Physician Agency and Inappropriate Antibiotic Prescriptions in Taiwan

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Abstract

As antimicrobial resistance becomes a global threat in public health, this paper shows physician agency is the main driver behind inappropriate antibiotic prescriptions. I used data from Taiwan with more than 10 million patient visits for viral upper respiratory tract infections and found that antibiotics were prescribed in 12% of the visits. Empirical results show that the inappropriate antibiotic prescriptions were more likely to be given by physician owners and dispensers. The number of doses prescribed is found to increase with the profit margin. The results also reveal that patients did not prefer to receive antibiotics, as their chances of returning to the same doctor would be reduced if they had received inappropriate antibiotics in the previous visit. Medical providers facing less competition were found to be more likely to prescribe inappropriate antibiotics given patients' sparse alternatives.

JEL: I11, I18, D82

Keywords: physician agency, pharmaceutical profit margin, health care competition, antibiotics

1. Introduction

Treating viral infections with antibiotics is an inappropriate use of antibiotics; it increases the risk of bacteria mutating and developing antimicrobial resistance (AMR). Medicines become ineffective and infections persist in the body, increasing the risk of spread to others. Likely results include the increased risk of chronic conditions, death, and longer hospital stays. The safety of procedures like cesarean sections and chemotherapy could be greatly reduced (Roope et al., 2019). AMR has been considered by the World Health Organization as an increasingly severe threat to health care worldwide that could even force people into poverty (WHO, 2018). Roope et al. (2019) also

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mentioned that AMR is jeopardizing modern health care and causing significant economic costs similar to those caused by climate change. They called for more economics research on the use of antibiotics and AMR due to the urgency of the matter and the lack of studies on the economic issues such as agency, public good and externality.

This paper studies the inappropriate use of antibiotics prescribed for upper respiratory tract infections (URTIs) like the common cold, nasal obstructions and sore throats. Even though antibiotics are ineffective in treating these viral infections, doctors still prescribed antibiotics for these conditions. Fleming-Dutra et al. (2016) examined outpatient visits in the U.S. during 2010-2011 and found that almost half of the antibiotic prescriptions for acute respiratory conditions in their sample were inappropriate. Pouwels et al. (2018) also found physicians in the U.K. overprescribing antibiotics for viral URTIs. Given the potential damage of AMR, the long-debated question is why do doctors still inappropriately prescribe antibiotics?

One common explanation is that patients ask for antibiotics. Stivers (2005) discussed literature that cite patients' and parents' pressure as a reason for inappropriate antibiotic prescriptions. Applied economic studies suggest indirect evidence supporting patients' demand for antibiotics, such as Filippini and Masiero (2012) that found consumers in Italy had low price elasticity of their demand for antibiotics; Panthöfer (2020) found that doctors use antibiotics as defensive medicine in the United States. Literature on the effect of health care competition on antibiotic use often considered patients' preferences for antibiotics as the premise and derived the related results. Theoretically, Albert (2021) suggested an optimal market structure of health providers based on the patients' requests for antibiotics. Empirically, antibiotics are considered as a quality measure of medical providers as patients perceive it. Competition is found to be positively related with antibiotic prescriptions using data from Sweden (Fogelberg, 2013), Taiwan (Bennett et al., 2015), and Norway (Zykoda, 2020).

Opposite to the above demand-side explanation that stresses patients' preferences for antibiotics even when unnecessary, other papers consider the inappropriate antibiotic prescriptions as a supply-side phenomenon where physician agency plays an important role (WHO, 2018; Roope et al., 2019). Park et al. (2005) found a policy that prohibited medication dispensing by physicians substantially reduced inappropriate antibiotic prescriptions in Korea. Using an audit study in China, Currie et al. (2011, 2012, 2014) found evidence indicating physicians wanted to prescribe antibiotics even when the demand-side factors were eliminated. Financial incentives were found to be the major reason behind these antibiotic prescriptions. Filippini et al. (2014) found that in Switzerland dispensing doctors prescribed more antibiotics than the other doctors. Ellegård et al. (2018) showed that in Sweden doctors' choices of antibiotics were strongly affected by the design of pay for performance. Accordingly, physician agency has been found to be an important factor behind inappropriate use of antibiotics worldwide.

This paper provides another evidence of physician agency being behind doctors' overprescriptions of antibiotics. It differs from the existing research by focusing on the data of viral URTIs where antibiotic prescriptions are inappropriate for certain. The data include more than 10 million patient visits for 15 types of viral URTIs for which prescribing antibiotics would be later regulated as inappropriate by the Centers for Disease Control (CDC) in Taiwan in 2015. In 12% of these visits during 1999 to 2011, antibiotics were prescribed. The data include the characteristics of physicians and the price and markup information on the antibiotics prescribed, which were rarely found in the previous research. The data reveal that the profit margin per dose is about 29% of the price of antibiotics. The inappropriate antibiotic prescriptions account for about 9% of the total amount reimbursed from the National Health Insurance Administration (NHIA) for URTIs per clinic, which suggests sufficient financial incentives for physicians as it is roughly a quarter of a doctor's monthly salary in Taiwan.

Empirical analysis controls for the characteristics of hospitals and clinics and also demographic and socioeconomic characteristics stressed in Filippini et al. (2009) and Zykota (2020). Empirical results suggest that physicians with stronger financial incentives prescribed more inappropriate prescriptions than other physicians; those with stronger financial incentives include physicians who are legally obliged for their practicing facility (physician owner) and the physicians who both prescribe and dispense drugs (physician dispenser). Empirical results also indicate physicians prescribed more doses of antibiotics when the markup was higher. Similarly, Trap and Hansen (2002) found that in Zimbabwe dispensing doctors prescribed a greater number of drugs for URTIs than the other doctors.

This paper is closely related to Bennett et al. (2015), who also used data from Taiwan. They focused on the competition between health care providers in Taiwan and discovered that antibiotics were prescribed in the more competitive markets. This paper differs from theirs by using only the data of URTIs and focusing on the inappropriate use of antibiotics. Competition was also found to increase inappropriate antibiotic prescriptions, but the effect changed after controlling for market fixed effects; inappropriate antibiotic prescriptions were more likely to be given in less competitive markets. The result is intuitive when considering physician agency and patients' potential preferences *against* inappropriate use of antibiotics. The providers with financial incentives were more likely to prescribe inappropriate antibiotics when the patients had fewer options in the less competitive markets, even when the patients did not prefer to receive antibiotics. This hypothesis is supported by the estimates of the interaction term between physician owner and competitiveness of the market measured by the Herfindahl–Hirschman Index (HHI).

While the patients' preferences to inappropriate use of antibiotics were not observed, the correlated random effect (CRE) method was applied to control for the patients' preferences in the empirical analysis. Patients being against inappropriate antibiotics is further supported by examining patients' decisions to return to the same doctor they had visited most recently. Empirical results reveal that inappropriate antibiotics reduced patients' likelihood to visit the same doctor again when they had another URTI. Although the results show that patients are more likely to revisit physician owners than the employed physicians, their chances of returning would be reduced if the physician owner prescribed antibiotics in their previous visit. Results using the next five or ten visits revealed a similar pattern. The results are different with Bennett et al. (2015) likely because of the inclusion of physician characteristics and market fixed effects.

The empirical results reveal that patients in Taiwan might not ask for antibiotics, especially after an administration's policy campaign and regulation on inappropriate use of antibiotics was implemented between 2000 and 2001 (Chang, 2003). Patients' knowledge on antibiotics and AMR were also found to reduce antibiotic prescriptions in China (Currie et al. 2011), Sweden (Ancillotti et al., 2018), and other European countries (Coenen et al., 2013). Huang et al. (2005) showed that in Taiwan the children with parents who were physicians or pharmacists received significantly fewer antibiotics than the other children. Kwon and Jun (2015) found that consumers in Korea visited less frequently the clinics that prescribed more of the unnecessary antibiotics after a mandatory disclosure of antibiotic prescription rates for the common cold.

Overall, the empirical evidence indicates that physicians in Taiwan faced a tradeoff between prescribing inappropriate antibiotics: to earn a profit margin at the risk of losing patients in the future. Before reaching this conclusion, the following section describes the background of regulation and education of antibiotic use in Taiwan. This section also includes the relevant details on the universal healthcare system in Taiwan, the National Health Insurance (NHI), and the pharmaceutical pricing and markup for the drugs covered by the NHI. Section 3 describes the data and summary statistics. Section 4 illustrates the empirical framework, while Section 5 presents the results. Section 6 concludes this paper.

