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Economic incentives in outpatient care and patient demand for pharmaceuticals

A study of antibiotics and addictive drugs prescriptions

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A dissertation for the degree of Philosophiae Doctor, August 2021

Abstract

The questions asked in this thesis relate to the economic incentives and characteristics of the health care market, which may result in suboptimal drug prescription. We consider two types of pharmaceuticals, such as antibiotics and addictive drugs. These pharmaceuticals are interesting because their use/misuse is associated with costs both at the individual and societal levels. The decision about the prescription of both antibiotics and addictive drugs is ideally made by a doctor, and over-the-counter sales are not available. A good share of the prescriptions is made in outpatient care or primary care (a part of outpatient care). This market is characterised by asymmetric information and may suffer from economic disincentives, which, together with patient-induced demand, may result in drug misuse. Thus there is a need for solutions aimed to facilitate optimal drug consumption, i.e. reducing consumption to a minimum consumption level, given that patients are effectively treated. This thesis considers several characteristics of the outpatient care market, such as free choice of provider, competition, and financial incentives within a health care centre to be important factors contributing to drug misuse. Knowledge about driving mechanisms is important for understanding how policies for more efficient antibiotic and addictive drugs consumption can be achieved. The first paper in the thesis relates to the ownership type of health care centres. It finds that private health care centres in the Västerbotten county of Sweden have a higher share of prescriptions for antibiotics than public ones. The second paper focuses on the competition between general practitioners and antibiotic prescription in Norwegian municipalities. The paper shows that the level of competition may be an important factor contributing to a more frequent antibiotic prescription. The third paper relates to the presence of free choice of the health care provider and uses the prescription data from Västerbotten county of Sweden to investigate patients' demand for addictive drugs and how a strategy to switch providers may affect individual drug consumption.

Acknowledgements

Taking PhD is an exciting but sometimes very exhausting task, especially while being far away from home. I would like to thank all those people who have been a part of this journey, who helped me to finally feel that Tromsø is my home as well, and those who encouraged me on the way to be an independent researcher. This way was quite challenging and not smooth at all, but I am glad that it happened to me.

First of all, I was one of those lucky PhD students who could propose the topic of the thesis and choose the supervisors myself. I am so happy about making the right choice. Andrea Mannberg and Øystein Myrland, I cannot imagine better supervisors for me than you. I am very grateful for all the support you gave me, both professional and mental. Øystein, thank you for being kind, helpful, sharing your experience, and supporting all my research ideas, even not the best ones. I always felt much more confident about myself after talking to you. Andrea, thank you so much for both giving me freedom and always being there for me when I needed help. Thank you for your guidance, empathy, care, and being a person I could always be open with. It means so much to me, and I won't ever stop being grateful to you.

Next, I would like to thank all my colleagues at the School of Business and Economics at UiT for creating a great working environment. Derek Clark, as the department leader at the time I started my PhD, you made me feel very much welcome at my new place of work. Thank you for that; it encouraged me a lot. Stein Østbye, thank you very much for the possibility to participate in your collaboration project with the Higher School of Economics, Moscow. I met so many wonderful people and made new friends during this unforgettable experience. I am also very grateful to Ingrid Dyrkorn Heimland. Your endless support helped me a lot during a difficult time in my life. I would like to express my gratitude to my fellow PhD students, especially Tatiana and Eirik, for a great time spent together and for many interesting discussions, both scientific and not at all.

My special thanks are to David Granlund from Umeå University, Sweden. This PhD project would not be possible without collaboration with you. Thank you very much for making it happen. Even though I have never met you in person, it was a great pleasure to work with you, and I've learned a lot from this.

I am very grateful to the friends I made in Tromsø. Anna, Sergey, Evgenia, Timofey, Katja, Ilia, Tatiana, Steven, Tannaz, Rano, Daria and Mark, thank you for the great time spent together and for supporting each other in everyday life. I am fortunate to have such friends like you.

My deepest gratitude goes to my parents – Olga and Vladimir, and my sister Sonja for their unconditional and endless love. You made me believe in my abilities and created space where I could always feel safe, supported and loved. This is why I have never feared failing and could easily accept all new challenges in my life. You are not only perfect parents but also grandparents. You helped me enormously with the kids despite living so far away.

