

An empirical analysis of habit and addiction to antibiotics

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Abstract

To some extent, antibiotics are similar to addictive goods. 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 behaviour towards antibiotics by exploring variations in the average consumption of antibiotics across Italian regions. Using a balanced panel dataset (2000-2009) for 20 Italian regions, we estimate a dynamic model where antibiotic consumption depends upon demographic and socio-economic 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.

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

JEL classification: C21, C23, I1

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1 Introduction

The increasing use of antibiotics and the consequent harmful effects of bacterial resistance have become a growing concern in many countries. Evidence suggests that bacterial resistance grows with antibiotic use and may regress when antibiotic consumption is controlled (Monroe and Polk, 2000; Mera et al., 2006). Although public interventions may be effective in controlling antibiotic consumption (Huttner et al., 2010), the effects on bacterial resistance cannot be assessed accurately at present. The consumption dynamics of antibiotics and its behavioral aspects are still unclear.

To some extent, antibiotics are similar to addictive goods since individuals may develop dependence or experience persistent attitudes towards consumption. Addiction is a negative side-effect of consumption where the characteristics of goods interact with the characteristics of individuals. Consumption of addictive goods is characterized by reinforcement - higher levels of consumption in the past increases the desire for present consumption - and tolerance - utility of a given level of consumption is lower when past consumption is higher - (Peper, 2004). In the case of antibiotics, current consumption may be affected by past consumption because of endogenous bacterial resistance. Past consumption increases bacterial resistance, i.e. the ‘capital stock’, which in turn reduces the effectiveness of antibiotic use over time (Laxminarayan and Brown, 2001).

To our knowledge, the empirical analysis on the use of antibiotics is limited to static models of consumption. Recent theoretical developments suggest, however, that dynamic aspects play an important role in understanding consumption behavior (Herrmann and Gaudet, 2009). The spread of antimicrobial resistance reduces antibiotic effectiveness on each individual (internal effect) as well as for other individuals in the community (external effect). The mechanism of transmission of antimicrobial resistance is described by the basic SIS epidemiological model (Wilenski and Msangi, 2003). The 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.

Econometric models may incorporate the influence of consumption habits on preferences over time (Spinnewyn, 1981). To include habits or addiction aspects in models of antibiotic consumption one can drop the assumption that an increase in current consumption has just an impact on current individual's utility and assume correlation between consumption and utility in subsequent periods.

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 supposed to affect present consumption only through the reduced level of antibiotic effectiveness. Conversely, patients could be aware of future implications of antibiotic use in terms of reduced antibiotic effectiveness. This hypothesis stems also from the idea that patients trust their doctors, whose superior knowledge on the implications of antibiotic treatment drives patients' decisions. This may imply that addiction to antibiotics is rational.

In the empirical exercise, past and future antibiotic consumption can either be taken into account by means of lagged and lead variables included in models of consumption. The approach based on lagged and lead variables has been considered, for instance, by Baltagi and Levin (1986) and Becker et al. (1994) to estimate the demand for cigarettes; by Johnson and Oskanen (1977) and Baltagi and Griffin (2002) to study the demand for alcohol.

The purpose of this article is to provide some evidence on habit and addictive behavior towards antibiotics by exploring variations in the average consumption of antibiotics across Italian regions. We propose a dynamic approach to capture adjustment in consumption and the speed of the adjustment. Using balanced panel data from 20 Italian regions between 2000 and 2009, we estimate myopic and rational models of antibiotic consumption in outpatient care. Estimations are carried out by means of suitable approaches for short dynamic panels. Our findings indicate evidence of habit formation in the consumption of antibiotics and prove consistent with the hypothesis of rational addiction to antibiotics.

The remaining of the paper is organized as follows. Section 2 provides an overview on 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 health care 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, 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 this, 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 which 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 time to recover.¹ Antibiotics have also external benefits since they are similar to preventive care. In this sense, the use of antibiotics may

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

contribute to reduce the spread of bacterial infections to other individuals, which increase 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 in turn reduces the effectiveness of antibiotics over time (Elbasha, 2003).

Although patients appear to be poorly informed on future costs and benefits of antibiotic consumption, doctors's 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 consumer's preferences in different time periods. They assume that a change in current consumption affects consumer's utility in the current period only and 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 taking also bacterial resistance into account.

Consider a simple model where 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 where 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. 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. Matuz et al. (2005) explore regional variations in antibiotic consumption in ambulatory care in Hungary. Finally, Filippini et al. (2009) estimate an econometric model of the demand for antibiotics using data from 240 small areas in Switzerland.

To our knowledge, the only study utilizing panel data and including bacterial resistance among explanatory variables is the recent investigation by Masiero et al. (2010) on socioeconomic determinants of antibiotic use in Europe. A limitation of this study is that the process of adjustment towards optimal levels of antibiotic consumption is neglected.

