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Antibiotic consumption and the role of dispensing physicians

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Abstract

Regulation of prescription and dispensing of antibiotics has a twin purpose: to enhance access to antibiotic treatment and to reduce inappropriate use of drugs. Nevertheless, incentives on antibiotics to dispensing physicians may lead to inefficiencies. We model the interaction between competing physicians (with and without dispensing of drugs) and patients exposed to bacterial infections when antibiotic treatment generates spatial consumption externalities. Then, we empirically investigate the impact of dispensing practices on antibiotic consumption by means of combined spatial-lag and spatial-error econometric estimators for panel data (SARAR). The investigation exploits data from small geographic areas in a country where both regimes - with and without dispensing physicians - are possible. We find evidence that dispensing practices increase antibiotic use after controlling for determinants of demand and access, and spatial effects. This suggests that health authorities have a margin to adjust economic incentives on dispensing practices in order to reduce antibiotic misuse.

JEL classification: I11; I18; D12; D21; D43; D81; D82

Keywords: Physician dispensing, Prescribing behaviour, Antibiotic use.

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1 Introduction

Prescribing and dispensing of drugs are the two primary aspects of access to primary health care. In most developed countries, the main role of family physicians is to prescribe drugs without direct dispensing. Doctors are not allowed to sell drugs directly to their patients in several OECD countries such as Italy, Germany and Scandinavian countries. Still, direct dispensing of drugs is possible within some countries. For instance, one Scottish region (Highland) includes almost 20% of the total number of dispensing doctors in Scotland (Information Services Division of the National Health System in Scotland, 2006). In Switzerland, physicians are allowed to sell drugs directly to their patients in most cantons, with some exceptions across the country.

The reason for separating drug prescribing and dispensing is to optimise drug treatment by avoiding a conflict of interest for the prescriber and by ensuring good practice in dispensing (Trap and Hansen, 2003). Since dispensing physicians may have an incentive to induce drug consumption in order to increase their revenues, it is suggested that a regulatory policy that allows physicians to sell drugs directly to the patient may lead to sub-optimal levels of drug consumption (Chou et al., 2003; Holloway, 2005; Morton-Jones and Pringle, 1993; Nelson, 1987). Abood (1989) shows that dispensing doctors charge higher retail prices, whereas Rischatsch and Trottmann (2009) suggest that dispensing physicians have a greater probability of prescribing drugs that offer high margin, when compared with non-dispensing physicians.

Nevertheless, the benefits of separating drug prescribing and dispensing are still unclear. Direct dispensing of drugs may increase patients' benefits because of improved access to drug treatment in areas where geographical barriers represent a problem. Moreover, there are important external effects of consumption which affect, in particular, the optimal use of anti-infective drugs. Among these drugs, consumption externalities are certainly relevant for antibiotics. These externalities can be summarized by the effect of bacterial resistance, which reduces antibiotic effectiveness, and the effect of infection prevention, which extends benefits from antibiotic use to other individuals (Rudholm, 2002). The recent literature on antibiotic manufacturers suggests, for instance, that incentives for pharmaceutical firms to minimise resistance are not optimal since companies enjoy a too short period of monopoly benefits from their antibiotic effectiveness (Herrmann, 2010). As with respect to the retailing market, the benefits of good prescribing practices and low levels of resistance to antibiotics generated by the separation of drug prescribing and dispensing must be weighed

against the costs of limited access and low levels of infection prevention.

The purpose of this article is to explore the role of practice regulation in enhancing access to antibiotic treatment and in reducing inappropriate use of antibiotics. We first propose a theoretical model to investigate the behaviour of different types of general practitioners in a competitive environment with imperfect information on the nature of patient infections. The goal of the theoretical model is to provide some insights and hypothesis on the prescribing behaviour of dispensing and not dispensing practices. For this reason we propose a full theoretical model rather than a reduced form model that can be directly estimated afterwards. The hypothesis derived by the theoretical model are then tested empirically.

We apply an infinite-periods horizontal product differentiation model (Hotelling, 1929) to the market for community antibiotic treatment by incorporating imperfect information about the type of infection, diagnosis errors and alternative treatments under a fee-for-service remuneration scheme for physicians. The market for outpatient antibiotic treatment we have in mind applies, for instance, to Switzerland where doctors receive a consultation fee which varies depending on the time allocated to the patient and the diagnostic tests performed. In such a case, dispensing doctors may include additional costs for drugs available with them in stock and gain a margin on antibiotics sold to the patient. We show that the interaction between imperfect information on the nature of a patient's infection and economic incentives to dispensing practices may increase the likelihood of antibiotic prescriptions, *ceteris paribus*. The rationale is that self-dispensing physicians may increase their revenue by selling more antibiotics under uncertainty on the nature of a patient's infection. To some extent, this effect may overcome the opposite effect of restrictions on antibiotic use due to difficulties in access to health care treatment in areas where the density of providers is relatively poor.

In the health economics literature, we are not aware of any theoretical approach to the behaviour of dispensing practices that considers competition among physicians under uncertainty on the nature of patient's infection and spatial aspects of drug consumption. Two studies (Liu et al., 2009; Rischatsch and Trottmann, 2009) investigate physician prescribing decisions in the choice between generic and brand-name drugs. Though, these studies assume that physicians act as monopolists and spatial aspects are neglected. Recently, Brekke, Holmas and Straume (2011) applied a vertical differentiation model to analyze the impact of regulation on prices and market shares of brand-names and generic drugs.

To investigate the impact of dispensing practices on outpatient antibiotic consumption

empirically, we use a demand model which takes into account the main determinants of antibiotic use. Moreover, we consider spatial aspects of consumption by means of an appropriate econometric estimator. We exploit data from small geographical areas in a country (Switzerland) where two regimes - prescribing physicians and dispensing physicians - are possible, which provides the ground for a natural experiment. Related to this exercise is the study by Windmeijer et al. (2006) who investigate the impact of promotional activities by pharmaceutical companies on GP prescription behaviours. The authors suggest that prescriptions are positively affected by promotion expenditure but do not consider different types of practices and focus on the market of anti-hypertensives and anti-depressant. Also, Trap and Hansen (2002) examine differences in the rationality of the prescription in relation to diagnosis and symptoms between dispensing and non dispensing doctors for one antibiotic substance (cotrimoxazole). Since dispensing doctors are found to prescribe an antibiotic 2.5 times more frequently than non dispensing doctors, the authors conclude that dispensing practices may lead to increasing health hazards and bacterial resistance. The authors do not account for access and consumption externalities.

Two previous empirical papers on the consumption of antibiotics relate to the current study, primarily because they exploit the same dataset although they address different research questions. Filippini et al. (2009a) investigate socioeconomic determinants of outpatient antibiotics across small areas in Switzerland. However, this paper neglects the prescribing behaviour of different types of practices, which is the focus of the present paper. Filippini et al. (2009b) model the demand for different antibiotic classes used for respiratory infections rather than the demand for total antibiotic consumption. The authors investigate elasticities to socioeconomic determinants of consumption and own- and cross-price elasticities between different groups of antibiotics.

Although one can hardly identify the socially optimal level of antibiotics empirically, it is advisable to adjust for external effects when investigating the behaviour of different types of practices. Spatial aspects of consumption are generally disregarded in empirical studies on drug prescription and consumption. Nonetheless, antibiotic drugs are generally used to treat respiratory and gastrointestinal infections which are among the most common infectious diseases acquired in the community. As discussed by Hess et al. (2002), these infections are characterized by a spreading process across regions, i.e. the infection initiates in one region and then spreads across other regions. As an example of the spatial spread of an infection see, for instance, Werneck et al. (2002). Spatial-econometric estimators in health economics have been recently applied by Lachaud (2007), Moscone et al. (2007),

and Moscone and Tosetti (2010a, 2010b). Moscone et al. (2007) and Moscone and Tosetti (2010a, 2010b) empirically investigate the determinants of regional health expenditures in the US and in England using panel data. Both studies suggest the importance of taking spatial aspects into account when modelling the utilization of health care services. We are aware of only one study investigating spillover effects of antibiotic consumption using Italian regional data (González Ortiz and Masiero, 2013).

The remaining of the article is organized as follows. In Section 2 we sketch the model and derive the equilibrium levels of antibiotic use for dispensing and non dispensing practices. Section 3 empirically investigates the impact of dispensing practices on antibiotic use and discusses the results. Section 4 concludes.

2 The theoretical framework: antibiotic treatment in general practice

Our model of the market for antibiotic treatment provided by primary care physicians (GPs) is an application of the standard Hotelling product differentiation model (Hotelling, 1929; Gravelle, 1999) in an infinite-period framework. We incorporate new features, such as imperfect information about the nature of the infection, doctor’s diagnosis errors, alternative types of treatment, and antibiotic consumption externalities. We focus on the interaction between patients and general practitioners in an infinite-period model when anti-infective treatment is needed.¹

At the beginning of each period, nature assigns a health problem (e. g. mild respiratory or gastro-intestinal infection), $i \in \{b, v\}$, to each of the 2θ individuals uniformly distributed along a unit line, where b is a *bacterial* infection and v represents a *viral* infection.² Consumers initially observe a symptom but cannot infer the type of infection they suffer from. To simplify the presentation, we assume that both types of infections are equally likely. Hence, the probability of having a bacterial infection is $p = p[i = b] = p[i = v] \equiv 1/2$. Each generation of consumers lives for two periods. Therefore, in each period there is a mass of 2θ consumers: a mass θ^y composed of young consumers and a mass θ^o composed of old consumers. The proportion of young consumers entering the market and the proportion of old consumers leaving the market in each period are the same, with $\theta^y = \theta^o = \theta$. As an

¹Anti-infective is a general term that encompasses antibacterials, antibiotics, antifungals, antiprotozoans and antivirals. In this paper we focus on the choice between antibacterials and antivirals and the terms antibacterials and antibiotics are used interchangeably.

²Dichotomous health problems are considered, for instance, in Jelovac (2001) where patients have the same probability of suffering from a “mild” illness as well as from a “severe” one.

exception, in the first period there is only one generation of consumers, θ , and all of them are young.