Finally, I would like to thank my husband Ilya. You are not only my love but the best friend anyone could ever ask for. You always believed in me, encouraged and supported me. The confidence that I can always count on you has always kept me going. Thank you for understanding me, for your trust and love – they mean a lot to me. I am truly thankful for having you in my life. Of course, I am very grateful to my wonderful daughters Katja and Julia for their love, tenderness, for being my inspiration, teaching me patience and wisdom, making me smile, and showing what is the most important in my life. I am happy to be your mother.

Yana Zykova

Abbreviations

ATC– Anatomical Therapeutic Chemical (ATC) Classification System

AR – Antibiotic Resistance

CAP – Capitation

CDC – The US Center for Disease Control and Prevention

CNS – Central Nervous System

DDD – Defined Daily Dose

DS – Doctor Shopping

FFS – Fee-for-service

GDP – Gross Domestic Product

GP – General Practitioner

HELFO – the Norwegian Health Economics Administration

HHI – Herfindahl-Hirschman index

RTI – Respiratory Tract Infection

PFP – Pay-for-Performance

WHO – World Health Organisation

List of papers

Name of candidate:

Yana Zykova

Papers

The following papers are included in my PhD thesis:

I: Granlund, D., & Zykova, Y. V. (2020). Can Private Provision of Primary Care Contribute to the Spread of Antibiotic Resistance? A Study of Antibiotic Prescription in Sweden. *PharmacoEconomics-Open*, 1-9.

II: Zykova, Y. Competition in primary care and prescription of antibiotics in Norway – advance manuscript.

III: Zykova, Y., Mannberg, A., Myrland, Ø. Effects of 'doctor shopping' behaviour on prescription of addictive drugs in Västerbotten, Sweden. Under revision in *Social Science and Medicine.*

Contributions (co-author statements)

	Paper 1	Paper 2	Paper 3
Idea	YZ, DG, AM	YZ	YZ
Conceptualization	YZ, DG	YZ	YZ, AM, ØM
Methodology	YZ, DG	YZ	YZ, ØM
Formal analysis	YZ, DG	YZ	YZ
Data curation	YZ, DG	YZ	YZ
Writing original draft	YZ, DG	YZ	YZ
Writing – Review and Editing	YZ, DG	YZ	YZ, AM
Visualisation	YZ, DG	YZ	YZ

AM = Andrea Mannberg

DG = David Granlund

YZ = Yana Zykova

ØM = Øystein Myrland

Other declarations

Conflict of interest: none

Parts of the text in sections 2.1, 3, 5 and 6 have been recycled/adapted from previously delivered by the author examination answers in the following subjects SVF-8600 'Philosophy of Science and Ethics' in spring 2016 at UIT, FSK-8002 'Scientific Writing' in autumn 2016 at UIT, FSK-8005 'Funding your research' in autumn 2016 at UIT, and the PhD project proposal.

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1 Introduction

Intake of some pharmaceuticals by an individual can impose costs on both the individual and society. This problem is highly relevant for antibiotics and addictive drugs. Nowadays, policy-makers consider antimicrobial resistance (AR) as one of the major public health problems in the world [1]. AR means that antibiotics become ineffective in treating infectious diseases, while the increasing AR rates are associated with intensive antibiotic consumption, including continuant misuse of these drugs. Misuse of addictive drugs also leads to a decrease in life expectancy and poor quality of life. Both problems are associated with a cost for society and create so-called externalities when individual activity affects other parties not involved in this activity. Therefore, it is important to make sure that such medications are not overused.

Normally, antibiotics and addictive drugs are prescribed by medical practitioners, and such prescriptions are monitored by the authorities responsible for this. Meanwhile, characteristics of the health care market and economic incentives may affect doctor-patient interaction and create room for inappropriate prescriptions.

