and lead values of price, income, and other covariates as instruments for past and future consumption. We then estimate Eqs. 7 and 8 using both the corrected LSDV and the FE2SLS approaches. We are fully aware that the estimation of (7) using the corrected LSDV estimator could produce biased results.

3.1 Data

The balanced panel data set for the 20 Italian regions was created using several sources. Data on regional outpatient antibiotic consumption, i.e., group J of the Anatomical Therapeutic Chemical Classification (ATC) of drugs, were collected from annual reports prepared by the Italian National Observatory on Drugs Utilization (Osmed). The per capita consumption is measured by the number of defined daily doses per 1000 inhabitants per day (DID). A defined daily dose

[9] Spatial aspects of consumption are not considered here. In a preliminary stage of this analysis we estimated a spatial dynamic model following two approaches: the corrected 2SLS approach suggested by Beenstock and Felsenstein (2007). However, the results were not encouraging. This could be due to the fact that our data set is characterized by a low T and a low N.

represents the standard dose necessary for one day of drug treatment in adults and is defined by an independent scientific committee answering to the WHO Collaborating Center for Drug Statistics Methodology. The DID measure can be interpreted as the number of persons (out of 1000) who are taking antibiotics on a given day.

Data on antibiotic consumption in Italy are available for the 10 years between 2000 and 2009. Summary statistics are provided in Table 1. The mean level of antibiotic consumption during the period was 23.70 DID. Antimicrobials use slightly increased over time, with a peak in 2009 (25.24) and a minimum in 2000 (22.36). A remarkable degree of heterogeneity in consumption is observed across the regions. Generally, regions in central Italy use more antibiotics per capita (25.12 DID) than regions in the north (18.53 DID) and less than southern regions and the islands (28.99 DID).

As mentioned in Section 2.1, antibiotics are included in class A by the Italian National Health Service (SSN), which means they require a doctor's prescription and are supplied virtually free of charge, in return for small patient co-payments. Information on co-payments is obtained from annual reports on pharmaceutical consumption and expenditure prepared by Osmed. Regional co-payments vary from 0 to 4 Euros with a national average of 0.87 Euros.

Data on the demographic structure of the population and density, per capita income, density of general practices, the number of working permits for immigrants, and the rate of infectious diseases are obtained from the Italian National Institute of Statistics (Istat). Data on these covariates are available for 9 years, between 2000 and 2008, with the exception of income and population density.

4 Results

In this section, we discuss the results obtained from the estimations of our models of habit and addiction to antibiotics. For the myopic model, estimations are carried out on the modified Equation 8, while the rational addiction model is directly estimated on (7). Both models are estimated by means of the corrected LSDV and the FE2SLS estimators discussed above. We summarize our findings in Table 2 for the myopic model and in Table 3 for the rational addiction model.

The estimates are shown together with p-values of the test statistics and standard errors. The number of observations used in the FE2SLS regressions is lower than the number of observations used in the LSDVC regressions, since lead values of explanatory variables are included among the set of instruments in the FE2SLS approach. First-stage regressions on the instruments yield significant joint F-tests and exhibit high R^2, 0.54 and 0.80, respectively for the myopic and the rational addiction models. Finally, the p-value of the Sargan-test statistics does not reject the null hypothesis and concludes that the overidentifying restriction is valid.

In the myopic model, the dynamics of antibiotic use is captured by the coefficient of the lagged variable of consumption, a_{t-1}. This is positive and highly significant in both the LSDVC and the FE2SLS regressions, which supports the hypothesis of habit to antibiotic consumption. The coefficient of income is also significant in the FE2SLS regression, at the 5% significance level. In accordance with the economic theory, we find a statistically significant and negative association between antibiotic consumption and co-payment, at least in the LSDVC estimation, even though the impact is relatively low.

Using the coefficient of co-payment we can calculate the short- and long-run elasticities. Short- and long-run price elasticities (ε_t and ε_∞) evaluated at the means of the data (a and P) can be calculated using the formulas derived by Becker et al. (1994) in their Appendix A and applied in Baltagi and Griffin (2001, 2002). For the short-run elasticity $\varepsilon_t = (da_t/dP_t)(P/a)$ with $da_t/dP_t = 2\beta_3/[1-2\beta_2+(1-4\beta_1\beta_2)^{0.5}]$, and for the long-run elasticity $\varepsilon_\infty = (da_\infty/dP)(P/a)$ with $da_\infty/dP = \beta_3/(1-\beta_1-\beta_2)$. For the myopic model, we use these formulas assuming that β_2 is zero.

Short- and long- run elasticities for myopic consumers are -0.02 and -0.03, respectively. The average long-run elasticity is approximately 1.5 times as large as the short-run elasticity. Using a natural experiment across Italian regions, Fiorio and Siciliani (2010) investigate the effect of co-payments on drug prescriptions. They find that an increase in the co-payment by one Euro reduces the per capita number of prescriptions by 4% and the per capita public pharmaceutical expenditures by 3.4%.