Individuals maximise their expected utility from consulting a doctor. In the market there are 2 general practice firms (GP j , with $j \in [l, r]$) of equal size, located at the two extreme points of the distance. General practitioners can either be allowed to sell drugs directly to their patients or not, depending on the legislative frame set by the health authority. In the latter case patients need to purchase the prescribed drugs from a pharmacy, which is located equidistantly from each practice, i.e. at $d = 1/2$.³

Patient's choice of a doctor depends on the perceived level of diagnosis accuracy. Patients differ with respect to their location and the type of infection. Hence, a patient is located at distance d_l from practice l and at distance $d_r = 1 - d_l$ from practice r . The differentiation parameter d can either be interpreted as a geographical distance between the individual and the provider location, it could be the distance between the individual's preferences and the characteristics of the provider that maximises his utility.

Following patients' choice of a practice, doctors make prescriptions based on a diagnosis signal. However, patients recover naturally from viral infections soon after a consultation. The scenario is illustrated in Figure 1. This scenario applies, for instance, to mild respiratory tract infections in the community, such as colds, rhynofaringites, mild pneumonia and otitis. In these cases, a treatment undertaken using healing drugs, suitable for instance to reduce body temperature (e.g. antipyretic or anti-inflammatory), cough (e.g. syrup) or nose constipation (e.g. spray), generally decreases the cost of illness because it offers quicker recovery and/or less discomfort. This type of treatment (NA) is usually prescribed and is independent of any antibiotic treatment. Conversely, treatment with antibiotics (A) is necessary to recover from a bacterial infection. However, antibiotics do not provide any benefit against viral infections. Since a doctor's diagnosis may not be initially correct, a second consultation is required later if the patient suffers from a bacterial infection and an antibiotic was not previously prescribed.

2.1 Information structure

The accuracy of a GP's prescription is related to the level of diagnostic services provided. We define $p_j^c \in [0, 1]$ as the probability of a correct diagnosis by GP j . More diagnostic services increase the probability of a correct diagnosis through the following simple rela-

³This implies that patients do not incur additional costs of transportation to buy drugs after a consultation with a GP. Clearly, we also hypothesize that pharmacies are not allowed to change a doctor's prescription.

relationship $p_j^c(e_j) = \beta e_j$, where e_j represents the level of diagnostic services provided by the practice and $\beta \in [0, 1]$ is a parameter. Consequently, the probability that the diagnosis is a bacterial infection and an antibiotic is correctly prescribed is $pp_j^c = \frac{1}{2}\beta e_j$. The probability of mistaken diagnosis will then be $\frac{1}{2}(1 - \beta e_j)$. We assume that doctors rely on diagnostic tests to decide upon the type of treatment to be prescribed. Alternatively, we could assume that doctors share the results of diagnostic tests with patients and cannot cheat on this information.

Patients are imperfectly informed about the level of diagnostic services (e_j) provided by the practice. They assume that the level of diagnostic services is $e_j \in [e^{\min}, e^{\max}]$, with e^{\min} and e^{\max} equally likely. Consequently, patients expect an average level of services $\hat{e}_j = \frac{1}{2}e^{\min} + \frac{1}{2}e^{\max} \equiv \bar{e}$. We normalise e_j to $1/\beta$ and set $e^{\min} = 0$ and $e^{\max} = 1/\beta$.

Patients are aware that higher intensity of diagnostic services increases the probability of a correct prescription but don't know the true level of e_j . They ask for a second consultation if they do not recover within some time from the initial consultation.

2.2 Expected net benefits of care

Primary health care services are covered by compulsory health insurance contracts and patients pay only a small fraction (α) of the total cost of care. General practitioners are paid under a pure fee-for-service scheme. The health care system we have in mind is akin to the Swiss market for outpatient care. In this system, a consultation with a doctor is usually characterized by a fixed fee (f) plus the cost of any prescribed drugs. Treatment with antipyretic/anti-inflammatory drugs is assumed not to vary with the type of infection; the cost of this treatment is set to zero. On the other hand, a course of treatment with antibiotics has a fixed cost of z ($z < f$). In Switzerland, patients copayments depends upon the type of insurance plan chosen since different deductible schemes are available. However, to simplify the analysis, we assume that the level of patients cost sharing does not vary across patients.

Patients incur distance costs td_j to purchase services from provider j , where t is the unit cost of distance. We summarise the costs implied by alternative treatments conditional upon the type of infection in Table 1. A treatment without antibiotics is denoted by *NA*. For instance, consider a patient with a viral infection consulting doctor j . If the GP decides to prescribe an antipyretic/anti-inflammatory without an antibiotic, the total cost of treatment includes the partial cost of a consultation (αf), plus the cost of distance (td_j). This gives $\alpha f + td_j$ in the first row of Table 1. However, if the GP makes a wrong diagnosis, the cost

of treatment increases by αz since an antibiotic is prescribed (second row of Table 1). The total cost will then be $\alpha(f + z) + td_j$.

A fully recovered patient has utility $u^h > 0$ defined in monetary terms. Consumers are myopic in that only diagnosis effort in the current period is considered. Using Table 1 we can write the expected net benefits from choosing doctor j as

$$\begin{aligned}\hat{u}_j &= u^h - \frac{1}{2}\beta\hat{e}_j(\alpha f + td_j + t\Delta x) - \frac{1}{2}\beta\hat{e}_j(\alpha f + \alpha z + td_j + t\Delta x) \\ &\quad - \frac{1}{2}(1 - \beta\hat{e}_j)(\alpha f + \alpha z + td_j + t\Delta x) - \frac{1}{2}(1 - \beta\hat{e}_j)(2\alpha f + \alpha z + 2td_j + 2t\Delta x) \\ &= u^h - \frac{1}{2}[(3 - \beta\bar{e})(\alpha f + td_j + t\Delta x) + (2 - \beta\bar{e})\alpha z].\end{aligned}\tag{1}$$

The terms inside the brackets of equation (1) indicate the costs of treatment when a viral infection is correctly diagnosed (first term), a bacterial infection is correctly diagnosed (second term), a viral infection is wrongly diagnosed and an antibiotic is prescribed (third term), and a bacterial infection is wrongly diagnosed so that patients need a second consultation (fourth term).⁴ Since patients purchase drugs from the pharmacy located halfway from the two GP practices, patients bear the additional cost of distance $t\Delta x$, where $\Delta x = |x_j - x_{PHA}| = 1/2$ is the distance that patients need to travel from the chosen practice j to the pharmacy (PHA). When patients need a second consultation because of wrong diagnosis, the cost of distance to the pharmacy doubles ($2t\Delta x$). Finally, $\Delta x = 0$ when GP practices are allowed to dispense drugs directly to the patients.

2.3 Demand for GP consultations by young patients

The structure of patients' information implies that a patient's choice of practice is based upon costly distance.⁵ Patients at distance $d_l \leq 1/2$ from GP l will prefer to consult GP l instead of GP r . Similarly, patients with distance $d_l > 1/2$ will choose GP r .

⁴Note that patients do not consider the possibility of switching to an alternative practice when a bacterial infection is wrongly diagnosed. The fourth term of equation (1) indicates that patients consult the same doctor twice if needed. This assumption seems plausible given the very short period between two sequential consultations (see footnote 8 for further details). Many spatial papers (e.g. Brekke et al., 2010) neglect switchings among firms when their implications are beyond the scope of the analysis. Also, patients are assumed to be myopic in the sense that they maximise utility to recover from current infections only and do not take future choices into account.

⁵Brekke, Nuscheler and Straume (2006, 2007) assume that a proportion of patients is uninformed and chooses a doctor according to distance. Gravelle and Masiero (2000) assume that patients observe practice quality with an error and then learn by experience. These models focus on capitated systems rather than fee-for service. Our assumption is useful to simplify the model and to focus on a patient's alternative strategies rather than the effects of competition among providers. We then ignore the impact of a patient's information structure on the choice of practice.

Doctor j 's initial demand for consultations by young patients in period t is then $\theta/2$. Note that one implicit assumption of this demand is that the market is always covered. This requires that the expected net benefits in (1) are positive for those patients located halfway from the two practices, whatever the level of diagnosis accuracy. We then hypothesize that u^h is large enough to ensure $\hat{u}(d = 1/2, e \geq 0) > 0$.⁶

Patients with a bacterial infection who receive a wrong diagnosis need an additional consultation to switch to antibiotic treatment. These patients realise that the infection has not been cured at some time after the first consultation. All these patients have now strong preference for antibiotic treatment. Total demand for consultations of GP l by young consumers in each period is then derived by adding the number of patients who need a second consultation to the initial number of consultations:⁷

$$D_{lt}^y(e_{lt}) = \frac{\theta}{2} \left[1 + \frac{1}{2}(1 - \beta e_{lt}) \right], \quad (2)$$

where $\frac{1}{2}(1 - \beta e_{lt})$ is the proportion of patients with a bacterial infection who need a second consultation because of wrong diagnosis. Similarly, we can write the demand for GP r as $D_{rt}^y(e_{rt}) = \theta [1 + (1 - \beta e_{rt})/2] / 2$.

2.4 Prevention and bacterial resistance externalities

At the beginning of each period, nature assigns a health problem to old patients in the market, like for young patients. However, old patients present a lower probability of infection because they have been exposed to antibiotics prescribed in the previous period. As a consequence, they benefit from the preventive effect of antibiotic use (Ellison and Hellerstein, 1999). We assume that the number of old patients with an infection decreases by a proportion $\phi \in [0, 1]$ of the number of young patients (now the old patients) receiving antibiotics in the previous period (from both practices). This can be derived from (2) considering that only half of the initial number of consultations by young patients from each GP lead eventually to an antibiotic prescription and some of the young patients also receive antibiotics because of wrong diagnosis. The number of young patients receiving antibiotics from both

⁶The assumption is quite realistic for the Swiss market for primary care, where the costs of access in rural areas are not such as to exclude some individuals from receiving antibiotic treatment. Even though the costs of access may generate some delay in receiving prompt treatment, individuals with bacterial infections must consult a general practitioner to purchase antibiotics and recover.