2. Institutional Background

2.1. Regulation and Education on the Inappropriate Use of Antibiotics in Taiwan

Antibiotics had been overprescribed in Taiwan in the late nineties, resulting in one of the highest prevalence of AMR in the world (Lauderdale et al., 2004). The Control Yuan of Taiwan, the supreme audit institution similar to the Government Accountability Office in the U.S., investigated the overprescription of antibiotics in Taiwan and impeached the then National Health Insurance

Administration, Ministry of Health and Welfare (NHIA) in 2000.[1] In response to this, the NHIA changed their reimbursement policy in February 2001 by requiring doctors who prescribed antibiotics for URTI's to submit additional evidence of a bacterial infection. The NHIA enforced this rule by auditing doctors who prescribed antibiotics frequently; this incentivized doctors to curtail unnecessary prescriptions to avoid the audits. Bennett et al. (2015) found the regulation made it less profitable for physicians to attract patients by prescribing antibiotics, but it did not completely eliminate competition as a determinant of antibiotic use.

In addition to the aforementioned policy regulating physicians prescribing antibiotics, Chang (2003) mentioned that in 2000 the NHIA in Taiwan started a series of policies that aimed to educate patients refrained from asking for antibiotics. The campaign was conducted widely through various media outlets. The related knowledge on appropriate use of antibiotics was also integrated into the teaching materials for middle schoolers. Chang (2003) showed that these education campaigns significantly reduced the inappropriate prescriptions of antibiotics in Taiwan. Accordingly, it is reasonable to consider the patients in Taiwan have gained knowledge on inappropriate use of antibiotics since 2000.

The government in Taiwan continued to monitor and regulate the antibiotic use in Taiwan after the regulation policy and education campaign in 2000. The Taiwan CDC published guidance for health care providers to follow that covered nearly everything about antibiotics, such as when to prescribe antibiotics for various conditions, the information technology used to restrict and control the use of antibiotics, how to measure and trace the level of drug resistance, and how to prevent conditions that required the use of antibiotics (Taiwan Centers for Disease Control, 2015). The guidance specifically defines the inappropriate use of antibiotics on the URTIs as prescribing antibiotics for condition recorded with an ICD code of 460, 462, 464, 465, 466, 487, or 490 as the main diagnosis. While the guidance was published after the sampling period in this paper, these restricted diagnoses provide a reference on what would be inappropriate use of antibiotics before its publication. The empirical analysis thus focuses on these conditions where prescriptions of antibiotics are considered as inappropriate.

2.2. The National Health Insurance in Taiwan

Taiwan implements a single payer, universal health care system administrated by the NHIA. Most of the medical providers provide health care services under contract with the NHIA. Patients pay premiums each month, conditional on their salary and dependencies, and pay roughly 15% of their medical expenses in each outpatient visit to a doctor. A typical visit to a clinic for a common

[1] The investigation case 098-0124 of the Control Yuan, https://www.cy.gov.tw/CyBsBoxContent2.aspx?n=718&s=522

cold costs about New Taiwan Dollar (NT$) 200, about US$7, which includes the registration fee paid to clinics and the copayment for services and drugs. Patients' copayment for drugs is capped at NT$200, regardless of the quantity of drugs prescribed, so patients' burdens from acquiring prescription drugs are really low under the NHI coverage.

For each patient's visit, medical providers file a claim that records the diagnoses and treatments for the patient. Associated fees are regulated by the NHIA and included in the claim, such as the service fees for doctors and pharmacists. Information regarding each prescription drug is recorded as separate logs associated with the claim, including the price of the drug and the number of units prescribed. The claim is then used to apply for reimbursement from the NHIA. These claims provide a record of the medical history of Taiwanese citizens under insurance coverage since 1995, and they form the National Health Insurance Research Database (NHIRD).

About two-third physicians in Taiwan were employed (Lu and Hsiao, 2003). Others are hospital or clinic owners. In the rest of the paper, I considered a physician as an owner if he or she was marked as legally obliged for his or her practicing facility in the basic information file in the NHIRD. While clinic owners are obviously responsive to their financial incentives, Cheng (2003) mentioned that most hospitals in Taiwan also provide their staff physicians incentives to generate more revenues. Bennett et al. (2015) compared the system used in Taiwan to the staff model HMO in the United States.

The Taiwanese government launched a "separating policy" that prohibits physicians in clinics to both prescribe and dispense drugs; on-site pharmacies in clinics with a licensed pharmacist were allowed to continue to dispense drugs (Chen et al., 2013). Many on-site pharmacies were opened in response to this exemption of the policy. Many "gateway pharmacies" were also opened by or integrated with clinics next door. Thus, most physicians in clinics remained fully responsive to their financial incentives from prescription drugs after the implementation of the separating policy. Accordingly, while each observed claim marks whether a prescription was released for patients to purchase drugs from pharmacies, it is likely that the profit margin still went to the physicians who gave the prescriptions. In the rest of the paper, I considered prescriptions marked as not released as being prescribed by a physician dispenser, but the true proportion of these physician dispensers could be higher.

Taiwan adopts a global budgeting system with retrospective payments for its NHI. Under this system, providers are paid by fee-for-service, but the service price is calculated by points instead of a dollar amount. The actual amount reimbursed for each service depends on the final point value that is calculated by dividing the predetermined budget with the total service amount. The point value can be larger or lower than one New Taiwan Dollar; however, pharmaceutical reimbursements are not discounted in the manner of the reimbursement for services and maintain a monetary value of NT$1. Accordingly, some medical providers had increased their drug prescriptions after the implementation of global budgeting (Chou et al., 2010). Besides, the annual budget for health care is distributed among four sectors, including dentistry, Chinese medicine, community clinics, and hospitals. The hospitals and clinics practicing Western medicine compete in the same markets but under separate budgets. The administration also encourages patients with less severe conditions to visit community clinics, while hospital resources were preserved for patients with more severe conditions. The empirical analysis includes these considerations by controlling for the hospital accreditation level, which can be academic medical center, metropolitan hospital, regional hospital or clinic.[2]

2.3. Pharmaceutical Price Adjustment and Markup

Prescription drugs covered by the NHI are listed in a national formulary that comprises about 20,000 drugs with 13 to 75 new drugs added each year (Hsieh, 2009). As a drug enters the formulary, its price is determined by a uniform pricing that follows a "generic grouping rule", which prices the pharmaceuticals by their patent status, bioavailability/bioequivalence (BA/BE) availability, and the median price in other countries (Hsu and Lu, 2015). Pricing rules regarding brand-name and generic drugs are different and conditional on their bio-equivalent test results. Information on the drugs in the NHI formulary including names, the history of regulated prices, forms, strengths and branded or generic version were collected from the NHIA website.[3]

The NHIA reimburses medical providers' prescriptions according to the regulated prices, but medical providers are allowed to negotiate their own procurement price with pharmaceutical providers. Medical providers are allowed to make a profit from prescription drugs; the difference between the reimbursement price and their acquisition price is considered as the markup from prescribing a certain drug. But the percentage of markup is subject to a given range, the "reasonable zone," regulated by the NHIA; it was capped at 16% before September 2007 and 15% afterwards. The NHIA regulates the markup by adjusting the reimbursement prices periodically in a way similar to the Japanese system described in Iizuka (2012). In particular, the NHIA surveys pharmaceutical providers and medical providers on their privately-negotiated procurement prices of drugs every one or two years. If the average procurement price of a drug from the survey results is less than 85% of the regulated price, i.e., the average markup of that drug exceeds the reasonable zone, NHIA would reduce the reimbursement price of the drug accordingly down to a level such that the providers would acquire only the 15% or 16% regulated markup. In particular,

[2] Tang (2021) discusses the global budgeting system in Taiwan and investigates providers' strategic interactions in this system.

[3] http://www.nhi.gov.tw/Query/query1.aspx?menu=18&menu_id=703, in Chinese.

the following pricing formula is used to adjust the reimbursement price:

$$P^R_{kt+1} = P^W_{kt} + r \times P^R_{kt} \tag{1}$$

P^R_{kt} and P^R_{kt+1} denote the observed regulated price for drug k at time t and $t+1$, respectively. The t's and $t+1$'s indicate the time before and after each price adjustment, which was implemented every one or two years. The price adjustment would adjust all the drugs whose prices are subject to change based on the survey results; if a drug's average markup is within the reasonable zone then its price would not be adjusted. There were some drugs whose prices were adjusted for reasons other than the markup regulation. Those changes are not considered as revealing markup thus not used in calculating the markup.

The NHIA made nine price adjustments during 1999 to 2011 on the first day of the following months: April 2000, April 2001, March 2003, November 2004, September 2005, November 2006, September 2007, October 2009, and December 2011. These dates are considered as the t's and $t+1$'s in Eq. (1). The unobserved average reported wholesale price P^W_{kt} can thus be inferred with observed regulated prices P^R_{kt+1} and P^R_{kt} and the reasonable zone r. In particular, if a drug's reimbursement price was changed after a price adjustment in time $t+1$, the unobserved P^W_{kt} can be calculated from the observed P^R_{kt} and P^R_{kt+1} using Eq. (1). If the price remained unchanged after a price adjustment in time t, then $P^R_{kt} = P^R_{kt+1}$ and the wholesale price would simply be $P^W_{kt} = (1-r) \times P^R_{kt}$. The markup M_{kt} of each drug k was thus calculated as follows:

$$\begin{aligned} M_{kt} &= r \times P^R_{kt} && \text{if } P^R_{kt+1} = P^R_{kt} \\ &= P^R_{kt} - P^W_{kt} && \text{if } P^R_{kt+1} \neq P^R_{kt}. \end{aligned} \tag{2}$$

The resulting markup variable was used as the main measure of physician agency in the empirical analysis. Figure 1 reveals the trend of the time averages of price, markup percentage and quantity prescribed of the antibiotics. The quarters with a price adjustment were marked. Average price trended downward throughout the sample period. Average markup percentage would increase and decrease, and it was negatively related with the price of the next quarter because the price would be adjusted downward when the markup was sufficiently high. The quantity of antibiotics prescribed did not change much during the sampling period; it has been slightly increasing. Figure 1 thus suggests that the increasing quantity prescribed might be more likely related to profit margin than to price.