This thesis investigates how health care market settings (with the focus on primary and outpatient care) may result in higher prescription levels of antibiotics and addictive drugs. The remainder of the thesis is organised as follows. Part 2 presents an overview of the use/misuse of antibiotics and addictive drugs and the associated externalities. Part 3 provides a discussion of how health care market conditions and incentives may affect drug prescription. Part 4 introduces the aims of the thesis. Part 5 discusses the characteristics of the health care market in Norway and Sweden. Parts 6, 7, 8 present methods, results and discussion, respectively. Finally, in Part 9 the research papers included in the thesis are enclosed.

2 Importance of the appropriate drug consumption

2.1 Antibiotics and antibiotic resistance

One of the earliest concerns about the use of antibiotics was announced in 1945 by Alexander Fleming in his Nobel Prize lecture:

> "The time may come when penicillin can be bought by anyone in the shops. Then there is the danger that the ignorant man may easily underdose himself and by exposing his microbes to non-lethal quantities of the drug make them resistant. Here is a hypothetical illustration. Mr. X. has a sore throat. He buys some penicillin and gives himself, not enough to kill the streptococci but enough to educate them to resist penicillin. He then infects his wife. Mrs. X gets pneumonia and is treated with penicillin. As the streptococci are now resistant to penicillin, the treatment fails. Mrs. X dies. Who is primarily responsible for Mrs. X's death?" [2].

Fleming A. Penicillin. Nobel Lecture, December 11, 1945

In the scenario described by Fleming, no one is supposed to be guilty. However, there are scenarios we can observe nowadays, which make the question about guilt highly relevant.

Health care made a significant step forward with the discovery of antibiotics. In 1928, Alexander Fleming observed the death of bacteria caused by the invasion of mould. Further, he made an extract of the mould, well-known as penicillin, which was supposed to treat bacterial infections. In 1941, penicillin was purified and produced in the sufficient for clinical trials amount by a group of scientists, led by Howard W. Florey and Ernst Chain [3]. It has been the start of the new era for humanity when infectious diseases were no longer among the primary cause of mortality. During the early days of antibiotics, people even believed that infectious diseases would be completely defeated in the future. However, the euphoria did not last long. Bacteria know and may learn how to defend themselves against antibiotics. When an antibiotic drug is used as a treatment, bacteria resistant to this drug survive, reproduce, and are even able to share the genes of resistance with other bacteria. These bacteria can further spread from one individual to another or to the environment. Moreover, the use of one antibiotic may increase the number of bacteria resistant to other antibiotics due to so-called cross-resistance. As a consequence, the more antibiotics that are consumed, the more selective pressure is put on bacteria, and the more likely is the growth of antibiotic resistance (AR). Thus, antibiotic drugs are becoming less and less effective in the treatment of infectious diseases due to their intensive consumption, which includes inappropriate prescription and abuse [4].

Relatively many antibiotics have been discovered since the 1930s. However, during the last decades, the number of new agents under development has decreased substantially, and today approaches zero [4, 5]. The rapid decline in antibiotic development can be explained by the presence of a market failure. There are several underlying causes of this failure. One cause is that antibiotic therapy is a quick fix compared to drugs for some other non-infectious chronic diseases (e.g. asthma, diabetes or hypertension) that a patient uses through all their life. Moreover, the life span of the antibiotics will be short in most cases due to the presence of AR, while the production of antibiotics may turn out to be inefficient from the start, which makes these drugs to be not profitable for the pharmaceutical companies in the short term [6]. One more reason for the decline in the discovery of new antibiotics is the regulatory barriers for clinical trials [5]. Moreover, medical practitioners try to avoid the use of newly discovered antibiotic classes as drugs of last resort due to the fear of AR. Thus, despite the high demand and social net benefit of new antibiotics, the private pay-off for developing the drug is quite low and uncertain [4, 5].

The rates of AR continue to grow, and the world is facing a reasonable fear of entering a "postantibiotic era" when common bacterial infections may no longer be effectively treated. For now, AR is one of the major public health problems worldwide, and there is a need for joint international actions in order to counteract its growth [7]. "If we do not act immediately we face a future that may resemble the days before these "miracle" drugs were developed; one in which people die of common infections, and where many medical interventions we take for granted – including surgery, chemotherapy, organ transplantation and care for premature infants – become impossible" [8].