⁷Patients may be disappointed because of health complications or loss of revenue due to antibiotic treatment delay. However, dissatisfaction does not lead patients to switch practices. The rationale is that patients are still sick and now expect to receive antibiotic treatment from any practice. Consequently, expected utility from any practice is the same and switching costs associated to time and trouble to leave a doctor and find another are higher than zero.

practices in the previous period is $D_{t-1}^{Ay}(e_{lt-1}, e_{rt-1}) = D_{lt-1}^{Ay} + D_{rt-1}^{Ay} = D_{lt-1}^y + D_{rt-1}^y - \theta/2$.⁸ Consequently, a proportion of individuals ϕD_{t-1}^{Ay} is healthy in the second period and does not need to consult a doctor.

Total demand for consultations for GP l in each period t can then be written by summing up the demand for consultations by young and old patients as

$$D_{lt}(e_{lt}, e_{lt-1}, e_{rt-1}) = D_{lt}^y + \left(\frac{\theta}{2} - \phi D_{t-1}^{Ay} \right) \left[1 + \frac{1}{2}(1 - \beta e_{lt}) \right]. \quad (3)$$

The term $\frac{1}{2}(1 - \beta e_{lt})$ within the squared brackets in (3) is the fraction of old patients with a bacterial infection who need a second consultation because of wrong diagnosis. Note that diagnosis effort in period $t - 1$ affects demand in the following period through D_{lt-1}^y . Total second-period demand for GP r can be derived similarly as above.

Note that dissatisfaction with antibiotic treatment delay does not lead patients to switch practices when old. Patients switching to alternative practices because of dissatisfaction is not an issue in our model. This seems plausible given the set of information available to the patient. Patients can hardly disentangle whether antibiotic treatment delay was due to a wrong diagnosis or to the need to avoid unnecessary treatment and bacterial resistance. Under uncertainty, practitioners can easily argue that their initial prescription was the most appropriate. Hence, we focus on the impact of key features of antibiotic consumption, i.e. externalities due to prevention and bacterial resistance.

The use of antibiotics in period $t - 1$ reduces the effectiveness of antibiotic treatment in the following period because bacterial resistance causes a negative externality. We capture this effect by assuming that practices face increasing costs to cure patients with resistant bacteria. Bacterial resistance affects antibiotic effectiveness in the following period and depends on patients previously treated with antibiotics. We summarise the total costs of bacterial resistance for GP l as $\rho D_{t-1}^{Ay} = \rho (D_{lt-1}^y + D_{rt-1}^y - \theta/2)$, where ρ is the cost generated by each young patient treated with antibiotics in the previous period.⁹

⁸ Adding the number of patients with a viral infection who receive an antibiotic because of wrong diagnosis, $\frac{\theta}{2} \frac{1}{2}(1 - \beta e_{jt-1})$, to the total number of young patients with a bacterial infection, $\theta/2$, we get $(D_{jt-1}^y - \theta/4)$. Considering both GPs, l and r , the total number of young patients receiving antibiotics is then $(D_{lt-1}^y - \theta/4) + (D_{rt-1}^y - \theta/4)$.

⁹The parameter ρ can also be interpreted as the value of providing good care to patients. Indeed, better diagnostic services in $t - 1$ reduce inappropriate antibiotic prescriptions and, consequently, reduce future risks for patients.

2.5 The physician's objective function

The general practitioner has an objective function which depends upon the benefits and costs of diagnostic services provided in each period and the costs generated by the reduced antibiotic effectiveness due to bacterial resistance. Using (3) we can write GP l 's intertemporal profit at time t as

$$\begin{aligned} V_{lt} &= \sum_{t=k}^{\infty} \delta^{t-k} \pi_{lt}(e_{lt}, e_{lt-1}, e_{rt-1}) \\ &= \sum_{t=k}^{\infty} \delta^{t-k} \left[(f - c) D_{lt}(e_{lt}, e_{lt-1}, e_{rt-1}) - \rho D_{t-1}^{Ay}(e_{lt-1}, e_{rt-1}) - \gamma e_{lt}^2 \right], \end{aligned} \quad (4)$$

where $\delta \in (0, 1]$ is the discount factor for future profits, c is the fixed marginal cost of a consultation ($c < f$) and γ is the marginal cost of diagnostic services. Note that $D_{l1} = D_{l1}^y$ since there are only young consumers in the market, and $D_{l0}^y = 0$.

Dispensing physicians may differ from other practitioners for at least two reasons. Doctors may incur some costs when keeping drugs on stock. In this sense they are more similar to a pharmacy than to non-dispensing practices. A shortage of stock implies risks in case patients are unable to receive the required treatment when needed. On the other hand, large stocks of drugs that have been hoarded increase the risk of getting closer to the expiry date. Unsold drugs may imply some costs for the practice.

In Switzerland, dispensing physicians get a mark-up on drugs prescribed. Obviously, dispensing doctors are subject to pressure from pharmaceutical companies to increase prescriptions to the same extent as other doctors.¹⁰

We modify the objective function of the general practitioner defined by (4) to include the expected costs and benefits of self-dispensing as

$$\begin{aligned} V_{lt}^d &= \sum_{t=k}^{\infty} \delta^{t-k} \left[(f - c) D_{lt}(e_{lt}, e_{lt-1}, e_{rt-1}) + (z - \eta) D_{lt}^A(e_{lt}, e_{lt-1}, e_{rt-1}) + \right. \\ &\quad \left. - \rho D_{t-1}^{Ay}(e_{lt-1}, e_{rt-1}) - \gamma e_{lt}^2 \right], \end{aligned} \quad (5)$$

where $D_{lt}^A = D_{lt} - (\theta - \phi D_{t-1}^{Ay})/2$ is the number of antibiotic treatments in period t . The number of antibiotic treatments sold is obtained by summing up the number of young and old patients with a bacterial infection (correctly diagnosed) plus the number of individuals with a viral infection with a wrong diagnosis, and the number of patients who require a

¹⁰Windmeijer et al. (2006) find that GP prescription behaviour is affected by pharmaceutical promotion but the magnitude of this effect is not assessed separately for dispensing and prescribing doctors.

second consultation because a bacterial infection was not initially diagnosed.¹¹ z is the unit price of drugs dispensed to the patient and $\eta \leq z$ represents the unit cost of drugs on stock.

We simplify equations (4) and (5) by setting $c = 0$ and $\eta = 0$. This is a convenient normalization to ease the discussion of the results in the following section without losing any substance.

2.6 Market equilibrium and the effect of dispensing practices

Practice firms can change their effort strategies over time. They take their competitors' strategies as given and non-cooperatively maximize their profits by choosing the level of diagnostic services. When choosing diagnosis effort firms not only take into account the effects on their current period profits but also on their demand and costs (bacterial resistance) in the following periods. This dependence needs to be taken into account when solving the model for the equilibrium levels of diagnostic efforts. Profits in period t depends upon diagnostic services in period $t - 1$ by both GPs. Also, the value function represented by the flow of all future profits depends on all future levels of diagnosis effort. Consequently, an equilibrium has to ensure that deviations from current period levels of effort in the future are not convenient. We require a perfect equilibrium, i.e. each GP selects the diagnosis effort that maximizes its intertemporal profit given the subsequent strategies of the other GP and itself, whose strategies depend only on the payoff-relevant history (Maskin and Tirole, 1988). Our pair of reaction functions (R_l and R_r) form a Markov perfect equilibrium if $e_{lt} = R_l(e_{rt-1})$ maximizes GP l 's intertemporal profit at any time, given e_{rt-1} and assuming that GP l will move according to R_l , and the same holds for GP r . To solve for a Markov perfect equilibrium, let $V_l^d(e_r)$ be the present discounted value of GP l 's profits given that last period GP r played e_r and that from this time forth both GPs play optimally, i.e. according to their Markov strategies, and let $V_l^d(e_l)$ be the present discounted value of GP l 's profits given that last period GP l played e_l and that hereafter both GPs play optimally. $V_r^d(e_l)$ and $V_r^d(e_r)$ are symmetric. Given that GP j 's choice of e_j is restricted to a bounded set, the following are necessary and sufficient conditions for the reaction and value functions to be consistent and correspond to an equilibrium: $V_l^d(e_r) = \max_{e_l} \{ \pi_l^d(e_l, e_r) + \delta V_l^d(e_l) \} = \pi_l^d(R_l(e_r), e_r) + \delta V_l^d(R_l(e_r))$ and $V_l^d(e_l) = \pi_l^d(e_l, R_r(e_l)) + \delta V_l^d(R_r(e_l))$.

¹¹From total demand for consultations, D_{lt} , we subtract the number of patients with a correct diagnosis not treated with antibiotics. These are $\theta/4$ young patients with viral infections and $(\theta/2 - \phi D_{t-1}^{Ay})/2$ old patients with viral infections.