As for the rational addiction model estimated using (7), we observe that the

coefficients of past and future consumption are significant and positive in both the LSDVC and the FE2SLS estimations, which rejects the myopic model in favor of the rational addiction model. The rate of infections is also significant at less than 10% level in both regressions, while income is only significant in the FE2SLS regression at the 10% significance level.

The coefficients of the population below 14 (POP_1) and above 74 (POP_3) are generally not significant, with the exception of POP_1 in the myopic LSDVC model. Negative signs of these coefficients may indicate that regions with a relatively large proportion of younger and elderly individuals are less likely to use antibiotics, ceteris paribus. The literature has suggested an increase in the utilization of healthcare services as people grow older. However, this relationship finds very weak support in some empirical studies (see, for instance, Di Matteo, 2005) as well as in studies of antibiotic use. There are some plausible explanations for this. First, individuals in the labor force may be more prone to use antibiotics because of time pressure. Second, individuals may be more careful when giving antibiotics to their children because of perceived risks. A similar consideration applies to elderly individuals.

Following Baltagi and Griffin (2001), we calculated the interest rate as $r = (1 - \delta)/\delta$, where δ is the ratio between the estimated coefficient of a_{t+1} and the estimated coefficient of a_{t-1}, as shown by Equation 6 in Section 3. The estimated coefficients of the lag and lead variables of antibiotic consumption suggest that the discount rate *(δ)* ranges from 0.88 in the corrected LSDV estimation to 0.92 in the FE2SLS approach. Accordingly, these figures indicate that the interest rate (r) varies from 8.7% to 13.6%. Support for the rational addictive behavior is reinforced by the positive and relatively close values of the interest rate. The magnitude of these figures is not implausible since the discount factor is lower than one, which gives positive interest rates.

The coefficient of copayment is significant in the corrected LSDV only, as in the myopic model. This coefficient could be biased, as explained above. Nevertheless, we can calculate short- and long-run price elasticities for rational agents using the formulas above. The short-run elasticity is around -0.05, while the long-run elasticity is about -0.14. Elasticities are relatively low compared to estimated

elasticities for cigarettes and alcohol consumption in many empirical studies. In contrast to cigarettes and alcohol consumption, antibiotics are generally perceived as being necessary and are purchased under a doctor's advice. Moreover, at least in the Italian healthcare system, consumers directly pay a small proportion of the full price of antibiotics that has been relatively stable over time. This could imply that consumers are not very sensitive to price changes.

The possible policy implication of smaller short-run rather that long-run co-payment elasticities is that there is scope for raising revenues from increasing co-payments on antibiotics in the short-run. Moreover, these gains are long lived since the long-run elasticity is also relatively low. However, co-payments on antibiotic use may not represent an effective instrument to reduce antibiotic consumption and control bacterial resistance. The low elasticity of demand for antibiotics suggests that policy measures not targeted at antibiotic co-payments may be more effective in controlling antibiotic consumption. These measures may include providing incentives and information to physicians and public campaigns for promoting careful use of antibiotics targeted at consumers. A recent review of public campaigns in high-income countries (Huttner et al., 2010) highlights evidence that public campaigns have been successful in reducing antibiotic consumption, but their effects on bacterial resistance have not yet been accurately assessed.

5 Conclusions

An improved understanding of the dynamics of antibiotic consumption may contribute to the shaping of appropriate measures of public interventions to optimize the use of antimicrobials. Recent theoretical studies on the economics of antibiotics suggest that consumers make inter-temporal decisions. In this paper, we proposed a dynamic approach to investigate antibiotic use in outpatient care, which hypothesizes that antibiotic consumption is affected by antibiotic inefficacy, i.e., the stock of bacterial resistance to antimicrobials.

We explored myopic and rational models of habit and addiction to antibiotics, which represents the main novelty of our analysis and provides a significant contribution to the existing empirical literature on antibiotic consumption. We

found positive and significant coefficients of past and future consumption, which supports the hypothesis of habit to antibiotic consumption and rejects the myopic model in favor of the rational addiction model. Evidence of rational addiction is reinforced by positive values of the interest rate.

As for policy implications, our results indicate that short- and long-run price elasticity estimates are relatively low, at least for small co-payments such as those in Italy. Therefore, increasing co-payments may not affect antibiotic consumption appreciably. Information provided by public campaigns about the future negative effects of antibiotic misuse targeting doctors and patients may, however, have a significant impact on the behavior of forward-looking consumers.