2.1.1 Use and misuse

Although the knowledge about the levels of AR and its causes and consequences is increasing, current research shows [9] that antibiotic drugs tend to be consumed inappropriately. Antibiotics are both used for humans and animals. Despite preventive efforts of the United Nations and the WHO, antibiotics are still used as growth promoters in livestock in many countries: since the 1950s, more than half of the antibiotics produced were consumed by agriculture [6].

In this thesis, we focus on the human use of antibiotics, which may also require improvements. First of all, one of the major challenges associated with the global human use of antibiotics is unequal access to these drugs in different parts of the world, both due to lack of supply and inability to afford them [10]. The majority of deaths from antibiotic-treatable infections happen in low- and middle-income countries. This number is approximately equal to 5.7 million, which is far higher than the estimated annual death of 700 000 caused by AR [11]. While some people suffer from the lack of access to these life-saving drugs, others use them for self-treatment. In some countries, it is still possible to buy antibiotics without a prescription [12-14]. When over-the-counter sales of antibiotics are restricted, there may still be challenges related to inappropriate use. Previous research shows that doctors tend to prescribe antibiotics, even when such treatment is likely inefficient. This is especially common to prescribe antibiotics to treat respiratory tract infections (RTI), while such infections are often caused not by bacteria but by viruses [15, 16]. It may also be common to prescribe antibiotics for self-limiting bacterial infections, while such infections can be treated without antibiotics. [17, 18].

2.1.2 Cost and externalities

AR creates a cost for society. Bush et al. (2011) report that in Europe, "the expenditure associated with these infections in terms of extra hospital costs and productivity losses exceeded €1.5 billion each year. In the United States, antibiotic-resistant infections are responsible for $20 billion per year in excess health care costs, $35 billion per year in societal costs and 8 million additional hospital days per year" [6]. The US Center for Disease Control and Prevention (CDC) estimates that AR bacteria are responsible for more than 2 million infections and 23,000 annual deaths in the US, and 25,000 annual deaths in Europe [19]. The predictions of the total economic costs created by AR are close to the cost associated with the increase of the global average surface temperature with 2°C compared to the preindustrial level [20]. According to the estimations by O'Neil, infections caused by AR bacteria will cause more death than cancer by 2050 and will lead to a 2-3.5 per cent reduction in a global GDP and cost $100 trillion, which is similar to the cost of the financial crisis in 2007-2008 [21].

When the behaviour of one party – negatively or positively – affects another party, and prices in the market do not reflect this cost, there exists a so-called externality. Externalities distort incentives and contribute to the over- or under-consumption/production of goods and services. As a consequence, the equilibrium on free markets characterised by external effects is not efficient.

Demand for and use of antibiotics creates substantial externalities. A positive externality of antibiotic use is that infections, which could spread to the community, are successfully treated in case of appropriate antibiotic therapy. A negative public health externality of antibiotic use by one person – is a decreased possibility of someone else being treated due to AR bacteria occurred after such use. Antibiotic use is associated with market failure not only on the demand side but also on the supply side. On the one hand, the increase in the use of antibiotics makes investments in new antibiotics more profitable. On the other hand, intensive use of antibiotics contributes to AR and makes private agents not willing to produce new drugs.

One way to explain the problem of antibiotic misuse is the following. Antibiotic effectiveness can be seen as a potentially renewable but finite common pool resource [22]. A classic example of a common pool resource – is a common parcel of land shared by cattle herders [23]. Each herder gets private benefits from his cows grazing on that land. They can increase their benefits by having more cows and using more of the common land. This will also create some private cost for the herder and social cost due to decreased soil fertility. Private marginal benefit, in this case, is higher than private marginal cost. According to standard economic theory, if individuals are rational, they do not consider the social cost. Such individuals will use common resource only for their own gain. This will lead to the depletion of the resource due to ill-structured property rights. This problem is known as the "tragedy of the commons" and is described for antibiotics as well [24, 25].