Because diagnosis effort affects profits in two subsequent periods and expected profits are the sum of concave functions in e_{lt} , we can write the following first-order conditions for GP l - the dynamic reaction function - using (5) as:

$$\begin{aligned}
\frac{\partial V_{lt}^d}{\partial e_{lt}} &= \frac{\partial \pi_{lt}^d(e_{lt}, e_{lt-1}^*, e_{rt-1}^*)}{\partial e_{lt}} + \delta \frac{\partial \pi_{lt+1}^d(e_{lt+1}^*, e_{lt}, e_{rt})}{\partial e_{lt}} \\
&= f \left[\frac{\partial D_{lt}(e_{lt}, e_{lt-1}^*, e_{rt-1}^*)}{\partial e_{lt}} + \delta \frac{\partial D_{lt+1}(e_{lt+1}^*, e_{lt}, e_{rt})}{\partial e_{lt}} \right] + \\
&+ z \left[\frac{\partial D_{lt}^A(e_{lt}, e_{lt-1}^*, e_{rt-1}^*)}{\partial e_{lt}} + \delta \frac{\partial D_{lt+1}^A(e_{lt+1}^*, e_{lt}, e_{rt})}{\partial e_{lt}} \right] + \\
&- \rho \frac{\partial D_t^{Ay}(e_{lt}, e_{rt})}{\partial e_{lt}} - 2\gamma e_{lt} = 0
\end{aligned} \tag{6}$$

and symmetrically for GP r .¹² Substituting for $\partial D_{lt}/\partial e_{lt}$, $\partial D_{lt+1}/\partial e_{lt}$, $\partial D_{lt}^A/\partial e_{lt}$, $\partial D_{lt+1}^A/\partial e_{lt}$, and $\partial D_t^{Ay}/\partial e_{lt}$ in (6) and solving for the level of diagnostic services assuming for simplicity $\delta = 1$ and imposing $\partial V_{lt}^d/\partial e_{lt} = \partial V_{lt+1}^d/\partial e_{lt+1} = 0$ and $\partial V_{rt}^d/\partial e_{rt} = \partial V_{rt+1}^d/\partial e_{rt+1} = 0$, we then get¹³

Proposition 1 *A symmetric Markov perfect equilibrium in the level of diagnostic services is defined by*

$$e_l^* = e_r^* = \frac{\left(\frac{7}{4}\phi - 1\right) f + \frac{1}{2}\rho - \left(1 - \frac{3}{2}\phi\right)z}{\frac{3\beta}{4}\phi(f+z) + \frac{4}{\theta\beta}\gamma}. \tag{7}$$

As expected, the equilibrium level of diagnostic services decreases with the marginal cost of effort (γ). Diagnostic services may decrease or increase with the fee for the consultation (f), depending on the magnitude of the prevention effect of antibiotic consumption (ϕ). Without positive externalities from antibiotic consumption ($\phi = 0$), the equilibrium level of diagnostic services decreases with the fee for the consultation. This is because a higher fee increases the marginal gains from consultations. Consequently, there are more incentives to reduce the diagnosis effort, which reduces diagnosis accuracy and increases the number of consultations.

The impact of positive and negative externalities from antibiotic consumption deserve some comments. Note that negative externalities caused by bacterial resistance (ρ) increase

¹²The second-order conditions are $\frac{\partial V_{lt}^2}{\partial^2 e_{lt}} = -2\gamma < 0$.

¹³Using (2) and (3) we get $\frac{\partial D_{lt}}{\partial e_{lt}} = -\frac{\beta}{2} \left(\theta - \phi D_{t-1}^{Ay} \right) = -\frac{\beta\theta}{2} \left\{ 1 - \phi \left[1 - \frac{\beta}{4} (e_{lt-1} + e_{rt-1}) \right] \right\}$ and $\frac{\partial D_{lt+1}}{\partial e_{lt}} = -\phi \left[1 + \frac{1}{2} (1 - \beta e_{lt+1}) \right] \frac{\partial D_{t+1}^{Ay}}{\partial e_{lt}}$. Since $\frac{\partial D_{t+1}^{Ay}}{\partial e_{lt}} = -\frac{\beta\theta}{4}$ we then get $\frac{\partial D_{lt+1}}{\partial e_{lt}} = \frac{\phi\theta\beta}{4} \left[1 + \frac{1}{2} (1 - \beta e_{lt+1}) \right]$. We have $\frac{\partial D_{lt}^A}{\partial e_{lt}} = \frac{\partial D_{lt}}{\partial e_{lt}}$ and $\frac{\partial D_{lt+1}^A}{\partial e_{lt}} = \frac{\partial D_{lt+1}}{\partial e_{lt}} - \frac{1}{2} \left(\theta - \phi \frac{\partial D_t^{Ay}}{\partial e_{lt}} \right) = \frac{\phi\theta\beta}{4} (1 - \frac{\beta}{2} e_{lt+1})$.

the equilibrium level of diagnostic services. If the cost of treating patients increases because of resistant bacteria, a higher level of diagnostic services is required to reduce the number of misdiagnosed viral infection and, consequently, the amount of antibiotic prescriptions in previous periods. An increase in diagnosis accuracy lowers the amount of inappropriate prescriptions that contribute to the generation of resistant bacteria. Note also that positive externalities of antibiotic use that decrease the fraction of infected patients in period $t + 1$ have a two-fold effect. First, ϕ decreases the demand for consultations in period $t + 1$. As a consequence, a higher level of diagnostic services is required to reduce the number of antibiotic prescriptions in period t that generate a negative effect on doctor's revenues in period $t + 1$ (the numerator of equation (7)). But second, an increase in ϕ also decreases the fraction of misdiagnosed infections in period $t + 1$, *ceteris paribus*, which leads to lower prescriptions of antibiotics and reduced gains. To offset this effect, doctors must reduce their level of diagnosis accuracy (the denominator of equation (7)). Note, however, that the marginal impact of ϕ at the numerator of (7) is larger than the marginal impact at the denominator. Hence, we have $\partial e^*/\partial \phi > 0$.

Dispensing practices have an effect on the equilibrium level of diagnosis accuracy through the price of drugs dispensed, measured by z . Note, however, that this effect depends on the magnitude of positive externalities from antibiotic consumption (ϕ), and the efficiency of services provided (β), which affects the denominator of (7). The result is not completely straightforward. Dispensing practices generally reduce the equilibrium level of diagnostic services as compared to not dispensing practices, provided that $\phi < 2/3$. The rationale is that a reduced level of services increases the number of antibiotic prescriptions in period t with relatively low impact on consultations in period $t + 1$ and, consequently, the gains from antibiotic sales are higher. This effect is magnified by the reduced incentive to provide accurate diagnosis (at the denominator of (7)) when there are gains from antibiotic sales. However, this result may not hold with strong prevention effects ($\phi > 2/3$) and low efficiency of diagnostic services ($\beta \rightarrow 0$). This is because the marginal impact of z at the numerator (7) becomes positive and prevails over the effect at the denominator.

Using the equilibrium level of diagnostic services in (7), we can derive the amount of antibiotic prescriptions per patient. The total number of antibiotic treatments in equilibrium in period t is $2D_t^{A*} = 2 \left[D_t^* - (\theta - \phi D_{t-1}^{Ay*})/2 \right]$. Substituting for D_t^* and D_{t-1}^{Ay*} and dividing by the total number of patients (2θ), we get the per capita antibiotic use as

$$a^* = \left(1 - \frac{\beta}{2} e^* \right) \left(1 - \phi + \frac{\beta \phi}{2} e^* \right). \quad (8)$$

Whether or not dispensing practices lead to higher levels of antibiotic use compared to not dispensing practices clearly depends upon the combined effect of financial incentives from antibiotic sales and externalities from antibiotic consumption. With negligible prevention effects ($\phi \rightarrow 0$) antibiotic prescriptions per capita are higher for dispensing practices as compared to not dispensing practices. Note that the second term between brackets of equation (8) tends to 1, whereas the first term increases since $\partial e^*/\partial z > 0$ when $\phi \rightarrow 0$. Conversely, when prevention effects are strong ($\phi \rightarrow 1$) the result is less straightforward. Note that the first and the second terms may move in opposite directions. Consequently, the hypothesis that dispensing practices increase antibiotic consumption through a reduced effort in diagnostic services does not follow straightforwardly from our theoretical results and will then be empirically investigated in the following section.

3 Empirical analysis

3.1 Econometric specification

To investigate further the impact of dispensing practices we now propose an empirical approach that exploits panel data from a country with a fee-for-service remuneration scheme for doctors and variations in the regime of dispensing drugs across the country. The effects of antibiotic consumption externalities are captured by means of a combined spatial-lag and spatial error econometric approach. As mentioned in the Introduction section, the goal of the theoretical model presented in Section 2 is to formulate some hypothesis on the prescribing behaviour of the practice rather than to derive a reduced form model to be directly estimated.

The theoretical framework (equation 7) suggests that the consumption of antibiotics is influenced by factors such as the price of antibiotics and the price of a consultation, the financial incentives attached to direct dispensing of drugs, and positive and negative externalities of antibiotic consumption that also exhibit a spatial dimension. Moreover, it is important to underline that the demand equation (8) has been derived for a market characterised by individuals with homogeneous socioeconomic variables such as income, age, and cultural factors.

The theoretical model may also suggest the need for some dynamic specification in the econometric approach. However, data at our disposal cover a relatively short period of time and the estimation of a dynamic model with spatial econometrics methods is not

straightforward. For this reason, we focus on static models.¹⁴

We have Swiss quarterly data on antibiotic consumption for the year 2002, disaggregated by 240 small geographic areas.¹⁵ Switzerland exhibits relatively low levels of antibiotic consumption compared to neighbouring European countries. The number of defined daily doses per 1000 inhabitants (*DID*) in 2002 is 32.05 in France, 24.38 in Italy, 13.76 in Germany, 11.75 in Austria, and only 9.00 in Switzerland (Masiero et al., 2010; Filippini et al., 2006). Nevertheless, as shown in Figure 2, the country is characterized by high heterogeneity in consumption across small areas. Latin regions (French- and Italian-speaking regions) generally exhibit higher levels of antibiotic consumption as compared to German-speaking regions.

To investigate the relationship between antibiotic consumption and dispensing practices we adopt a representative consumer approach, namely for each area we define the dependent variable as the per capita antibiotic consumption. Further, the econometric specification of the demand for antibiotics includes some socioeconomic variables that vary across the areas.¹⁶

In order to estimate the impact of dispensing and not dispensing physicians on antibiotic consumption, the empirical model includes variables representing the difference in practice styles and incentives attached to the possibility of direct dispensing of drugs. We use a log-log functional form and, therefore, the estimated coefficients can be interpreted as elasticities.

We initially specify the following model:

$$\begin{aligned} \ln DID_{jt} = & \beta_0 + \beta_1 \ln Y_{jt} + \beta_2 \ln POP_{1jt} + \beta_3 \ln POP_{2jt} + \beta_4 \ln POP_{4jt} & (9) \\ & + \beta_5 \ln POP_{5jt} + \beta_6 \ln INF_{jt} + \beta_7 \ln DPHY_{jt} + \beta_8 \ln DPHA_{jt} \\ & + \beta_9 \ln PA_{jt} + \beta_{10} \ln PC_{jt} + \beta_{11} DBOR_{jt} + \beta_{12} DLAT_{jt} \\ & + \beta_{13} DHOS_{jt} + \beta_{14} NODISP_{jt} + \beta_{15} DISP50_{jt} + \varepsilon_{jt}. \end{aligned}$$

¹⁴For a dynamic approach to antibiotic consumption we refer the reader to a recent paper by Filippini and Masiero (2012).