2.3.2 Models of myopic addiction

Recent theoretical studies on the economics of antibiotics model consumption assuming inter-temporal decisions (Laxminarayan and Weitzman, 2002; Herrmann, 2010). Although the empirical literature is rich of 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 undergone antibiotic treatment in the past are more likely to consider the use of antibiotics in the current period.² However, individuals ignore future benefits and costs of their decisions and, therefore, are 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 are available on levels of antimicrobial resistance and agents

²This may be explained by some physical or psychological effects which persist over time. It may also reflect physician's attitude toward antibiotic prescriptions. Under uncertainty on the nature of patient's infection, antibiotic therapy may appear to have been beneficial even though patient's 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.

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 according to the following relationship:³

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

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

³This simple relationship assumes that the effect on antibiotic efficacy generated by consumption of other agents are negligible or hidden to 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).

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

time, individuals know that more therapies have to be considered before finding the effective one to cure the infection.⁵

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

$$\sum_{t=1}^{\infty} \delta^{t-1} U_t. \quad (3)$$

In equation (3), forward-looking agents are assumed to be time consistent. This means that current preferences regarding future behavior are in accordance with 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 carry out 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:

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

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:

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

⁵Throughout 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.

⁶Two extreme kind 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.

where P_t is antibiotic copayment 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. Assuming the utility function is quadratic, we then solve the first-order conditions for a_t and derive a first-difference equation where current antibiotic consumption is a function of past and future consumption, copayment, and unobservable variables.⁷

The first-difference equation derived by Becker et al. (1994) can be modified to investigate the dynamics of antibiotic consumption. We include socioeconomic aspects such as income, age, the local supply of health care, and the prevalence of community-acquired infections. For our empirical implementation we write the following equation:

$$a_{it} = \beta_0 + \beta_1 a_{it-1} + \beta_2 a_{it+1} + \beta_3 P_{it} + \beta_4 Y_{it} + \beta_5 POP_{1it} + \beta_6 POP_{3it} + \beta_7 DPOP_{it} + \beta_8 DPH_{it} + \beta_9 INF_{it} + \beta_{10} IMM_{it} + v_{it}, \quad (6)$$

where a_{it} is the level of antibiotic use in the i th region ($i = 1, \dots, 20$) 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 v_{it} is a disturbance term.

One can easily limit the focus to myopic consumers by combining equations (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 (6) by dropping the lead term a_{t+1} :

$$a_{it} = \beta_0 + \beta_1 a_{it-1} + \beta_2 P_{it} + \beta_3 Y_{it} + \beta_4 POP_{1it} + \beta_5 POP_{3it} + \beta_6 DPOP_{it} + \beta_7 DPH_{it} + \beta_8 INF_{it} + \beta_9 IMM_{it} + v_{it}. \quad (7)$$

⁷See equation (4) in Becker et al. (1994) for details. A similar approach is used by Baltagi and Griffin (2002) to investigate liquor consumption.

For the estimation of myopic and rational models of addiction to antibiotics we have a balanced panel data set for the 20 Italian 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 (6)-(7) using LSDV or RE estimators is not appropriate. This is because the inclusion of a lagged variable in equation (7) and the inclusion of a lagged and a lead variables in equation (6) among explanatory variables 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.⁸ 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).⁹

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 (7), 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 or equal to 20 and N lower or equal to 50, as it is our case, the Anderson-Hsiao and the Kiviet corrected LSDV (LSDVC) estimators are better 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 . 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).

Our panel includes 20 regions for the period 2000 – 2009. Given the charac-

⁸For a discussion of this issue and for a presentation of econometric models for panel data see Baltagi (2001).

⁹For a discussion on this issue, see Harris et al. (2008), p. 269.

teristics of the panel, we choose the LSDVC and the FE2SLS estimators for our myopic model of addiction defined by (7).¹⁰

For the estimation of the dynamic model in (6), 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 are 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 equations (6) and (7) using both the corrected LSDV and the FE2SLS approaches. We are clearly aware that the estimation of (6) using the corrected LSDV estimator could produce biased results.

3.1 Data

The balanced panel data set for the 20 Italian regions has been 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 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 10 years, between 2000 and 2009. Summary statistics are provided in Table 1. The mean level of antibiotic consumption during the period was 23.24 DID . Antimicrobials use

¹⁰Spatial 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 .

has slightly increased over time, with a peak in 2009 (25.70) 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, against small patient's copayments. Information on copayments are obtained from annual reports on pharmaceutical consumption and expenditure prepared by Osmed. Regional copayments vary from 0 to 4 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 (7), while the rational addiction model is directly estimated on (6). 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.

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 coefficients of income are also significant in both estimations.

In accordance with the economic theory, we find a statistically significant

and negative association between antibiotic consumption and copayment, at least in the LSDVC estimation, even though the impact is relatively low. Using the coefficient of copayment of this estimation, we calculated the short- and the long-run elasticities, which are respectively -0.02 and -0.03 . The average long-run elasticity is approximately 1.5 times as large as the short-run elasticity.¹¹ Using a natural experiment across Italian regions, Fiorio and Siciliani (2010) investigate the effect of copayments on drug prescriptions. They find that an increase in the copayment 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 (6), 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 in both regressions.