Externalities linked to antibiotic use arise because the private marginal cost of consumption is lower than the social marginal cost since AR bacteria that develop due to use of antibiotics by one individual have little effect on that person but can spread to others members of the society. The difference between private and social marginal costs is exacerbated if health care is publicly funded because this means that the patient does not pay the full cost of treatment. In addition, overuse of antibiotics reduces the positive public health externality associated with efficient antibiotic therapy, during which bacteria that otherwise could be transmitted to other members of the society are killed. In order to stop overusing the common good, policy-makers aim to change a private cost and make it equal to the social one, i.e. to internalise the externality.

Creating incentives for optimal antibiotic use is not only a technical challenge but also an ethical problem that requires balancing the rights of different parties to use antibiotics [26-28], and the common economic solutions may not work in the case of antibiotics. Describing the problem of "tragedy of the commons" for antibiotics, Hollis and Maybarduk [25] suggest classic conservation mechanisms used in this case, such as privatising and taxation. However, several authors argue that these mechanisms cannot be applied to the market of antibiotics. For example, Selgelid [29] claims that not all individuals have equal access to antibiotics as a public good. Moreover, in some countries, a combination of such factors as population density, uncontrolled antimicrobial use (e.g. due to limited access to health care), lack of clean water supply and processing of sewage and industrial waste create an environment for selection and dissemination of AR bacteria. The regulations mentioned above may imply that such countries with high antibiotic consumption have to compensate countries with low consumption, while AR disproportionally affects them. Usually, the production of antibiotics is located in low-income countries, which may cause a higher level of AR there. Moreover, the health care system of low-income countries cannot afford more diagnostic and disease control tools and are less likely to address the problem of AR themselves, while the above-mentioned regulations will limit their access to high-quality antibiotics [26]. In addition, people can travel between different parts of the world and can spread AR bacteria. Selgelid [29] claims that health is a good, which all individuals should have equal access to. Thus, AR is a common and urgent problem that has to be solved by joint efforts [6], and there is a need for more tailored solutions than classical conservational mechanisms.

2.2 Addictive drugs

2.2.1 Use and misuse

Similarly to antibiotics, abuse of addictive drugs causes substantial externalities. Addictive drugs are a heterogeneous group of drugs that may be prescribed for different purposes. Among the most common addictive prescription drugs are opioids, which are used as painkillers (e.g. morphine, oxycodone, codeine, fentanyl); central nervous system (CNS) depressants, which slow down the activity of CNS and are used to treat panic, anxiety, acute stress or sleep disorders (e.g. benzodiazepines, barbiturates); CNS stimulants, which increase brain activity and are mainly used to treat attention deficit hyperactivity disorder (include amphetamines and amphetamine-like stimulants) [30]. The misuse of addictive drugs is considered to be an important and growing problem worldwide [31]. For example, in Norway, more than one per cent of the population consumed amphetamine-type stimulants in 2008 [31]. Addictive drugs are prescribed to treat a variety of medical conditions, which makes it difficult to identify that part of the population that uses these drugs for non-medical purposes. According to research from the US, those who are over 18 and reported non-medical use of prescription drugs are likely to be married females older than 35 with higher income and more educated [32]. Those who have been prescribed addictive drugs to treat a medical condition have a higher risk of non-medical use of these drugs [30]. Moreover, mental disorders, family, genetic vulnerability and childhood abuse may also increase the risk of using prescriptions non-medically [33-35].

Patients may become addicted to prescription drugs because they have poor knowledge about the effects of treatment. For example, adolescents may think that addictive drugs prescribed by physicians are safer than illegal drugs because people use them as medication [36]. About one-third of adolescents believe that prescription drugs are non-addictive [37]. Among adults, poor knowledge and perception of the safety of the prescribed medication may also make them increase the dose without consulting a physician or conduct self-medication by the leftover. This behaviour may lead to the patient becomes addicted to the prescribed drug. Such behaviour is hardly detected by others, e.g. physicians or family. Another form of prescribed drug misuse is that those who get a prescription may share their drugs with others (e.g. trying to help friends or family members suffering from pain) or even sell them [38]. Intake of addictive drugs during a long period leads to tolerance development when a person needs to increase the dose in order to maintain the same effect.