¹⁵Switzerland is a federal state made of 26 cantons (states) with remarkable differences in terms of organization of the health care system and health care policy. Generally, a canton is made up of between 10 and 20 small areas. The population varies between 4,980 and 125,275 inhabitants per area. Each area has at least 4 pharmacies and/or drugstores. Direct dispensing is not allowed in some cantons like Geneva, Vaud, Balle ville, Ticino and Aargau. In some areas of the other cantons direct dispensing is permitted.

¹⁶The literature on determinants of the demand for physician's services emphasises the role of socioeconomic characteristics of the population and practice styles (Hunt-McCool et al., 1994; Carlsen and Grytten 1998; Grytten and Sorensen, 2003). More closely to antibiotics, the literature suggests that cultural aspects may influence the use of antibiotics. For instance, Italian children receive more courses of antibiotics than Danish children (Resi et al. 2003; Thrane et al., 2003).

DID_{jt} is the per capita outpatient antibiotic use in the j^{th} market area ($j = 1, \dots, J$) measured in defined daily doses per 1000 inhabitants, and ε_{jt} is the usual error term that will be specified later.¹⁷ $DPHY_{jt}$ and $DPHA_{jt}$ are respectively the density of physicians and pharmacies in the area; and PA_{jt} is the price of a defined daily dose of antibiotic and PC_{jt} represents the price of a standard consultation with a general practitioner defined at cantonal level and captured by the point values (weights) calculated for the reimbursement of services provided by general practitioners in 2001.¹⁸ POP_{ljt} is the percentage of population in the l age range and INF_{jt} is the incidence of bacterial infections (campylobacter and salmonella).¹⁹ The latter variable is a proxy for the probability of a correct diagnosis. We do not have more precise information, for instance, on potential need. Diagnosis accuracy improves when the incidence of bacterial infections is high since the probability to prescribe an antibiotic when it is not needed is lower. In the empirical specification we use the average incidence of bacterial infections calculated over the years 1999-2001.

Further, the model (9) considers some explanatory variables not explicitly defined in the theoretical model (8). Y_{jt} is the average income in the area; $DBOR_{jt}$, $DLAT_{jt}$, and $DHOS_{jt}$ are dummy variables. The first one captures any borderland effect with neighbouring countries. The second considers whether an area is characterised by Latin culture (French- and Italian-speaking), or German culture. The third dummy accounts for at least one hospital in the area.

In order to capture the presence of practices that can sell drugs directly to their patients, we use two approaches. The first approach is based on dummy variables and is specified in equation (9). In this case, two dummy variables, $NODISP_{jt}$ and $DISP50_{jt}$, are introduced in the model to capture the impact of direct dispensing of drugs. $NODISP_{jt}$ takes value equal to 1 if there are no dispensing practices in the area, 0 otherwise; $DISP50_{jt}$ takes value equal to 1 if the proportion of dispensing practices in the area is greater than 50%. The intermediate case where the proportion of dispensing practices is greater than 0 and lower

¹⁷Clearly, the model does not allow to disentangle the possible mismatch between antibiotic prescriptions, antibiotic sales and antibiotic use since detailed data on these figures are not available. We assume patient's non-compliance to be a negligible factor.

¹⁸In Switzerland, a detailed fee-for-service system with more than 4600 items is applied for the reimbursement of health care providers. A given number of points is assigned to each type of service according to time, complexity and facilities. The cantons apply different values to the basic point, which reflects the heterogeneity in the costs of services across the country. Therefore, the point value can be interpreted as a proxy for the price of a consultation.

¹⁹These are the leading causes of gastrointestinal infections. Since data are not available at local level, we use information at cantonal level.

than 50% represents our benchmark.²⁰ As for the second approach, we use a continuous variable ($DISP_{jt}$) that represents the rate of dispensing practice. Following this approach, the two previous dummy variables, $NODISP_{jt}$ and $DISP50_{jt}$, are substituted for $DISP_{jt}$ in equation (9). Dispensing variables should capture the presence of a positive mark-up on antibiotic prescriptions gained by dispensing practices as compared to not dispensing practices.

In Figure 3 we show the proportion of dispensing practices in small areas across the country. Note that the association between antibiotic consumption depicted in the previous map 2 and the presence of dispensing practices does not appear as straightforward as probably expected.

To check whether there is an interaction between GPs monopoly power and the integration of prescribing and dispensing, we also test interaction terms between the density of physicians and dispensing variables in equation (9). The results are discussed in the following section 3.2 together with other findings.

For the estimation of equation (9) we have quarterly data for the dependent variable - per capita antibiotic use - and for one independent variable - the price of a daily dose -, whereas for the remaining explanatory variables only yearly data are available.²¹ Therefore, we resolve to estimate equation (9) on a quarterly basis. A summary statistics of variables used in the empirical analysis is provided in Table 2.

The correct econometric approach to the estimation of equation (9) has to deal with three main issues: the possible endogeneity of price, the presence of unobserved heterogeneity variables, such as infection variables, and the possible spatial correlation of antibiotic consumption across regions. Although the price of each antibiotic product does not vary across geographic areas in Switzerland, the average price for a daily dose of antibiotics differs because geographic regions vary in the consumption mix of different antibiotic categories. Consequently, the price for a daily dose can be endogenous. Although both the Wu-Hausman F-test and the Durbin-Wu-Hausman χ^2 -test do not clearly reject the null hypothesis of price exogeneity, we deal with this potential endogeneity problem by treating the price as an endogenous variable and instrument it with the lagged value of price and the exogenous regressors.

²⁰To investigate the robustness of our estimations, we also considered alternative coding choices. A dummy variable that takes value equal to 1 if there are dispensing practices in the area, and 0 otherwise, is used to overcome the possible critique of setting an arbitrary threshold to 50%. The results are confirmed.

²¹It is worth noting that the quarterly variation of most explanatory variables, such as income per capita and demographic structure, is actually low.

One additional argument that should be clarified is the potential reverse causality between the presence of dispensing practices and the consumption of antibiotics. If areas with a majority of dispensing practices are significantly different in terms of antibiotic consumption, we assume that causality runs from dispensing to antibiotic consumption. Although regulators allow for dispensing because of need, there are at least two reasons why causality cannot run from consumption to dispensing. First, the institutional decision to allow for direct dispensing of antibiotics is not a short-run intervention. This relates to the structure of the primary care market in different geographical areas, which is relatively stable over time, and, consequently, can be treated as exogenous as with respect to the consumption of antibiotics. Second, in Switzerland, the decision to allow for direct dispensing is not a federal competence. Regional regulators independently decide on the organization of the primary care market. Direct dispensing of drugs requires parliament approval, that is a national law has to be passed and is subject to a referendum.

With regard to choice of the econometric approach, we decided to follow a two step approach. In the first stage, we used classical non spatial econometric models for panel data, whereas in the second stage, we applied spatial panel data models.

It should be noted that in the econometric literature on panel data, we can find various types of models. Generally, we can distinguish the following estimators: the OLS, the between (BE), the fixed effects (FE) and the random effects (RE).²² To account for unobserved heterogeneity, the best approaches are to econometrically specify the model (12) with either market area-specific fixed effects (FE) or with market area-specific random effects (RE).

FE models lend themselves well to situations with unobserved characteristics that remain relatively stable over time. RE models do not impose that heterogeneity be approximately constant within a unit over time, but have another important limitation. Specifically, they assume that the state-specific individual effects are assumed to be uncorrelated with the explanatory variables. In practice, the state-specific term may contain unobserved factors that are correlated with the explanatory variables. If so, the resulting RE coefficients are biased. By contrast, the preferred estimation technique with FE, yields unbiased estimated coefficients even in the presence of such correlations. In order to choose between the fixed-effects model and the random-effects model we applied the Hausman test. This test checks the null hypothesis that the explanatory variables and the individual-specific

²²For a detailed presentation of the econometric methods that have been used to analyses panel data, Greene (2008) and Baltagi (2006).

error terms are uncorrelated. The result of the test shows that the differences in coefficients between the two models are not systematic, thus implying that the random effects model is to be preferred. Moreover, the within variation of the majority of the variables included in the model is low and this could imply a low statistical efficiency of the fixed effects model. Therefore, model (12) has been estimated using a RE model. Further, given the fact that we are estimating model (12) using quarterly data where the majority of the explanatory variables do not vary over time, we decided to use, for comparison purposes and to check the robustness of the results, also the BE estimator. In this case, the estimation of model (12) using quarterly data only for 2002 is equivalent to the estimation of model (12) using cross-sectional data for 2002. Generally, the results are very similar to the random effects model and, therefore, we do not show them in the tables that report the empirical results.

As for spatial aspects, it is worth noting that regional antibiotic consumption may be affected by individuals' and physicians' attitudes towards antibiotic consumption as well as the presence of infection disease in adjacent regions. The implications of spillover effects in antibiotic consumption have been recently investigated by González Ortiz and Masiero (2013) using Italian data. Spatial externality problems can be taken into account by means of adequate spatial econometrics estimators.²³ To incorporate spatial effects into our regression model we can follow two approaches: the spatial-lag model and the spatial-error model or, as proposed by Kapoor et al. (2007), an econometric model that combine these two models. In this paper we adopt the random effects spatial error and spatial lag models.²⁴ As suggested by Moscone and Knapp (2005), the spatial error model is relevant when the distribution of residuals in different regions displays spatial correlation. Residual may be spatially correlated if aggregated shocks hit regional health authorities or there are unobservable risk factors concentrated across the areas. In our case, this effect may be due, for instance, to an infectious disease breakdown spreading across the country.