3. Data

3.1. Sample Descriptions

The data used in the analysis are a sample from the NHIRD. The database consists of the information from each claim filed by medical providers for reimbursement, and it includes almost the entire population of Taiwan because of the universal coverage. I used a sample of 0.6 million randomly drawn patients from 1999 to 2011. The population size in Taiwan is about 23.57 million people in 2021.

To focus on the physicians' choices concerning antibiotic prescriptions, I used only part of the original sample as follows: First, I downloaded from the NHIA drug inquiry website listed in footnote 3 for information from all the antibiotic drugs covered by the NHI whose ATC codes start with j01. Second, I merged the j01 drugs with the original sample by the drug ID. The merged dataset thus revealed the claims that included antibiotics prescriptions. Because each claim also recorded the type of disease diagnosed, I was able to calculate the total number of antibiotic prescriptions by each disease. For example, out of more than 1 billion observations that had an antibiotic prescription, more than 2 million antibiotic prescriptions were for patients diagnosed with acute sinusitis. Among the top 100 diseases ranked by their number of antibiotic prescriptions in the sample, 15 of them are viral URTI diseases for which the CDC guidance book states that antibiotic treatment is inappropriate. These include ICD9 codes 460, 462, 464.0, 464.10, 464.20, 465.0, 465.8, 465.9, 466, 466.0, 466.1, and 487.1, and A codes A311, A320 and A322. The claims associated with these diagnoses were then kept for further analysis. Because each claim could record up to three diagnoses, it is likely that some antibiotic prescriptions were reasonable when one of the 15 diseases was diagnosed along with other conditions. I thus excluded the claims having any diagnosis recorded other than the 15 diseases. Notice that not only the claims with antibiotic prescriptions were kept, but all the visits for these conditions were used for analysis. Table 1 reports the observations by diagnosis and the order of diagnosis in the claim.

Third, each visit could include multiple records, with each record includes one type of prescription drug. I thus gathered all the information from a visit into one record and kept only one observation for each visit. I added up the total price of all the antibiotics prescribed in a visit, the total markup acquired from these drugs and the total quantity of antibiotics prescribed in a visit. In addition, because some claims might be for follow-up prescriptions from the same visit for patients to obtain more drugs later, I removed any duplicate claims recorded by the same physician and patient on the same visit date. Fourth, I kept only the first visit in a month for a patient as the visits in the same month are likely subsequent visits for the same illness ordered by the doctor. Because this paper also studies patient retention, visits not in the same month are more likely a new illness and patients could decide whether to see the previous doctor.

3.2. Summary Statistics

Table 2 reports the summary statistics of the sample. Among the nearly 11 million visits, about 12% of the visits in the sample involved inappropriate prescriptions of antibiotics. Almost 85% of the visits were recorded after February 2001, when the Taiwanese government imposed stricter restrictions on antibiotic prescriptions for URTIs. About 79% of the visits were administrated by physician owners, who likely owned clinics as almost 96% of the visits in the sample were made to clinics. About 75% of the visits were made to physician dispensers, and only in 25% of the visits were patients released to fill prescriptions elsewhere. Figure 2 reveals that most of the inappropriate prescriptions were given by physician dispensers or owners, or both. It suggests physician agency as the main reason behind inappropriate use of antibiotics in Taiwan. The policy implemented in 2001 significantly reduced the inappropriate prescriptions, and the reduction came mostly from the physician owners and dispensers. The total percentage of inappropriate use of antibiotics became steady around 5% after 2005. The percentage prescribed by the other physicians remained small and constant throughout the sampling period.

Table 2 also reports the statistics of patients, hospitals and clinics, and markets. The markets are quite competitive as indicated by the average HHI. Most of the visits were made to private clinics. The average number of appearances for a patient in the sample is about 35 times, or 3 to 4 times a year. This variable accounts for the health status of a patient, particularly her medical history with regard to URTIs. In less than half of the visits, the patients returned to the doctors they saw in the previous visit for URTIs. The percentage increases to 75% and 84% when considering whether the patient returned to the same doctor in the next five and ten visits, respectively.[4] As a patient visited a doctor for URTIs about 4 times a year, the next five and ten visits were likely made in the next year and the next two years, respectively.

Table 3 reports the summary statistics of the visits with inappropriate antibiotic prescriptions. On average, the total price of the antibiotics given in these visits is about NT$7, where the markup is NT$2, or a 29% markup percentage per dose. As the average amount reimbursed for antibiotic prescriptions is about NT$92, the markup would be about NT$27 per visit. Considering the average amount reimbursed per visit with antibiotics is about 345 points in the sample, and the point value would be discounted by 10% on average for the clinic sector under global budgeting

[4]There are missing values when calculating return in the next visit because the data do not reveal the next visit in each patient's last observation. Patients revisiting in the next five visits would not require each patient to have at least five visits, however, as long as the patient returned to the same doctor in one of her next four or fewer visits. But if the patient did not return to the doctor in her observed visits, and the observed visits are fewer than five, then the revisit variable of this particular observation was counted as missing.

from 2001 to 2011, the markup from inappropriate antibiotic prescriptions account for about 9% of the total reimbursement amount per visit on average. From the official statistics reported by the Ministry of Health and Welfare, the average number of visits to a clinic for URTIs is 1,538 and the average reimbursed points for URTIs were about 515,724 a month.[5] Thus, assuming a clinic prescribed inappropriate antibiotics for all the visits, the total markup earned by prescribing inappropriate antibiotics would be about NT$41,526, or US$1,277 using the average exchange rate between 1999 and 2011, 32.53. For comparison, the average monthly salary of a doctor in Taiwan reported by the Ministry of Labor in 2019 is NT$164,289, or US$5,323 with the 2019 exchange rate.[6] Thus, the profit margin from inappropriate antibiotic prescriptions per clinic is about one quarter of a doctor's monthly salary in Taiwan. As the average number of clinics in Taiwan during the sampling period is 4,408, it would cost the NHI about NT$183 million or US$5.63 million a month if every clinic prescribed inappropriate antibiotics like the average clinic. Considering the average monthly budget for clinics was NT$6.692 billion during 2001 to 2011, the inappropriate antibiotic prescriptions could cost about 3% of the budget.

Table 3 also reveals that 82% of the visits were to physician owners. About 56% of the visits were made after the regulation policy implemented in February 2001. Nearly 89% of the patients were given antibiotics from physician dispensers. The patients were given more than eight doses per visit. These antibiotics seem to be given by younger providers with less experience than the average ones in the full sample reported in Table 2. The markets are also less competitive than the ones calculated using the full sample. Other statistics reported in Table 3 are similar to those of the full sample.

4. Empirical Model

This section first lays out a probit model with latent utility as a physician's objective function. A physician is assumed to maximize both her own profit and a patient's utility when writing an inappropriate prescription of antibiotics. If antibiotics were given, I proceeded to examine the determinants of the prescribed number of doses of these antibiotics, especially the price and markup of the antibiotics. A sample selection model was applied because the quantity was observed only when the antibiotics were prescribed. As the sample is a panel data with repeated observations from the same patients, correlated random effects were included in the empirical model to control for patients' time-invariant, unobserved heterogeneity, for example, their socioeconomic status.

[5] The statistics are obtained from `https://dep.mohw.gov.tw/DOS/np-1918-113.html` and `https://dep.mohw.gov.tw/DOS/np-1865-113.html` (in Chinese). I used the reported number of total visits and reimbursement points of URTIs from 1999 to 2011 and divided by the number of clinics of Otorhinolaryngology, pediatrics and general practice per year.

[6] `https://statdb.mol.gov.tw/html/svy08/0835all.pdf` (in Chinese)

At last, patients' returning chance to the same doctor is examined using a probit model. The likelihood is considered as a function of antibiotic prescriptions and physician agency, along with the other determinants.