2.2.2 Cost and externalities

Addiction and non-medical use of addictive drugs may have a variety of individual and social consequences. Abuse of these drugs may cause and worsen mental health problems [32], reduce life quality and lead to death (both in the long and short term) [30]. For example, the inappropriate use of prescription opioids in the US has placed a significant burden on the health care system and contributed to one of the most severe public health crisis the country has faced. In 2015, opioid overdose led to about 52 000 deaths in the US, which is comparable with the loss in the Vietnam War during four years [39]. The number of emergency departments visits related to these narcotic painkillers more than doubled from 2004 to 2008 [40]. Direct health care cost estimates are eight times higher for people involved in the abuse of prescription opioids than for those not involved, while the total social cost estimates were $9.5 billion in 2005 [41]. Inappropriate use of addictive prescription drugs is associated with crime, violence, aggressive behaviour [42]. Among adolescents, those who report non-medical use of prescription drugs are more likely to skip school or being involved in other kinds of risky behaviour, e.g. bringing drugs to school, promiscuous sex, alcohol abuse, and drunk driving [32].

Even though doctors mostly believe that they are able to identify the non-medical use of addictive drugs prescribed, more than 90 per cent of physicians failed to detect addiction, according to a study from the US [30, 32]. Moreover, it was difficult for almost half of the physicians to discuss the question of drug abuse with the patients and only about 55 per cent of physicians at least sometimes obtain patient's records from the previous doctor when prescribing the addictive drugs on a long-term basis.

3 Health care market conditions and the effects on drug prescription

Although antibiotics and addictive drugs are available in some countries without a prescription [6], normally, they are prescribed by doctors. Patients' demand for prescribed medications may still be high, and the drugs may be prescribed inappropriately. Indeed, abuse of prescribed addictive medications is a growing problem in both developed and developing countries [31]. For example, in 2013, the death rate from the use of prescribed opioids with suicidal intent in the US was about 0.6 % and 0.8 % in the age groups from 20 to 59 and 60+, respectively [43]. Misuse of prescribed antibiotics may also happen. For example, in a recent study, Pouwels *et al.* (2018) found a substantial antibiotic overprescription in British primary care, such that the difference between the actual prescription rate and the ideal was 31-77 percentage points depending on the condition [44].

Further, we discuss how health care market settings may limit or facilitate prescription drugs abuse. We focus on prescriptions in outpatient care because it is usually the first contact point for patients with the associated diseases. Primary care constitutes a major part of human antibiotic use [45] and deals with a large set of patients with symptoms for which antibiotics can be ineffective but still used. A significant part of the long-term prescriptions of opioids, anxiolytics or sleeping drugs also happens in primary care.

3.1 Asymmetric information and the principal-agent problem

The interaction between providers and patients can be described by a principal-agent relationship [46]. The patient, as a principal, chooses the provider as an agent to make a decision about treatment on a principal's behalf. When making a decision about prescription, the provider has to make a choice between patients' welfare, policy directives to prescribe the most cost-effective treatment and directives to restrict drug use. Meanwhile, the patient (principal) expects the provider to be a perfect agent who use their knowledge to maximise the principal's utility; but the principal is usually not informed about the effect of treatment on health and society and the above-mentioned directives.

Given the presence of asymmetric information, the agent may choose to act in their own utility, which quite often does not align with the interests of the principal. This is called a principal-agent problem. Thus, in a simple principal-agent problem, the provider, against their perception of the best care for the patient, may want to influence the patient's demand curve and shift it towards the self-interest of the provider. The level of the provider-induced demand usually depends on the degree of information asymmetry or the gap in knowledge between the principal and the agent. The higher is the level of the information asymmetry between patient and physician – the more physician would deviate from being a perfect agent. These dynamics are commonly observed when the provider's remuneration is based on fee-for-service (FFS). Under FFS, physicians are paid for each procedure or service that a patient receives, and the revenues depend on the number of patient visits and the tests conducted, while costs depend on the total time used on each patient. In accordance with this prediction, FFS has, in general, been found to be associated with the overprovision of services [47].