The estimated coefficients of the lag and lead variables of antibiotic consumption suggest that the discount rates ranges from 0.88 in the corrected LSDV estimation to 0.92 in the FE2SLS approach. Accordingly, these figures indicate that the interest rate varies from 8.33% to 12.5% . Support for the rational-addictive behavior is reinforced by the positive and relatively close values of the interest rate.

The coefficient of copayment is significant in the corrected LSDV only, like for the myopic model. This coefficient could be biased, as explained above. Nevertheless, we calculate short- and long-run price elasticities for rational agents. The short-run elasticity is around -0.03 , while the long-run elasticity is about -0.04 . 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 necessary and are purchased under doctor's advise. Moreover, at least in the Italian health care system, consumers directly face a small proportion of the full price of antibiotics which has been relatively stable over time. This could imply that consumers are not very sensitive to price changes.

¹¹The elasticities are computed at the means of the data and using the formulas proposed by Becker et. al. (1994).

5 Conclusions

Antibiotic misuse increases the threat of bacterial resistance which in turn reduces antibiotic effectiveness over time (Elbasha, 2003). 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). The understanding of the dynamics of antibiotic consumption may contribute to the shaping of appropriate measures of public interventions 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. Static models of antibiotic demand do not consider the process of adjustment towards optimal levels of antibiotic consumption. In this paper, we propose 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. The level of inefficacy represents a bad which is indirectly measurable by means of past and future antibiotic use.

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.

In our regressions, we find positive and significant coefficients of past and future consumption, which supports the hypothesis of habit to antibiotic consumption and reject the myopic model in favour 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 copayments like in Italy. Therefore, increasing copayments may not affect antibiotic consumption remarkably. Information provided by public campaigns about the future negative effects

of antibiotic misuse 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
<i>DID</i>	Defined daily doses per 1000 inhabitants	22.36 (4.66)	23.37 (5.28)	23.19 (5.21)	23.16 (5.09)	22.96 (5.07)	23.65 (5.22)	23.68 (5.52)	24.37 (5.34)	25.01 (5.54)	25.24 (5.71)
<i>Y</i>	Income per capita (in Euro)	20291.71 (5203.70)	21259.57 (5365.84)	21912.71 (5509.91)	22393.58 (5634.77)	23109.98 (5817.21)	23538.60 (5844.97)	24409.48 (5893.22)	25245.67 (6088.59)	25473.37 (6150.55)	24586.05 (5772.91)
<i>POP₁</i>	Proportion of population aged 0-14	14.02 (2.38)	13.97 (2.24)	13.94 (2.09)	13.88 (1.96)	13.82 (1.83)	13.78 (1.71)	13.75 (1.60)	13.70 (1.49)	13.67 (1.40)	-
<i>POP₂</i>	Proportion of population aged 15-74	77.51 (1.29)	77.29 (1.19)	77.05 (1.11)	76.88 (1.05)	76.76 (1.00)	76.59 (0.96)	76.39 (0.93)	76.26 (0.90)	76.14 (0.86)	-
<i>POP₃</i>	Proportion of population aged above 74	8.47 (1.68)	8.74 (1.70)	9.01 (1.70)	9.24 (1.69)	9.41 (1.67)	9.63 (1.64)	9.86 (1.61)	10.04 (1.58)	10.19 (1.54)	-
<i>DPOP</i>	Population density	174.37 (106.17)	174.42 (106.16)	174.92 (106.45)	176.21 (107.28)	177.82 (108.43)	179.09 (109.35)	180.06 (110.16)	181.27 (111.04)	182.58 (111.78)	183.99 (112.79)
<i>IMM</i>	Number of working permits per 100 inhabitants	1.98 (1.00)	2.27 (1.18)	2.38 (1.26)	2.47 (1.37)	3.14 (1.70)	3.71 (2.04)	4.11 (2.27)	4.47 (2.48)	5.24 (2.74)	-
<i>INF</i>	Rate of infectious diseases per 100000 inhabitants	354.77 (235.91)	316.97 (224.02)	317.70 (152.28)	329.04 (173.01)	302.99 (168.50)	216.25 (109.35)	236.13 (144.24)	213.90 (156.63)	208.76 (171.41)	-
<i>DPH</i>	Density of physicians per 1000 inhabitants	0.83 (0.06)	0.83 (0.06)	0.83 (0.056)	0.83 (0.06)	0.82 (0.06)	0.82 (0.06)	0.82 (0.06)	0.82 (0.06)	0.82 (0.06)	-
<i>P</i>	Copayment	1.50 (0)	0 (0)	0.83 (0.92)	0.85 (0.92)	0.95 (0.94)	0.70 (0.92)	0.65 (0.93)	0.95 (1.19)	1.1 (1.18)	1.17 (1.31)

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

Table 1: Descriptive statistics.

Variables	LSDVC			FE2SLS		
	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.

Variables	LSDVC			FE2SLS		
	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.