Consider a physician j choosing between prescribing inappropriate antibiotics ($A = 1$) or not ($A = 0$) for patient i in t visit. Define $U_{jt} = U_{jt}(u_{it}, \pi_{jt})$ as this physician j's utility gain from prescribing antibiotics to patient i, which is a function of patient i's utility u_{it} and provider j's financial incentives, π_{jt}. Assume the utility function is linear as follows:

$$U_{jt}(A_{it} = z) = \gamma_1 u_{it}(A = z) + \gamma_2 \pi_{jt}(A = z), \tag{3}$$

where z={0,1}. I normalized $U_{jt}(A_{it} = 0) = 0$ as not prescribing antibiotics generated no profits for physicians and likely no utility for the patient, too. γ_1 and γ_2 represent the weights given by the provider to the patient's utility and his financial incentives, respectively. The coefficients indicate the level of physician agency; $\gamma_1 < \gamma_2$ indicates physician j may prescribe antibiotics to receive π_{jt} even it hurts u_{it}.

The patient's utility gain from inappropriate antibiotics should be nonpositive because they were ineffective against the viral URTIs and likely created antimicrobial resistance. Patients would also have to pay for these antibiotics, but the drug expense is low under the NHI coverage so I ignored the monetary burden to the patients. Nevertheless, antibiotics could bring positive utility to the patients if they would like to receive medications even when they are ineffective. That is the demand side explanation for inappropriate antibiotic prescriptions. As this is an empirical question, a patient's utility is modeled as follows:

$$u_{it} = \beta_i X_{it} + c_i \tag{4}$$

X_{it} includes the observed patient characteristics such as age and sex. As patients' preferences concerning antibiotics are not revealed in the data, I used c_i in the model to represent this preference and considered it to be time invariant.

The provider's financial incentive π_{jt} represents the benefits provider j receives from prescribing antibiotics in the t visit, and is empirically modeled as follows:

$$\pi_{jt} = \beta_O O_{jt} + \beta_D D_{jt} + \beta_H HHI_{jt} + \beta_j X_{jt}. \tag{5}$$

Physician owner (O_{jt}) and dispenser (D_{jt}) indicate providers with higher financial incentives than the others. The competitiveness of a market, HHI_{jt}, affects the size of π_{jt} because physicians might want to prescribe more antibiotics in more competitive markets if that is what patients would prefer. However, in less competitive markets physicians would also be likely to prescribe more antibiotics because patients have few alternatives regardless of their preferences. So the sign of β_H would reveal providers' likelihood of inappropriate antibiotic use and market competition.

X_{jt} in Eq. (5) includes the other providers' characteristics such as their experience and age. The characteristics of the hospitals or clinics where provider j practices, including public ownership, operation years, and accreditation level, are also included in X_{jt}. Market characteristics are also included such as population density measured in per square kilometers, number of households, sex ratio, numbers of births and deaths each year and average annual household income. As a result, a provider's utility from prescribing antibiotics in Eq. (3) becomes

$$U_{jt}(A_{it}=1) = \gamma_1(\beta_i X_{it} + c_i) + \gamma_2 \pi_{jt}(\beta_O O_{jt} + \beta_D D_{jt} + \beta_H HHI_{jt} + \beta_j X_{jt}). \tag{6}$$

Notice $U_{jt}(A_{it}=0)$ is normalized to zero; thus, Eq. (6) is also the difference between $U_{jt}(A_{it}=1)$ and $U_{jt}(A_{it}=0)$.

To empirically examine the proposed model, randomness is introduced into the deterministic provider's prescription decision function, Eq. (6). Specifically, patients and providers are allowed to be heterogeneous in their utilities by introducing ε_{it} and ε_{jt}, respectively. These can be considered as the providers' and patients' unobserved characteristics that would affect providers' prescribing decisions. Because the data reveal whether antibiotics were prescribed in a visit but not the latent utility, the empirical model is further extended to be

$$\begin{aligned}
&Prob[A_{ijt}=1 \mid O_{jt}, D_{jt}, HHI_{jt}, X_{it}, X_{jt}] \\
&= Prob[U_{jt} > 0 \mid O_{jt}, D_{jt}, HHI_{jt}, X_{it}, X_{jt}] \\
&= Prob[\gamma_1(\beta_i X_{it}) + \gamma_2(\beta_O O_{jt} + \beta_D D_{jt} + \beta_H HHI_{jt} + \beta_j X_{jt}) + \gamma_1(c_i + \varepsilon_{it}) + \gamma_2 \varepsilon_{jt} > 0],
\end{aligned} \tag{7}$$

where $A_{ijt} = 1$ indicates that physician j prescribes antibiotics for patient i in the t visit. A physician would prescribe antibiotics when the physician gained more utility from prescribing antibiotics than from not prescribing them. Physicians' weights on utility and profit, γ_1 and γ_2, are left unidentified in the model but do not affect the interpretation of the signs of the estimates.

If $c_i + \varepsilon_{it}$ and ε_{jt} are independent with a normal distribution, then simple probit can be applied to estimate Eq. (7). However, this method involves the assumption that no correlation exists among patients of a given physician, which might bias this probit estimate if correlation exists (Hellerstein, 1998). For example, patients' preferences toward antibiotics would likely affect a provider's prescription decision if the provider tends to retain patients by prescribing antibiotics. To control for this potential correlation, I applied Chamberlain's correlated random effects probit model, which was introduced in Wooldridge (2010). A patient's unobserved, time-invariant characteristic c_i is specifically modeled as function of the time averages of the observed, time-variant variables in X_{it}, X_{jt} O_j, D_j and HHI_j. Since the sample consists of patients' medical histories, patients' visits were used as the unit of time to calculate the CRE as follows:

$$c_i \mid O_j, D_j, HHI_j, X_i, X_j \sim Normal(\psi_1 + \psi_o \overline{O_j} + \psi_D \overline{D_j} + \psi_H \overline{HHI_j} + \psi_2 \overline{X_i} + \psi_3 \overline{X_j} + \beta_L L_{ij}, \sigma_a^2), \quad (8)$$

where the upper bar of a variable indicates the time average of that variable. L_{ij} contains indicator variables that control for the fixed effects of a physician's diagnosis of a patient and the market of a hospital or clinic. σ_a^2 is the conditional variance from the mean variables in Eq. (8). The time averages control for the possible correlations between patients' preferences and the physician's unobserved characteristics. This enables the traditional random effect estimates to be consistent. This also has a lower computational burden compared to applying a fixed-effect probit or logit method that uses patient-specific fixed effects to proxy for c_i in the large sample analyzed in this paper. The coefficients of the mean variables in Eq. (8) also allow for the interpretation on the potential relationship between a patient's preference to inappropriate antibiotics and the patient's and doctor's characteristics.

As physicians' antibiotic prescriptions are likely affected by the price and markup of the prescription drugs, I examined physicians' choices on the intensive margin after investigating their choices on the extensive margin using Eq. (7). Consider the quantity of antibiotic k prescribed by physician j for patient i at t visit as Q_{ijkt}, which is a linear function of physicians' and patients' characteristics as follows:

$$Q_{ijkt} = \phi_P P_{kt} + \phi_M M_{kt} + \phi_i X_{it} + \phi_O O_{jt} + \phi_D D_{jt} + \phi_H HHI_{jt} + \phi_j X_{jt} + \varepsilon_{ijkt}. \quad (9)$$

P_{kt} and M_{kt} are the price and markup percentage of antibiotic k, respectively. The other control variables are the same as in Eq. (7). Because $Q_{ijkt} > 0$ only when $A_{ijt} = 1$, I estimated Heckman's sample selection model using full maximum likelihood estimation. Essentially, Eq. (7) is the select model while Eq. (9) is estimated jointly with the additional term of the inverse Mills ratio. CRE can also be included in both Eqs. (7) and (9) to control for the unobserved, time-invariant fixed effects.

Patients' returning chances to the same doctor in the next visit, next five visits and next ten visits are also examined. A probit model is applied similar to Eq. (7), where A_{ijt} is used as the key independent variable on the patients' returning likelihood. The model can be considered as a patient's decision to return, where she considers her utility as a function of her characteristics and the physician's characteristics.

5. Empirical Results

5.1. Probability of Inappropriate Antibiotic Prescriptions

Table 4 reports the empirical results on the determinants of inappropriate antibiotic prescriptions. Some observations were dropped after controlling for market fixed effects because three markets had no variations in the dependent variable. The first column of Table 4 reports the results when excluding market fixed effects. The estimate shows that competition increased antibiotics prescriptions, which is similar to Bennett et al. (2015). But after controlling for market fixed effects, the second column reveals that competition decreased physicians' probability of prescribing antibiotics. Since the market fixed effects control for unobserved, time-invariant heterogeneity within the same market, such as the residents' preference for antibiotics, the coefficient estimate of HHI reported in column 1 might be the effect from market preference; for example, residents in the markets that are more competitive also prefer to receive antibiotics. After this effect was controlled for, the estimate in column 2 reveals that physicians prescribed more antibiotics when facing less competition.

Column 3 of Table 4 further reports the results when including physician characteristics. The sign of the estimate of HHI remained similar to that of column 2. Physician owners are found to be more likely than other physicians to prescribe antibiotics; the marginal effect estimate is nearly 1%. Physician dispensers are also more likely than other physicians to prescribe inappropriate antibiotics. These results indicate inappropriate antibiotic prescriptions were more likely to be given by the physicians with strong financial incentives. In addition, column 3 also shows that the restriction policy implemented in February 2001 reduced inappropriate antibiotic prescriptions.