3.2 Patients-induced demand for pharmaceuticals

In the case of pharmaceuticals prescription, the principal-agent problem becomes more complex. It is associated with patient-induced demand when a provider knows that a poorly-informed patient may expect the prescription.

Studies show that some patients do have inadequate knowledge about the clinical indication for and the consequences of antibiotic treatment [48-50]. According to a study by Mazińska et al. [51] about public knowledge about antibiotics, about 20% of the sample did not know that antibiotics can kill bacteria, while 60% of the respondents believed that antibiotics could treat viral infection. Moreover, patients may have a positive previous experience with antibiotic treatment, even when this treatment was unnecessary. When patients take antibiotics for self-limiting infections (both bacterial and viral), their perception of the necessity of antibiotic treatment may suffer from the observer's bias. Thus, patients may demand antibiotics when it is not needed.

As it has been discussed before, patients may have poor knowledge about addictive drugs as well, and therefore the problem of information asymmetry may also be relevant when, e.g. an uninformed patients ask for a "stronger" drug to treat their conditions. When patients become addicted to their drugs, patient-induced demand may be extremely high even in the absence of information asymmetry.

3.3 Reimbursement and the ownership type

In the case of prescribed pharmaceuticals, the principal-agent problem is complicated not only by patient-induced demand but also by policy directives. In this case, the provider has to play a role of a 'double agent', where another principal is a policy-maker, who can be both responsible for the antibiotic or addictive drugs stewardship or have other healthcare efficiency goals not related to drug use. These policies may not only impose an ethical cost on the provider but may also be based on economic incentives. The reimbursement mechanism is an important policy tool that may affect the general practitioner's (GP) behaviour. Policy-makers believe that by manipulating the reimbursement mechanism, they may achieve certain objectives aimed to improve the quality of care.

For example, Ellegård et al. [52] found that reimbursement schemes for healthcare providers based on antibiotic-related Pay-for-Performance (PFP) indicators stimulate more appropriate antibiotic prescriptions. However, there are other reimbursement mechanisms, which may impose reputational and financial implications for providers if they do not give patients the desired drug.

The main types of GPs reimbursement used worldwide are salary, capitation (CAP), previously-mentioned FFS, or a mixture of them [53]. Physicians working under salary receive a fixed payment from working a defined number of hours per year and usually have no financial motivation to increase the number of visits by attracting patients or satisfying their needs. CAP is based on the number of registered patients, which may encourage GPs to have longer patient lists and shorter consultations. Therefore, both salaried payments and CAP can encourage cost containment and result in the under-provision of treatment [54]. To avoid this and to increase the supplier-induced demand, FFS is usually implemented [55]. Under both FFS and CAP, providers have incentives to attract patients by satisfying their needs. This strategy may allow GPs to increase the number of visits, the number of registered patients, and, hence, to maximise profit. Therefore, if patients demand antibiotics for viral infections or addictive drugs for non-medical use, the financial incentives in the market can contribute to the over-prescription of these drugs [56]. Moreover, FFS and CAP may motivate GPs to have more and shorter consultations, while it may be time-consuming for GPs to argue with the patients about the necessity of the demanded drug.

Most of the papers about the effect of financial incentives on antibiotic prescription consider antibiotic-related PFP indicators (when physicians, hospitals, or other healthcare providers' payments depends on some performance measure) and find that they improve prescription behaviour PFP [57, 58]. However, there is a gap in the literature about the relationship between the primary payment scheme types (salary, FFS, CAP) and drug prescription in primary care. For example, Hutchinson and Foley [59] found that physicians working under FFS have higher antibiotic prescription rates than salaried physicians, while there are no (to our knowledge) studies about the relationship between reimbursement type and addictive drugs prescription.

Physicians do not always get a direct profit from each patient consultation, but the reimbursement schemes like FFS and CAP apply to a clinic they work at. Sometimes physicians have to follow the additional recommendations from their employer, which may also be reinforced by the financial incentives, e.g. inside the health care centre. In this case, the clinic ownership type may play an important role. For example, Silverman et al. [60] and Devereaux et al. [61] found that the share of private hospitals is positively correlated with health expenditures, while Granlund [62] found that private doctors and doctors from private clinics were more likely to veto substitution to generic drugs, which allowed patients to receive co-payment for the brand name version of the drug under pharmaceutical insurance. Granlund [62] concluded that the effect observed could be explained by stronger incentives for private physicians to please their patients.