We expect the spatial error coefficient to be positive, because infectious disease breakdown in the neighbourhood of area j will determine an increase of antibiotic consumption

²³For a general introduction and discussion of spatial econometrics, see Anselin (1988, 2001). For an application of spatial econometric methods in health economics see Moscone and Knapp (2005), Moscone, Knapp and Tosetti (2007), Costa-Font and Moscone (2008), Filippini et. al. (2009a, 2009b).

²⁴In order to test the presence of spatial autocorrelation we considered several preliminary tests. The Moran's I statistic as described by Kelejian and Prucha (2001) were applied to check for spatial correlation in the residuals. We also employed the testing procedure described in Baltagi et al. (2007). Both tests reject the null hypothesis of no spatial correlation in the residuals at 1% significance level (p-value 0.01). In order to test for spatial correlation in the dependent variable, we applied the test described in Baltagi and Long (2008). The test rejects the null hypothesis of no spatial correlation in the dependent variable at less than 5% significance level (p-value = 0.018).

in the area. On the other side, we expect the spatial lag coefficient to be negative, because of the presence of spatial spillovers. A general increase of the consumption of antibiotics in a neighborhood area decreases the need to consume antibiotics because the probability of contagions decreases.

The econometric specification of the RE model for panel data with J cross-sectional units observed over T time periods including spatial effects, also referred as SARAR model and proposed by Kapoor et al. (2007), is defined as

$$DID = \lambda \cdot (W \otimes I_T) \cdot DID + X \cdot \beta + u \quad (10)$$

$$u = \rho \cdot (M \otimes I_T) \cdot u + \varepsilon \quad (11)$$

$$\varepsilon = \mu \otimes e_T + v \quad (12)$$

where DID is a $Jx1$ vector of observations on antibiotic consumption per capita; X is the JxQ matrix of explanatory variables; β is the vector of regression parameters; W and M are the matrix of spatial weights; u is a vector of spatially lagged residuals; μ is a vector of individual effects and v is a vector of i.i.d. residuals; finally λ and γ are the spatial lag and spatial error respectively.

Concerning ε , following assumptions are made:

$$\varepsilon = \mu \otimes e_T + v \quad (13)$$

$$E(\mu) = 0 \quad (14)$$

$$E(\mu \cdot \mu') = \sigma_\mu^2 \cdot I_J \quad (15)$$

$$E(v) = 0 \quad (16)$$

$$E(v \cdot v') = \sigma_v^2 \cdot I_{JT} \quad (17)$$

$$E(v' \cdot (\mu \otimes e_T)) = 0 \quad (18)$$

where μ is a $(Jx1)$ vector of individual (random) effects with zero mean, zero covariance and variance σ_μ^2 . Further, μ_j and v_{jt} are i.i.d. with finite fourth moments. It is assumed that the matrices $I_J - \lambda W$ and $I_J - \rho M$ are invertible (non-singular) and that λ , ρ are bounded in absolute value.

As expected the Wu-Hausman F-test rejects the null hypothesis of exogeneity of the spatially lagged dependent variable at less than 0.1% significance level. To deal with endogeneity, we also treat the spatially lagged dependent variable as endogenous, together with price, and instrument it with the spatially lagged exogenous regressors and lagged price. Note that we can only use three quarters for our estimations since the lagged price

is included as an instrument. 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.

For the estimation of the spatial econometric models above we follow the approach suggested by Kapoor et al. (2007), and use a generalized moment estimator. Moreover, since current STATA commands do not combine the estimation of spatial-lag and spatial-error models, we developed additional STATA codes to estimate our models.

3.2 Estimation results

Before focusing on the effect of dispensing practices, we briefly summarize the main results from the estimation of equation (9) using the random effects model with and without spatial error and spatial lag effects described by (10)-(12). In Table 3 we report the parameter estimates obtained using the random effects models that do not consider spatial effects. Models with spatial effects are summarized in Table 4. Further, we report the results obtained using the two approaches to account for dispensing practices in separate columns. In the first column we show the results with the dummy variable approach, whereas in the second column a continuous dispensing variable is considered.

Generally, the value of the parameters and the number of significant parameters in spatial models are relatively close to those reported for the non spatial models. When we take spatial effects into account, the values of the income parameters are higher than the values reported in Table 3. Further, in both spatial models the age structure of the population seems to have a lower impact on the per capita antibiotic sales than in models without spatial effects.

To provide more details on the estimated parameters, we start by looking at the effect of income. Income elasticity varies between 0.13 (non-spatial models, not significant) and 0.27 (spatial models, significant at less than 5%), which supports the hypothesis that antibiotics are normal goods.²⁵ Our result is in accordance with other findings in the literature (Nilson and Laurell, 2005; Henricson et al., 1998; Thrane et al., 2003).

Concerning the impact of the age structure of the population on antibiotic consumption we can observe that only young and elderly people seem to have a clear impact. A higher proportion of children between 0 and 14 years of age increases antibiotic consumption in an area. Conversely, antibiotics are less likely to be prescribed in areas that have a larger

²⁵Baye et al. (1997) find higher income elasticity (1.33) that may be related to differences in the population under study and the type of antibiotics considered (only penicillins and tetracyclines).

proportion of individuals who are over 74 years of age compared to the baseline class.²⁶

In all model specifications the coefficient of the incidence of infections exhibits the expected positive sign but is poorly significant.

The values of price elasticity of antibiotics obtained in the between model are close to the estimates of Baye et al. (1997), who found negative compensated (-0.785) and uncompensated (-0.916) own-price effects for anti-infectives. Ellison et al. (1997) calculate price elasticities irrespective of drug (cephalosporins) expenditure using US wholesales data from 1985 to 1991. Their estimates range between -0.38 and -4.34 . Our estimated price elasticities range between 0.14 (non-spatial models, not significant) to -0.55 (spatial models, significant). The coefficient on price of doctor consultations is not significant. Although expensive consultations imply higher diagnosis effort, which may reduce inappropriate prescriptions of antibiotics, this hypothesis is not confirmed by our results.

The physicians' density is positively and significantly associated with local per capita antibiotic use. Estimated elasticities vary between 0.08 and 0.13 . Similarly, an increase in the density of pharmacies leads to higher levels of per capita outpatient antibiotic use in the area. The estimated coefficient ranges between 0.61 and 0.69 .

As for the impact of direct dispensing of drugs, the results reported in Table 4 for spatial models confirm the results reported in 3. We find that the proportion of practices without dispensing (*NODISP*) has a negative effect on antibiotic sales in both models, although the coefficient is not significant. Consequently, we cannot reject the hypothesis that areas without dispensing practices and areas with a relatively small proportion of dispensing practices (below 50%) exhibit similar levels of antibiotic consumption per capita. However, when the proportion of dispensing practices is relatively high (more than 50%), the effect on consumption is positive and significant. The estimated coefficients suggest that in market areas where the proportion of dispensing practices is relatively high, antibiotic consumption is 1.30 to 1.37 times higher than in the other market areas, respectively for non spatial and spatial model specifications. This effect is confirmed by the results obtained using a continuous variable representing the share of dispensing practices in each market areas.²⁷ The value of the estimated price elasticity varies between 0.58 and 0.68 and is highly significant. This value suggests that a one percent increase in the proportion of

²⁶Similar results are obtained, for instance, by Mousquès et al. (2003), who investigate a panel of general practitioners prescribing antibiotics for rhynopharyngeal infections.

²⁷Interaction terms between the density of physicians and dispensing variables are always insignificant, both in spatial and non-spatial regressions. This is somehow expected since the density of physicians and dispensing covariates are highly significant. Most of the variation is then captured by these variables included separately and little is left for their interaction.

dispensing practices will increase the per capita antibiotic sales by 0.58% to 0.68%.

The estimates of the spatial error coefficient (ρ) and the estimates of the spatial lag coefficient (λ) are statistically significant and carry the expected sign.²⁸ The positive spatial error coefficient may suggest that unobservable aspects or random shocks, such as a disease outbreak in surrounding areas, will determine an increase of antibiotic consumption in area i . Other more deterministic spatial spillovers are captured by the negative spatial lag coefficient. In this case an increase in the consumption of antibiotics in neighborhood areas decreases antibiotic consumption in area i . This may indicate that the probability of contagions decreases due to the preventive effect of antibiotic consumption.

It is worth noticing that the negative correlation between the rate of dispensing practices and the density of pharmacies in the areas is remarkable. One could then argue that dispensing practices are meant to improve access to drugs when pharmacies are lacking. Note, however, that in our model specifications we control for access in general. Indeed, the estimated coefficient for dispensing practices is adjusted for the density of pharmacies as well as for the density of all practices. This suggests that direct dispensing of drugs may increase antibiotic consumption beyond the levels usually attained by some satisfactory access to medical services. One could also argue that the density of pharmacies is not a good indicator for access to antibiotic treatment in the area. Indeed, travelling costs for patients may vary consistently. Consider, for instance, two small areas of the same size but different number of pharmacies and inhabitants. The two areas may have the same number of pharmacies per inhabitant, i.e. the same density. However, the average patient's distance from the pharmacy may differ. To address this point we run separate regressions with the density of the population as an additional regressor. This allows to better captures the level of urbanization of the areas and, consequently, can be used as a proxy for travelling distances. The variable is never significant, nor does it change the results of the other covariates significantly. We are then confident that our estimates of the effect of dispensing practices on antibiotic consumption is quite robust to any possible misspecification related to access to medical treatment.

4 Conclusions

Prescribing and dispensing of drugs are important aspects of access to primary health care. In most developed countries, these aspects are kept separate and doctors are not allowed

²⁸To investigate the robustness of these results we also estimate spatial lag models and a spatial error models separately. The estimates confirm the results reported in Table 4.

to sell drugs directly to their patients. The separation of prescribing drugs and dispensing drugs has recently proved to be effective in reducing drug expenditure, for instance in Taiwan (Chou et al., 2003). However, the separation of drug prescribing and dispensing may be costly in terms of limited access to drug treatment and low levels of infection prevention. In Switzerland, physicians are allowed to sell drugs directly to their patients in most cantons, with some exceptions across the country.