Column 4 of Table 4 reports the results considering the interactive effects between physician owner and HHI. The results indicate that the owners are more likely to prescribe antibiotics and the effect increases with less competition. The result is intuitive because, even if the patients do not prefer antibiotics, physicians are still likely to prescribe them as the patients have fewer alternatives in their local markets. The estimate of HHI became negative after controlling for its interaction with physician ownership, meaning patients would be less likely to receive antibiotics from employed physicians as market competition increases. These results show that inappropriate antibiotic prescriptions are more likely to be given when physicians' financial incentives are strong and the market competition is not fierce.

Table 4 also reports the other important determinants of inappropriate antibiotics prescriptions. Physicians with more experience are less likely to prescribe unnecessary antibiotics. But after controlling for experience, older physicians are more likely to prescribe antibiotics. Public owned facilities are more likely to prescribe antibiotics. Hospitals are less likely than clinics to prescribe inappropriate antibiotics, and the probability decreased with their accreditation level. Patients who are prone to URTIs are less likely to be given antibiotics. Male and older patients are more likely to receive antibiotics.

Table 4 reveals that the market characteristics are statistically significant factors in determining the chance to be given antibiotic prescriptions. In markets that are richer and less populated with fewer households and have a higher ratio of women, patients' likelihood to receive antibiotics tends to increase. The numbers of births and deaths are also positively related to the chance of being given antibiotics, but the statistical significance varies across specifications. Because market fixed effects are controlled for in most regressions, these estimates reflect how the time-varying characteristics affect the probability of receiving antibiotics.

Table 5 reports the results when controlling for correlated random effects. The specifications of columns 1 to 3 are similar to columns 2 to 4 of Table 4 except for the addition of CREs. As discussed in the empirical model section, the coefficient estimates of the CREs can be interpreted as the correlations between these fixed effects and a patient's unobserved heterogeneity for antibiotics prescriptions. For example, the negative owner-CRE estimates reveal that physician owners reduced patients' utility from receiving antibiotics. The positive estimate of owners thus indicates that, controlling for patients' preferences, owners are still more likely to prescribe antibiotics. Whether the physician would make an antibiotic prescription thus depended on the difference between γ_1 and γ_2 in Eq. (3). But the estimates show that physicians faced the tradeoff between their profit and the patients' utility when prescribing inappropriate antibiotics.

The other statistical significant CREs show that patients are more willing to receive antibiotics from older doctors. The patient age-CRE estimate shows that older patients did not prefer to receive antibiotics. Patients in the areas that have greater populations, higher men-women ratios, fewer households and more deaths are more likely than other patients to have a negative preference against antibiotic prescriptions.

5.2. Quantity of Inappropriate Antibiotic Prescriptions

Table 6 reports the results using the sample selection model on the quantity of antibiotics prescribed. The model was estimated by using full MLE, and the first stage results were not reported because they are essentially similar to the results reported in Tables 4 and 5. The results show that the prescription quantity decreases with the price of antibiotics but increases with the markup acquired by the providers. This indicates that physicians responded to the markup acquired from prescribed antibiotics, even when the reimbursement price was not high. This result is not affected by controlling for CREs in the first and second stage as shown in the second and third columns of Table 6. The CREs in the second stage control for physicians' unobserved, time-invariant heterogeneity when treating a given patient. Thus, the negative and positive estimates of the price-CRE and markup-CRE indicate providers' preferences to less expensive antibiotics with high markup percentages.

The other coefficient estimates are similar across three specifications reported in Table 6. Physicians reduced the quantity prescribed after February 2001. Physicians who both prescribed and dispensed drugs gave higher quantities of antibiotics than the other physicians. Physician owners also prescribed more antibiotics than the other physicians, but they would prescribe fewer for frequent patients as shown by the negative estimate of owner-CRE. This estimate is consistent with the owner-CRE estimates reported in Table 5 and are also consistent with the results reported later for patient retention. Table 6 also reveals that inexperienced and older physicians are more likely to prescribe more antibiotics.

Regarding hospital characteristics, I did not find statistically significant effects from HHI on prescription quantity. Public and more established providers prescribed higher quantities of antibiotics than other providers, while the quantity decreases as the accreditation level increases. Patients that are more prone to URTIs or men received higher quantities of antibiotics. Older patients also received higher quantities of antibiotics, but the effect decreases as providers preferred to give fewer antibiotics to older patients that visited the same doctor frequently. Markets that have higher household incomes, lower population densities, more women, fewer households, and more births and deaths also received higher quantities of antibiotics in general. The CRE estimates are mostly the same with the level estimates despite the number of households.

5.3. Patient Retention and Inappropriate Antibiotic Prescriptions

Tables 4 to 6 reveal that physician agency is one of the main reasons behind inappropriate antibiotic prescriptions. Physicians with strong financial incentives are more likely than others to prescribe antibiotics. But the CRE estimates indicate physicians may face the tradeoff between their profits and patients' negative utility. This subsection presents another empirical evidence showing that patients did not prefer to receive antibiotics; patients would be less likely to visit doctors who prescribed inappropriate antibiotics in the previous visit. The results reveal the tradeoff for the doctors is to earn the profit from prescribing antibiotics this time at the expense of the patient possibly not visiting next time.

Table 7 reveals that prescribing inappropriate antibiotics would reduce a patient's returning chance to the same doctor. The results are robust across specifications. In particular, column (1) reports the result when excluding physician characteristics. Columns (2) and (3) report the results with physician characteristics, and column (3) also includes the interaction terms between antibiotics and owner. Column (4) reports the results when controlling for CREs. These results point out that patients were more likely to return to the physicians with strong financial incentives, including physician owners and physicians who both prescribed and dispense drugs. While reasons behind this increased returning chance were not observed, the reason is probably not antibiotics. The coefficient estimates of the interaction term show that patients' returning chances to physician owners were reduced if antibiotics were prescribed. Accordingly, while physician agency would increase the probability to prescribe antibiotics as shown in Tables 4 and 5, doctors face the tradeoff between acquiring profit from prescribing inappropriate antibiotics and being more likely to have future visits from the same patients.

Table 7 provides another evidence supporting the physician's tradeoff. In a less competitive market, patients would have to return to the same doctor regardless of their preference toward antibiotics because there were not many other options in the market. Table 7 indicates this possibility as patients' returning chance is higher when the market is less competitive. Table 7 also shows that patients were more likely to revisit older and less experienced physicians and physicians in private hospitals and clinics. Patients were less likely to revisit hospitals than clinics probably because patients visited hospitals when they were really sick. It is also likely because clinics are closer to the patients. Besides, patients that are older, prone to URTIs, or male were also more likely to revisit the same doctor. Table 7 also reveals that patients in markets that were less wealthy or more populated were more likely to visit the same doctors. When considering the dependent variable to be revisits to the same doctor in the next five visits or the next ten visits, the signs of the estimates are similar to the ones reported in Table 7. Thus, Table 8 reports the abridged results. It shows patients' likelihood to return to the same doctor did not increase with time.

6. Conclusions

Antimicrobial resistance is an prominence threat to global health. This research focuses on one likely reason behind its widespread, the physician agency problem. While physician agency has been extensively studied, few researches investigate its effect on physicians writing appropriate prescriptions. In this paper, I focused on inappropriate antibiotic prescriptions in Taiwan. I found physician agency is an important factor behind the inappropriate use of antibiotics in Taiwan. Patients are less likely to return to the same doctor if inappropriate antibiotics were prescribed the previous time, so the physician faced a tradeoff when prescribing inappropriate antibiotics: to earn a high profit margin and face the risk of losing patients in the future.

I used data with more than 10 million patient visits for 15 types of viral upper respiratory tract infections for which prescribing antibiotics would be inappropriate, and antibiotics were prescribed about 12% of the visits. Empirical results show that inappropriate antibiotic prescriptions were more likely to be given by physician owners and dispensers. Inappropriate antibiotic prescriptions were also more likely to be given from the medical providers who faced less competition, thus indicating providers with more monopoly power would be less worried about losing patients. The argument is further supported by the results showing that inappropriate antibiotics reduced patients' revisits to the same doctor.

Policy implications from the results of this paper are straightforward: First, the administration could exclude or reduce the payments for inappropriate antibiotic prescriptions. The NHIA already planned to do so for acute rhinosinusitis in 2021. Second, the administration could lower the price and markup of the antibiotics that are frequently prescribed inappropriately. Third, more audits on physician owners and dispensers and the medical providers facing less competition locally should effectively discourage inappropriate antibiotic prescriptions. At last, policy campaigns and education on the appropriate use of antibiotics are useful to reduce the overprescription of antibiotics.