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Variable	Description	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
DID	Defined daily doses per 1000	22.36	23.37	23.19	23.16	22.96	23.65	23.68	24.37	25.01	25.24
	inhabitants	(4.66)	(5.28)	(5.21)	(5.09)	(5.07)	(5.22)	(5.52)	(5.34)	(5.54)	(5.71)
Y	Income per capita (in Euro)	20291.71	21259.57	21912.71	22393.58	23109.98	23538.60	24409.48	25245.67	25473.37	24586.05
		(5203.70)	(5365.84)	(5509.91)	(5634.77)	(5817.21)	(5844.97)	(5893.22)	(6088.59)	(6150.55)	(5772.91)
POP_1	Proportion of population	14.02	13.97	13.94	13.88	13.82	13.78	13.75	13.70	13.67	-
	ages 0-14	(2.38)	(2.24)	(2.09)	(1.96)	(1.83)	(1.71)	(1.60)	(1.49)	(1.40)	-
POP_2	Proportion of population	77.51	77.29	77.05	76.88	76.76	76.59	76.39	76.26	76.14	-
	ages 15-74	(1.29)	(1.19)	(1.11)	(1.05)	(1.00)	(0.96)	(0.93)	(0.90)	(0.86)	-
POP_3	Proportion of population	8.47	8.74	9.01	9.24	9.41	9.63	9.86	10.04	10.19	-
	ages above 74	(1.68)	(1.70)	(1.70)	(1.69)	(1.67)	(1.64)	(1.61)	(1.58)	(1.54)	-
$DPOP$	Population density	174.37	174.42	174.92	176.21	177.82	179.09	180.06	181.27	182.58	183.99
		(106.17)	(106.16)	(106.45)	(107.28)	(108.43)	(109.35)	(110.16)	(111.04)	(111.78)	(112.79)
IMM	Number of working permits	1.98	2.27	(2.38)	2.47	3.14	3.71	4.11	4.47	5.24	-
	per 100 inhabitants	(1.00)	(1.18)	(1.26)	(1.37)	(1.70)	(2.04)	(2.27)	(2.48)	(2.74)	-
INF	Rate of infectious diseases	354.77	316.97	317.70	329.04	302.99	216.25	236.13	213.90	208.76	-
	per 100000 inhabitants	(235.91)	(224.02)	(152.28)	(173.01)	(168.50)	(109.35)	(144.24)	(156.63)	(171.41)	-
DPH	Density of physicians	0.83	0.83	0.83	0.83	0.82	0.82	0.82	0.82	0.82	-
	per 1000 inhabitants	(0.06)	(0.06)	(0.056)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	-
P	Copayment	1.50	0	0.83	0.85	0.95	0.70	0.65	0.95	1.1	1.17
		(0)	(0)	(0.92)	(0.92)	(0.94)	(0.92)	(0.93)	(1.19)	(1.18)	(1.31)

Notes: Figures represent mean value by year. Standard errors are in parenthesis.

Table 1: Descriptive statistics.

	LSDVC Obs. 140			FE2SLS Obs. 120		
Variables	Coefficients	St. Err.	p-value	Coefficients	St. Err.	p-value
Constant	-	-	-	14.39705	13.60300	0.290
P	-0.217246	0.095916	0.024	-0.065501	0.127598	0.608
Y	0.000193	0.000159	0.224	0.000585	0.000237	0.013
POP_1	-0.706939	0.349829	0.043	-0.155507	0.541298	0.774
POP_3	-0.606525	0.467679	0.195	-0.137834	0.838389	0.869
DPOP	-0.035590	0.027385	0.194	-0.025877	0.036700	0.481
DPH	1.832944	4.422422	0.679	-3.736097	5.937115	0.529
INF	-0.000861	0.000851	0.312	-0.001344	0.001046	0.199
IMM	0.342392	0.149850	0.022	-0.367148	0.247223	0.138
a_{t-1}	0.492594	0.092653	0.000	0.354114	0.166113	0.033

Notes: The instruments used in the $FE2SLS$ regression are P_t, Y_t, POP_{1t}, POP_{3t}, $DPOP_t$, DPH_t, INF_t, IMM_t, and their one- and two-period lags and future values. First-stage regressions on the instruments yield significant joint F-tests. Moreover, the p-value of the Sargan-test statistics does not reject the null hypothesis and concludes that the overidentifying restriction is valid.

Table 2: Parameter estimates of myopic models of habit to antibiotics.

	LSDVC Obs. 140			FE2SLS Obs. 120		
Variables	Coefficients	St. Err.	p-value	Coefficients	St. Err.	p-value
Constant	-	-	-	0.990672	14.05327	0.944
P	-0.191576	0.086065	0.026	-0.121166	0.122829	0.324
Y	0.000008	0.000147	0.956	0.000437	0.000232	0.060
POP_1	-0.269570	0.324759	0.407	0.400516	0.518027	0.938
POP_3	-0.469742	0.426974	0.271	-0.367230	0.797943	0.645
DPOP	-0.008220	4.034917	0.738	0.007821	0.037502	0.835
DPH	1.534188	0.170049	0.704	-0.490277	5.775167	0.932
INF	-0.001320	0.000781	0.091	-0.002019	0.001029	0.050
IMM	0.206112	0.138807	0.138	-0.434565	0.235284	0.065
a_{t-1}	0.474151	0.078549	0.000	0.364383	0.156979	0.020
a_{t+1}	0.417266	0.080337	0.000	0.334489	0.141954	0.018

Notes: The instruments used in the $FE2SLS$ regression are P_t, Y_t, POP_{1t}, POP_{3t}, $DPOP_t$, DPH_t, INF_t, IMM_t, and their one- and two-period lags and future values. First-stage regressions on the instruments yield significant joint F-tests. Moreover, the p-value of the Sargan-test statistics does not reject the null hypothesis and concludes that the overidentifying restriction is valid.

Table 3: Parameter estimates of rational models of addiction to antibiotics.