In this paper, we investigated dispensing practices using a theoretical and an empirical approach. For this purpose, we extended the classical Hotelling product differentiation model (Hotelling, 1929; Gravelle, 1999) with horizontal and vertical dimensions. We allowed for different types of general practitioners (with and without direct dispensing), imperfect information on the nature of patient's infection (viral or bacterial), and positive and negative externalities from antibiotic consumption. GPs we allowed to reduce errors in prescribing by increasing the level of diagnostic services provided to their patients. We showed that the interaction between consumption externalities and incentives to dispensing practices may reduce diagnosis accuracy and, consequently, increase the likelihood of antibiotic prescriptions.

Using data on antibiotic consumption from small geographical areas from a country (Switzerland) with a fee-for-service remuneration scheme for doctors and two prescribing regimes - with and without dispensing practices -, we examined the effects of dispensing practices empirically. Our econometric approach relies on spatial models for panel data where spatial aspects (both spatial lag and spatial error effects) of infectious diseases and antibiotic consumption are taken into account by appropriate spatial-econometrics estimators (Moscone et al., 2007; Moscone and Tosetti, 2010a). Findings indicate that dispensing practices induce higher rates of antibiotic use, after controlling for patient characteristics, epidemiological factors, and access to drug treatment.

The rationale behind a higher consumption of antibiotics under a dispensing regime may be that dispensing practices benefit more from antibiotic prescriptions because they gain a margin from antibiotic sales. This leads to lower diagnosis effort which increases mistaken diagnosis and, consequently, raises antibiotic prescriptions and reduces antibiotic effectiveness (higher bacterial resistance). This effect is probably only partially mitigated by the positive externality from antibiotic consumption that reduce prescriptions needed by other individuals and in following periods. There will be scope for additional incentives to dispensing practices to reduce the inappropriate use of antibiotics and contain the threat of bacterial resistance.

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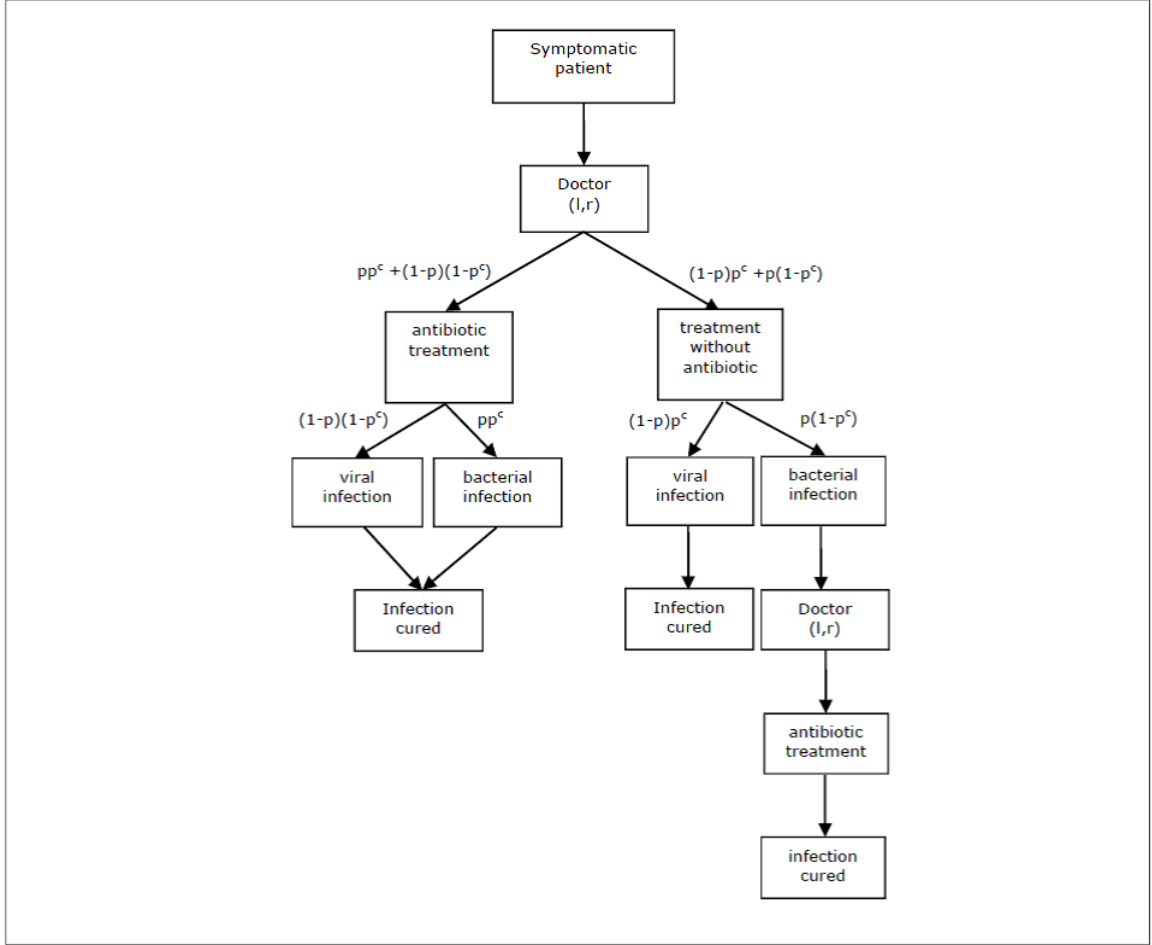


Figure 1: Doctor's strategies to tackle a mild respiratory/gastro-intestinal infection.

| Infection | Prescription | Cost of different treatment's strategies |
|-----------|--------------|--|
| v | NA | $\alpha f + td_j$ |
| v | A | $\alpha(f + z) + td_j$ |
| b | A | $\alpha(f + z) + td_j$ |
| b | $NA+A$ | $2(\alpha f + td_j) + \alpha z$ |

Table 1: The total cost of treatment depends upon doctor's prescription strategy (A =antibiotics, NA =antipyretic/anti-inflammatory only) and the type of patient's infection (b =bacterial, v =viral).

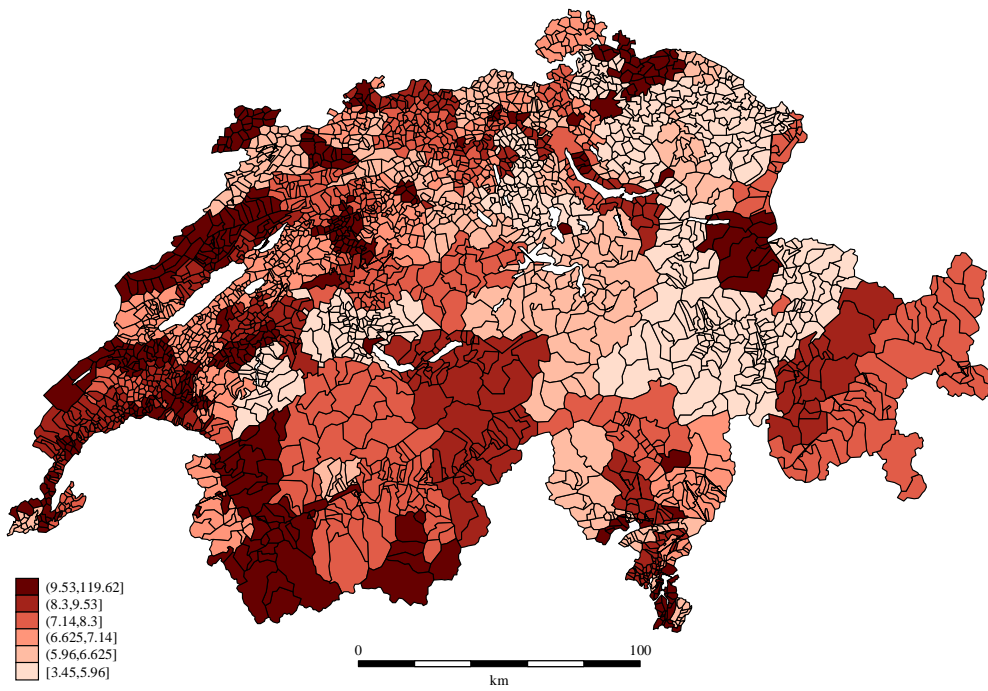


Figure 2: Outpatient antibiotic use across small areas in Switzerland (year 2002), measured in defined daily doses per 1000 inhabitants (DID).

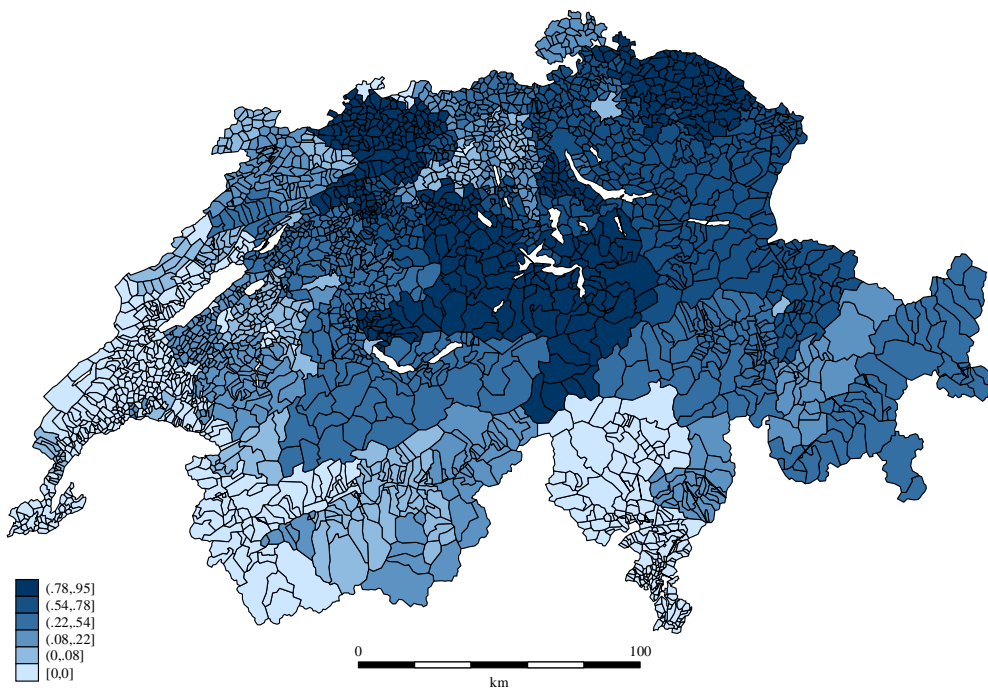


Figure 3: Proportion of dispensing practices among all GP practices across small geographic areas in Switzerland (year 2002).