This paper did not investigate whether raising the copayment on drug expenses or removing the insurance coverage for some frequently prescribed antibiotics would reduce the inappropriate use of antibiotics. But patients would have to be more thoughtful when given costly antibiotics. This paper confines the scope within inappropriate antibiotic use for URTIs. But antibiotic prescriptions for other conditions could also be inappropriate. In this paper, a prescription was deemed either appropriate or inappropriate, but there could be a range of appropriateness rated for each antibiotic prescription for various diagnoses. This paper also did not examine the effect of physician agency on antimicrobial resistance due to inappropriate antibiotic prescriptions. Further research is required to find the socially desired level of antibiotics with proper regulations on physician agency.

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Tables and Figures

Table 1 Total Observations by Diagnosis

ICD9/A code	First Diagnosis	Second Diagnosis	Third Diagnosis
460	1,656,207	97,336	10,539
462	694,060	70,161	6,659
464.0	296,052	24,791	5,607
464.10	244,844	37,034	2,004
464.20	90,706	10,141	895
465.0	548,113	40,598	3,056
465.8	313,427	10,733	1,592
465.9	5,292,821	102,961	7,557
466	19,616	3,043	143
466.0	1,081,142	155,461	10,958
466.1	94,102	12,938	1,900
487.1	349,310	9,973	711
A311	134,361	2,001	62
A320	92,201	2,203	35
A322	87,429	874	144
Total Observations	10,994,391	580,248	51,862

Table 2 Summary Statistics

Variables	Mean	SD	Observations
Drug			
Antibiotics	0.117	0.321	10,994,391
Restriction policy	0.846	0.361	
Physician			
Owner	0.789	0.408	
Dispenser	0.750	0.433	
Experience	13.843	15.225	
Age	49.154	13.178	
Hospital			
HHI	4.033	4.747	
Public	0.015	0.120	
Age	8.989	7.261	
Academic medical center	0.006	0.078	
Metropolitan hospitals	0.013	0.112	
Regional hospitals	0.024	0.155	
Clinics	0.957	0.204	
Patient			
Number of appearances	35.124	22.341	
Age	27.724	21.964	
Sex	0.461	0.499	
Market			
Household income (millions)	0.788	0.189	
Density (thousands)	7.988	8.868	
Sex ratio (m/f)	102.217	5.655	
Number of households (thousands)	56.465	43.332	
Number of births (thousands)	1.618	1.197	
Number of deaths (thousands)	0.851	0.536	
Retention			
Revisit in the next visit	0.498	0.500	10,431,547
Revisit in the next five visits	0.752	0.432	9,482,885
Revisit in the next ten visits	0.841	0.366	8,849,737

Table 3 Summary Statistics of Antibiotic Prescriptions

Variables	Mean	SD	Observations
Drug			
Total price	6.773	16.362	1,284,040
Total markup	1.975	5.110	
Total quantity prescribed	8.350	33.115	
Markup percentage	0.281	0.152	
Restriction policy	0.557	0.497	
Physician			
Owner	0.820	0.384	
Dispenser	0.886	0.318	
Experience	9.657	5.323	
Age	47.415	10.069	
Hospital			
HHI	4.498	5.423	
Public	0.012	0.110	
Age	8.905	7.477	
Academic medical center	0.004	0.060	
Metropolitan hospital	0.009	0.095	
Regional hospital	0.027	0.161	
Clinic	0.961	0.194	
Patient			
Number of appearances	32.931	21.461	
Age	26.765	20.473	
Sex	0.464	0.499	
Market			
Household income (millions)	0.789	0.192	
Density (thousands)	8.678	9.336	
Sex ratio (m/f)	102.769	5.503	
Number of households (thousands)	55.948	41.453	
Number of Births (thousands)	1.861	1.324	
Number of Deaths (thousands)	0.836	0.504	
Retention			
Revisit in the next visit	0.490	0.500	1,252,408
Revisit in the next five visits	0.719	0.450	1,178,771
Revisit in the next ten visits	0.802	0.399	1,108,773

Table 4: Probit Model (Dependent Variable: Antibiotics=1)

Dependent Variable	*(1)*	*(2)*	*(3)*	*(4)*
Physician				
Owner			0.047***	0.037***
			(0.002)	(0.003)
Owner*HHI				0.002***
				(0.000)
Dispenser			0.282***	0.282***
			(0.003)	(0.003)
Experience			-0.017***	-0.017***
			(0.000)	(0.000)
Age			0.008***	0.008***
			(0.000)	(0.000)
Restriction policy			-0.268***	-0.268***
			(0.004)	(0.004)
Hospital				
HHI	-0.002***	0.000*	0.001***	-0.001***
	(0.000)	(0.000)	(0.000)	(0.000)
Public	0.076***	0.081***	0.088***	0.087***
	(0.008)	(0.008)	(0.008)	(0.008)
Age	0.011***	0.011***	0.011***	0.011***
	(0.000)	(0.0010)	(0.000)	(0.000)
Academic medical center	-0.571***	-0.611***	-0.608***	-0.604***
	(0.010)	(0.011)	(0.011)	(0.011)
Metropolitan hospital	-0.452***	-0.432***	-0.445***	-0.446***
	(0.008)	(0.008)	(0.008)	(0.008)
Regional hospital	-0.234***	-0.241***	-0.266***	-0.265***
	(0.005)	(0.005)	(0.005)	(0.005)

(*Continued*)

Table 4: Probit Model (Dependent Variable: Antibiotics=1)

Dependent Variable	*(1)*	*(2)*	*(3)*	*(4)*
Patient				
Number of Appearances	-0.002***	-0.002***	-0.002***	-0.002***
	(0.000)	(0.000)	(0.000)	(0.000)
Age	0.000***	0.000***	0.000***	0.000***
	(0.000)	(0.000)	(0.000)	(0.000)
Sex	0.012***	0.013***	0.008***	0.008***
	(0.002)	(0.002)	(0.002)	(0.002)
Market				
Household income (millions)	0.137***	0.195***	0.192***	0.194***
	(0.008)	(0.028)	(0.028)	(0.028)
Density (thousands)	0.004***	-0.012***	-0.011***	-0.011***
	(0.000)	(0.001)	(0.002)	(0.002)
Sex ratio (m/f)	0.004***	-0.003**	-0.003**	-0.003**
	(0.000)	(0.001)	(0.001)	(0.001)
Number of households (thousands)	-0.001***	-0.004***	-0.003***	-0.003***
	(0.000)	(0.000)	(0.000)	(0.000)
Number of births (thousands)	0.000	0.069***	0.066***	0.066***
	(0.003)	(0.005)	(0.005)	(0.005)
Number of deaths (thousands)	0.063***	0.118***	0.026	0.025
	(0.008)	(0.021)	(0.021)	(0.021)
Fixed Effects				
Year, Quarter, Diagnosis	YES	YES	YES	YES
Market	NO	YES	YES	YES
Total Observations	10,994,391	10,994,333[a]	10,994,333[a]	10,994,333[a]

Note: a. Some observations were dropped because three markets had no variations in the dependent variable. Standard errors in parentheses, * p<0.1, ** p<0.05, *** $p < 0.01$

Table 5: Panel Probit Model
(Dependent Variable: Antibiotics=1)

Dependent Variable	*(1)*	*(2)*	*(3)*
Physician			
Owner		0.053***	0.044***
		(0.002)	(0.003)
Owner (CRE)		-0.032***	-0.031***
		(0.006)	(0.006)
Owner*HHI			0.002***
			(0.000)
Dispenser		0.283***	0.283***
		(0.003)	(0.003)
Dispenser (CRE)		-0.001	-0.002
		(0.005)	(0.005)
Experience		-0.017***	-0.017***
		(0.000)	(0.000)
Experience (CRE)		0.000	0.000
		(0.000)	(0.000)
Age		0.008***	0.008***
		(0.000)	(0.000)
Age (CRE)		0.001***	0.001***
		(0.000)	(0.000)
Restriction policy		-0.269***	-0.269***
		(0.004)	(0.004)

(*Continued*)

Table 5: Panel Probit Model (Dependent Variable: Antibiotics=1)

Dependent Variable	*(1)*	*(2)*	*(3)*
Hospital			
HHI	0.000*	0.001***	-0.001***
	(0.000)	(0.000)	(0.000)
HHI (CRE)	-0.000	0.000	0.000
	(0.001)	(0.001)	(0.001)
Public	0.081***	0.087***	0.086***
	(0.008)	(0.008)	(0.008)
Age	0.011***	0.011***	0.011***
	(0.000)	(0.000)	(0.000)
Age (CRE)	0.001***	0.000	0.000
	(0.000)	(0.000)	(0.000)
Academic medical center	-0.609***	-0.606***	-0.602***
	(0.011)	(0.011)	(0.011)
Metropolitan hospital	-0.430***	-0.445***	-0.446***
	(0.008)	(0.008)	(0.008)
Regional hospital	-0.239***	-0.266***	-0.265***
	(0.005)	(0.005)	(0.005)
Patient			
Number of Appearances	-0.002***	-0.002***	-0.002***
	(0.000)	(0.000)	(0.000)
Age	0.006***	0.006***	0.006***
	(0.001)	(0.001)	(0.001)
Age (CRE)	-0.005***	-0.006***	-0.006***
	(0.001)	(0.001)	(0.001)
Sex	0.013***	0.008***	0.008***
	(0.002)	(0.002)	(0.002)

(*Continued*)

Table 5: Panel Probit Model (Dependent Variable: Antibiotics=1)

Dependent Variable	*(1)*	*(2)*	*(3)*
Market			
Household income (millions)	0.192***	0.188***	0.190***
	(0.028)	(0.028)	(0.028)
Household income (CRE)	0.015	0.021	0.020
	(0.016)	(0.016)	(0.016)
Density (thousands)	-0.012***	-0.011***	-0.011***
	(0.001)	(0.002)	(0.002)
Density (CRE)	-0.001***	-0.001***	-0.001***
	(0.000)	(0.000)	(0.000)
Sex ratio (m/f)	-0.003**	-0.003**	-0.003**
	(0.001)	(0.001)	(0.001)
Sex ratio (CRE)	0.000	0.000	-0.000
	(0.001)	(0.001)	(0.001)
Number of households (thousands)	-0.004***	-0.003***	-0.003***
	(0.000)	(0.000)	(0.000)
Number of households (CRE)	0.001**	0.001***	0.001***
	(0.000)	(0.000)	(0.000)
Number of births (thousands)	0.068***	0.065***	0.065***
	(0.005)	(0.005)	(0.005)
Number of births (CRE)	0.006	0.005	0.005
	(0.006)	(0.006)	(0.006)
Number of deaths (thousands)	0.126***	0.037*	0.036*
	(0.021)	(0.021)	(0.021)
Number of deaths (CRE)	-0.057***	-0.085***	-0.085***
	(0.016)	(0.016)	(0.016)
Test of CRE(χ^2)	146.31***	261.27***	259.21***
Fixed Effects			
Year, Quarter, Diagnosis, Market	YES	YES	YES
Total Observations	10,994,333		

Standard errors in parentheses, * p<0.1, ** p<0.05, *** $p < 0.01$

Table 6: Sample Selection Model (Dependent Variable: Total Quantity of Antibiotics Prescribed)

Dependent Variable	*No CRE*	*CRE in First Stage*	*CRE in Both Stages*
Drug			
Total price	-0.073***	-0.073***	-0.065***
	(0.001)	(0.001)	(0.001)
Total price (CRE)			-0.013***
			(0.001)
Markup percentage	0.563***	0.557***	0.267***
	(0.056)	(0.056)	(0.056)
Markup percentage (CRE)			0.644***
			(0.078)
Restriction policy	-7.964***	-7.960***	-7.964***
	(0.684)	(0.683)	(0.685)
Physician			
Owner	1.534***	1.539***	1.682***
	(0.161)	(0.161)	(0.173)
Owner (CRE)			-0.723***
			(0.246)
Dispenser	8.799***	8.798***	8.893***
	(0.776)	(0.776)	(0.810)
Dispenser (CRE)			-0.295
			(0.275))
Experience	-0.543***	-0.543***	-0.547***
	(0.047)	(0.047)	(0.047)
Experience (CRE)			0.011
			(0.007)
Age	0.235***	0.235***	0.221***
	(0.020)	(0.020)	(0.020)
Age (CRE)			0.041***
			(0.009)

(*Continued*)

Table 6: Sample Selection Model (Dependent Variable: Total Quantity of Antibiotics Prescribed)

Dependent Variable	*No CRE*	*CRE in First Stage*	*CRE in Both Stages*
Hospital			
HHI	-0.001	-0.001	-0.002
	(0.007)	(0.007)	(0.007)
HHI (CRE)			0.005
			(0.018)
Public	3.751***	3.742***	3.720***
	(0.369)	(0.369)	(0.369)
Age	0.370***	0.370***	0.360***
	(0.034)	(0.034)	(0.033)
Age (CRE)			0.020
			(0.014)
Academic medical center	-16.145***	-16.095***	-16.024***
	(1.555)	(1.555)	(1.550)
Metropolitan hospitals	-11.707***	-11.696***	-11.680***
	(1.131)	(1.131)	(1.127)
Regional hospitals	-6.919***	-6.917***	-6.876***
	(0.685)	(0.685)	(0.682)
Patient			
Number of Appearances	-0.083***	-0.083***	-0.080***
	(0.006)	(0.006)	(0.006)
Age	0.052***	0.052***	0.350***
	(0.002)	(0.002)	(0.038)
Age(CRE)			-0.301***
			(0.039)
Sex	0.234***	0.235***	0.216***
	(0.084)	(0.084)	(0.083)

(*Continued*)

Table 6: Sample Selection Model (Dependent Variable: Total Quantity of Antibiotics Prescribed)

Dependent Variable	*No CRE*	*CRE in First Stage*	*CRE in Both Stages*
Market			
Household income (millions)	7.615***	7.665***	7.203***
	(1.257)	(1.261)	(1.245)
Household income (CRE)			1.733**
			(0.796)
Density (thousands)	-0.585***	-0.584***	-0.583***
	(0.081)	(0.081)	(0.080)
Density (CRE)			-0.067***
			(0.024)
Sex ratio (m/f)	-0.142***	-0.141***	-0.145***
	(0.045)	(0.045)	(0.045)
Sex ratio (CRE)			0.022
			(0.022)
Number of households (thousands)	-0.200***	-0.199***	-0.197***
	(0.029)	(0.029)	(0.029)
Number of households (CRE)			0.021*
			(0.012)
Number of births (thousands)	1.541***	1.542***	1.430***
	(0.215)	(0.215)	(0.216)
Number of births (CRE)			0.563**
			(0.223)
Number of deaths (thousands)	9.502***	9.473***	9.780***
	(1.641)	(1.640)	(1.667)
Number of death (CRE)			-2.519***
			(0.602)
Test of CRE(χ^2)		100.28***	3631.47***
Inverse Mills Ratio	36.723	36.721	36.393
	(3.187)	(3.187)	(3.181)
Fixed Effects			
Year, Quarter, Diagnosis, Market	YES	YES	YES
Total Observations	10,994,391		

Standard errors in parentheses, * p<0.1, ** p<0.05, *** $p < 0.01$

Table 7: Probit Model (Dependent Variable: Patient's Revisit to the Previous Doctor in Her Next Visit=1)

Dependent Variable	*(1)*	*(2)*	*(3)*	*(4)*
Drug				
Antibiotics	-0.024***	-0.038***	-0.015***	-0.016***
	(0.002)	(0.002)	(0.004)	(0.004)
Restriction policy		-0.001	-0.001	-0.001
		(0.003)	(0.003)	(0.003)
Physician				
Owner		0.611***	0.614***	0.456***
		(0.002)	(0.002)	(0.002)
Owner (CRE)				0.749***
				(0.006)
Antibiotics*Owner			-0.027***	-0.026***
			(0.004)	(0.004)
Dispenser		0.152***	0.151***	0.122***
		(0.002)	(0.002)	(0.002)
Dispenser (CRE)				0.051***
				(0.004)
Experience		-0.001***	-0.001***	0.000
		(0.000)	(0.000)	(0.000)
Experience (CRE)				-0.003***
				(0.000)
Age		0.001***	0.001***	-0.001***
		(0.000)	(0.000)	(0.000)
Age (CRE)				0.006***
				(0.000)

(*Continued*)

Table 7: Probit Model (Dependent Variable: Patient's Revisit to the Previous Doctor in Her Next Visit=1)

Dependent Variable	*(1)*	*(2)*	*(3)*	*(4)*
Hospital				
HHI	-0.000	0.001***	0.001***	0.001***
	(0.000)	(0.000)	(0.000)	(0.000)
HHI (CRE)				0.000
				(0.000)
Public	-0.256***	-0.204***	-0.204***	-0.192***
	(0.009)	(0.008)	(0.008)	(0.009)
Age	0.008***	0.006***	0.006***	0.002***
	(0.000)	(0.000)	(0.000)	(0.000)
Age (CRE)				0.006***
				(0.000)
Academic medical center	-1.305***	-0.850***	-0.849***	-0.840***
	(0.014)	(0.014)	(0.014)	(0.015)
Metropolitan hospital	-1.125***	-0.665***	-0.665***	-0.643***
	(0.009)	(0.009)	(0.009)	(0.009)
Regional hospital	-0.825***	-0.467***	-0.467***	-0.420***
	(0.005)	(0.005)	(0.005)	(0.006)
Patient				
Number of Appearances	0.007***	0.007***	0.007***	0.007***
	(0.000)	(0.000)	(0.000)	(0.000)
Age	0.004***	0.003***	0.003***	0.002***
	(0.000)	(0.000)	(0.000)	(0.001)
Age (CRE)				-0.000
				(0.001)
Sex	0.062***	0.063***	0.063***	0.065***
	(0.002)	(0.002)	(0.002)	(0.002)

(*Continued*)

Table 7: Probit Model (Dependent Variable: Patient's Revisit to the Previous Doctor in Her Next Visit=1)