| Variable | Description | Mean | Std dev. |
|------------------------|---|--------|----------|
| <i>DID</i> | Defined daily doses per 1000 inhabitants | 11.714 | 13.061 |
| <i>Y</i> | Income per capita defined in CHF | 23465 | 6849.4 |
| <i>POP₁</i> | Proportion of 0-14 in total population | 0.1658 | 0.0243 |
| <i>POP₂</i> | Proportion of 15-25 in total population | 0.1247 | 0.0173 |
| <i>POP₃</i> | Proportion of 26-59 in total population | 0.4956 | 0.0314 |
| <i>POP₄</i> | Proportion of 60-74 in total population | 0.1363 | 0.0213 |
| <i>POP₅</i> | Proportion of over 74 in total population | 0.0776 | 0.0190 |
| <i>INF</i> | Incidence of common gastrointestinal infections (salmonella and campylobacter) in 100000 inhabitants | 114.69 | 22.580 |
| <i>DPHY</i> | Density of physicians for 100000 inhabitants | 565.21 | 1052.5 |
| <i>DPHA</i> | Density of pharmacies for 100000 inhabitants | 35.098 | 39.112 |
| <i>PA</i> | Price of a defined daily dose | 3.7112 | 0.3113 |
| <i>PC</i> | Price of GP consultations | 0.9074 | 0.0526 |
| <i>DBOR</i> | Whether or not the area borders other countries | 0.125 | 0.0107 |
| <i>DLAT</i> | Whether an area has a Latin (French and Italian) or a German culture | 0.4375 | 0.0160 |
| <i>DHOS</i> | Whether or not there is at least one hospital in the area | 0.7417 | 0.0141 |
| <i>NODISP</i> | Whether or not there are no dispensing practices in the area | 0.4083 | 0.0159 |
| <i>DISP50</i> | Whether or not there is a majority of dispensing practices in the area | 0.2333 | 0.0137 |
| <i>DISP</i> | % of dispensing practices across all practices in the area | 0.2187 | 0.0100 |

Table 2: Variables notation and summary statistics.

| Random-effects IV regressions | | | | | | |
|-------------------------------|--------------------|-----------|---------|--------------------------------|-----------|---------|
| | Dispensing dummies | | | Continuous dispensing variable | | |
| Number of obs. | 720 | | | 720 | | |
| Number of groups | 240 | | | 240 | | |
| R ² within | 0.6599 | | | 0.6545 | | |
| R ² between | 0.7369 | | | 0.7497 | | |
| R ² overall | 0.7333 | | | 0.7452 | | |
| Covariates | Coefficients | St. Err. | p-value | Coefficients | St. Err. | p-value |
| Constant | -2.198744 | 1.427119 | 0.123 | -3.024184 | 1.437677 | 0.035 |
| Y | 0.1341392 | 0.1086522 | 0.217 | 0.1494742 | 0.1065245 | 0.161 |
| POP ₁ | 0.7770858 | 0.2902369 | 0.007 | 0.707528 | 0.2854014 | 0.013 |
| POP ₂ | -0.3992381 | 0.2628232 | 0.129 | -0.4388904 | 0.258685 | 0.090 |
| POP ₄ | -0.0832129 | 0.2108611 | 0.693 | -0.1966698 | 0.2121132 | 0.354 |
| POP ₅ | -0.2448346 | 0.1039692 | 0.019 | -0.2192098 | 0.1017727 | 0.031 |
| INF | 0.0146288 | 0.0420017 | 0.728 | 0.0329257 | 0.0410286 | 0.422 |
| DPHY | 0.1271244 | 0.0340157 | 0.000 | 0.1181553 | 0.0334417 | 0.000 |
| DPHA | 0.6092891 | 0.0513577 | 0.000 | 0.6456287 | 0.0515961 | 0.000 |
| PA | 0.1435792 | 0.7619403 | 0.851 | 0.192503 | 0.817172 | 0.814 |
| PC | 0.2545297 | 0.4248651 | 0.549 | 0.3310219 | 0.4261601 | 0.437 |
| DBOR | -0.0001904 | 0.0583645 | 0.997 | 0.0076729 | 0.0560429 | 0.891 |
| DLAT | -0.0618509 | 0.0921805 | 0.502 | -0.034946 | 0.0872025 | 0.689 |
| DHOSP | -0.0006248 | 0.0560705 | 0.991 | -0.0011009 | 0.0554195 | 0.984 |
| NODISP | -0.0441112 | 0.0614449 | 0.473 | | | |
| DISP50 | 0.2993839 | 0.0602715 | 0.000 | | | |
| DISP | | | | 0.5856185 | 0.0938454 | 0.000 |
| dt ₂ | -0.1982564 | 0.0143699 | 0.000 | -0.1974589 | 0.015179 | 0.000 |
| dt ₃ | -0.1824587 | 0.0149339 | 0.000 | -0.1816195 | 0.0157927 | 0.000 |
| σ_κ | 0.25347992 | | | 0.24544706 | | |
| σ_ϵ | 0.07584716 | | | 0.07584716 | | |
| σ^2 due to μ_i | 0.91782296 | | | 0.91283258 | | |

Notes: The instruments used in the random-effects IV regressions (*RE2SLS*) are the lagged variable of price (PA_{t-1}), Y_t , POP_{1t} , POP_{2t} , POP_{4t} , POP_{5t} , INF_t , $DPHY_t$, $DPHA_t$, PC_t , $DBOR_t$, $DLAT_t$, $DHOSP_t$, $NODISP_t$, $DISP50_t$ ($DISP_t$ in the continuous variable regression), dt_2 , and dt_3 . First-stage regressions on the instruments yield significant joint F-tests.

Table 3: Parameter estimates of random-effects IV regressions (*RE2SLS*).

| Spatial random-effects IV regressions | | | | | | |
|---------------------------------------|--------------------|-----------|---------|--------------------------------|-----------|---------|
| | Dispensing dummies | | | Continuous dispensing variable | | |
| Number of obs. | 720 | | | 720 | | |
| Number of groups | 240 | | | 240 | | |
| R ² within | 0.4055 | | | 0.4076 | | |
| R ² between | 0.7921 | | | 0.8005 | | |
| R ² overall | 0.7839 | | | 0.7923 | | |
| Covariates | Coefficients | St. Err. | p-value | Coefficients | St. Err. | p-value |
| Constant | -0.5600248 | 0.7059426 | 0.428 | -0.931256 | 0.6927078 | 0.179 |
| Y | 0.2506859 | 0.1172455 | 0.033 | 0.2670415 | 0.1139665 | 0.019 |
| POP ₁ | 0.4642093 | 0.267977 | 0.083 | 0.4615374 | 0.2614212 | 0.077 |
| POP ₂ | -0.349267 | 0.2318164 | 0.132 | -0.4088315 | 0.2255809 | 0.070 |
| POP ₄ | -0.1101778 | 0.1879261 | 0.558 | -0.1769792 | 0.1842804 | 0.337 |
| POP ₅ | -0.2025597 | 0.0939734 | 0.031 | -0.1504447 | 0.0928847 | 0.105 |
| INF | 0.0072868 | 0.0549224 | 0.894 | 0.0310215 | 0.0539316 | 0.565 |
| DPHY | 0.0788513 | 0.027162 | 0.004 | 0.0768944 | 0.0264956 | 0.004 |
| DPHA | 0.6536462 | 0.0468989 | 0.000 | 0.6916768 | 0.0469933 | 0.000 |
| PA | -0.5476143 | 0.3067118 | 0.074 | -0.4935378 | 0.3062494 | 0.107 |
| PC | 0.0614923 | 0.4785733 | 0.898 | 0.1189752 | 0.4670196 | 0.799 |
| DBOR | 0.0275946 | 0.0605708 | 0.649 | 0.0554975 | 0.0593344 | 0.350 |
| DLAT | 0.0678903 | 0.0898894 | 0.450 | 0.1175204 | 0.0818143 | 0.151 |
| DHOSP | 0.0100526 | 0.0462533 | 0.828 | 0.0089593 | 0.0451583 | 0.843 |
| NODISP | 0.0075422 | 0.0545024 | 0.890 | | | |
| DISP50 | 0.3738889 | 0.0632064 | 0.000 | | | |
| DISP | | | | 0.6853876 | 0.0992924 | 0.000 |
| dt ₂ | -0.1355012 | 0.0108294 | 0.000 | -0.1326363 | 0.0107027 | 0.000 |
| dt ₃ | -0.1270158 | 0.0104178 | 0.000 | -0.1242904 | 0.0103106 | 0.000 |
| λ | -0.3537783 | 0.0891222 | 0.000 | -0.3323822 | 0.0871533 | 0.000 |
| ρ | 0.5346576 | 0.0534699 | 0.063 | 0.5346576 | 0.0534699 | 0.063 |
| σ _κ | 0.23122444 | | | 0.22573567 | | |
| σ _ε | 0.070791 | | | 0.070791 | | |
| σ ² due to μ _i | 0.91430063 | | | 0.91046009 | | |

Notes: The instruments used in the spatial random-effects IV regressions (*SRE2SLS*) are the lagged variable of price (PA_{t-1}), Y_t , POP_{1t} , POP_{2t} , POP_{4t} , POP_{5t} , INF_t , $DPHY_t$, $DPHA_t$, PC_t , $DBOR_t$, $DLAT_t$, $DHOSP_t$, $NODISP_t$, $DISP_{50t}$ ($DISP_t$ in the continuous variable regression), dt_2 , dt_3 , and their spatial lags. 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 4: Parameter estimates of spatial random-effects IV regressions (*SRE2SLS*).

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