Dependent Variable	*(1)*	*(2)*	*(3)*	*(4)*
Market				
Household income (millions)	-0.103***	-0.113***	-0.113***	-0.124***
	(0.021)	(0.020)	(0.020)	(0.020)
Household income (CRE)				0.041***
				(0.012)
Density (thousands)	0.004***	0.003**	0.003***	0.004***
	(0.001)	(0.001)	(0.001)	(0.001)
Density (CRE)				0.000
				(0.000)
Sex ratio (m/f)	-0.006***	-0.006***	-0.006***	-0.004***
	(0.001)	(0.001)	(0.001)	(0.001)
Sex ratio (CRE)				-0.009***
				(0.000)
Number of households (thousands)	-0.002***	-0.000	-0.000	0.001**
	(0.000)	(0.000)	(0.000)	(0.000)
Number of households (CRE)				-0.003***
				(0.000)
Number of births (thousands)	-0.018***	-0.010***	-0.010***	-0.011***
	(0.004)	(0.004)	(0.004)	(0.004)
Number of births (CRE)				0.027***
				(0.005)
Number of deaths (thousands)	0.057***	-0.022	-0.022	-0.050***
	(0.015)	(0.014)	(0.014)	(0.014)
Number of deaths (CRE)				0.205***
				(0.012)
Test of CRE(χ^2)				24014.27***
Fixed Effects				
Year, Quarter, Diagnosis, Market	YES	YES	YES	YES
Total Observations	10,431,547			

Standard errors in parentheses, * p<0.1, ** p<0.05, ***$p < 0.01$

Table 8: Probit Model (Dependent Variable: Patient's Revisit to the Previous Doctor in Her Next Five or Ten Visit=1)

Dependent Variable (Next Five)	*(1)*	*(2)*	*(3)*	*(4)[a]*
Antibiotics	-0.027***	-0.039***	-0.019***	-0.023***
	(0.002)	(0.002)	(0.004)	(0.004)
Owner		0.523***	0.527***	0.471***
		(0.002)	(0.002)	(0.002)
Owner (CRE)				0.260***
				(0.005)
Antibiotics*Owner			-0.025***	-0.020***
			(0.004)	(0.004)
Prescription Dispenser		0.122***	0.122***	0.100***
		(0.002)	(0.002)	(0.002)
Prescription Dispenser (CRE)				0.055***
				(0.004)
HHI	0.002***	0.003***	0.003***	0.002***
	(0.000)	(0.000)	(0.000)	(0.000)
HHI (CRE)				0.007***
				(0.000)
Total Observations	9,482,885			
Dependent Variable (Next Ten)	*(1)*	*(2)*	*(3)*	*(4)[a]*
Antibiotics	-0.025***	-0.036***	-0.023***	-0.029***
	(0.002)	(0.002)	(0.004)	(0.004)
Owner		0.497***	0.499***	0.481***
		(0.002)	(0.002)	(0.002)
Owner (CRE)				0.053***
				(0.006)
Antibiotics*Owner			-0.017***	-0.009***
			(0.004)	(0.004)
Dispenser		0.109***	0.109***	0.077***
		(0.002)	(0.002)	(0.002)
Dispenser (CRE)				0.102***
				(0.005)
HHI	0.003***	0.004***	0.004***	0.003***
	(0.000)	(0.000)	(0.000)	(0.000)
HHI (CRE)				0.013***
				(0.001)
Total Observations	8,849,721[b]			

a. Patient age-CRE was not included because estimation could not reach convergence. b. One market has no variation in dependent variable. Standard errors in parentheses, * $p<0.1$, ** $p<0.05$, *** $p<0.01$

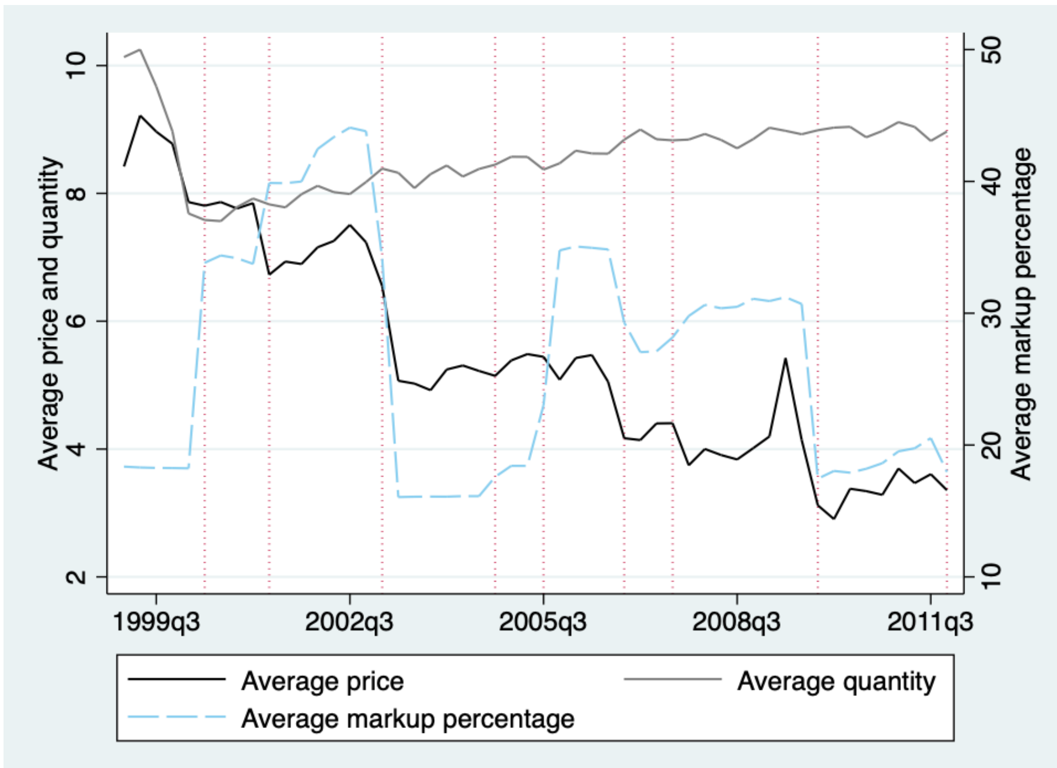

Figure 1: Trends of Average Price, Markup Percentage and Quantity Prescribed of the Antibiotic Prescriptions

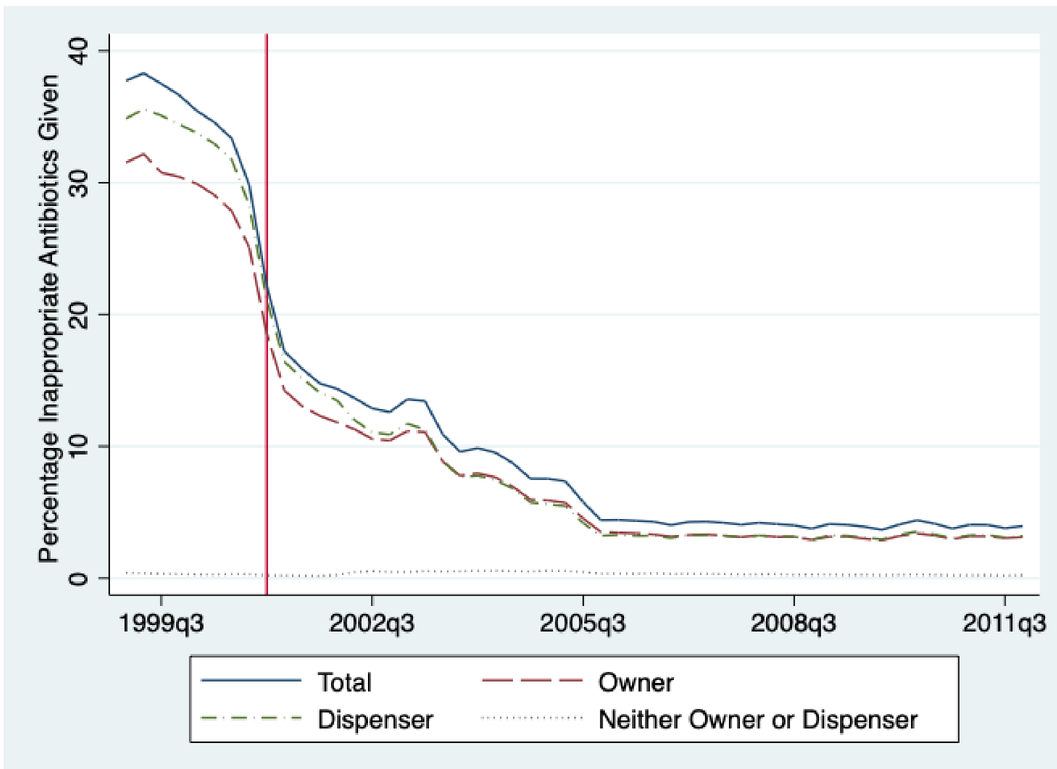

Figure 2: Trend of Inappropriate Use of Antibiotics by Physician Owner and Dispenser