3.4 Free choice of the provider, competition and gatekeeping

When the reimbursement system involves a mixture of CAP and FFS, such factors as the access to the free choice of provider, the level of competition between providers and their gatekeeping function may also play an important role in contributing to the problem of suboptimal drug prescription.

Free choice of provider is an important characteristic of primary care. The free choice can refer to several different things, e.g. choice to register or visit a certain GP or health care centre, choice of GP within a centre the patient is registered with or availability of primary care services [63]. The primary reason for registering with a specific GP is a possibility to be followed over time by a doctor familiar with the patient's health status and condition [64]. When changing their GP, patients consider the following factors important: distance to home/workplace, recommendation and expectations and dissatisfaction with the treatment [63]. Patients may have different preferences for health care, and free choice of provider is an important condition for achieving market efficiency because it improves access to primary care as well as gives patients the possibility to choose the provider according to their needs [65]. However, this may also lead to the suboptimal prescription of drugs. Indeed, studies show that GPs' decisions may not solely rely on facts related to the effectiveness of the prescribed drug but also on patient demand, e.g. GPs may prescribe antibiotics if they think that patient expects it [15, 66]. In the paper by Kohut et al. [67], it was found that physicians considered patients' demand to be the main factor for unnecessary antibiotic prescription among physicians and mention the following reasons of physicians' responding to it. Doctors may not want to spend time arguing with patients. Some of the doctors have emotional reasons and believe that it is not possible to satisfy patients without an antibiotic prescription, while others have economic reasons to do this. Since addictive prescribed drugs abuse is a growing problem, it means that doctors respond to patients' demand for the addictive drugs as well. However, to our knowledge, there is a gap in the literature about the reasons for such overprescription from the doctors' side. Most of the studies refer to the difficulty in distinguishing between drug-seeking behaviour and patients' medically legitimate need for the drug as well as the lack of training in managing such patients [68], but some studies also mention economic incentives [69]. When a free choice of primary care provider is available, patients may switch between them to get the desired drugs, which is usually called doctor shopping (DS) [70].

Thus, free choice of provider together with economic incentives within a health care centre is expected to increase competition between providers in the market. Ideally, competition is aimed to improve the quality of care by making providers more sensitive to patients' needs. However, such needs may include not only the desire for improvement in health but also sub-optimal demand for addictive drugs and antibiotics from patients who consider prescription as a sign of the care quality.

The literature about the effects of competition in the health care market is broad, focusing on quality, costs, prices, and health outcomes, while most of the studies are from the US [71]. However, there is a lack of studies about competition and the prescription of drugs. The main challenge for the studies about competition in the health care market is related to the proper definition of the competition and its measurement. Moreover, such measures should be based on specific market conditions.

Another important issue, which, together with other market conditions, may play an important role in drug prescription, is the gatekeeping function of primary care. On the one hand, the absence of gatekeeping gives patients direct access to specialists and, hence, may increase overprovision of care. On the other hand, a very strong gatekeeping role of GPs may lead to poor health outcomes and undertreatment. When it comes to drug prescriptions, it is important to understand the incentives in secondary care. If secondary care specialists have financial incentives to please patients, the number of prescribed drugs may be even higher due to stronger competition in the health care market. Even if there are no such incentives, the absence of gatekeeping increases patients' chance to get the desired drug by DS.

3.5 Insurance and high-cost protection

An important health care market characteristic is insurance. It gives patients financial protection against high healthcare spending. However, it may cause imperfection of the market. When patients' expenses are covered by insurance (public or private), a moral hazard problem arises, and patients can overconsume health care services. In order to limit such overconsumption, patients are usually asked to pay a part of their expenses out of pocket. However, in some countries there exists a high-cost protection limit. This limit means that patients get their health care spending covered by the insurance after they have reached a certain limit of expenditures, which may include pharmaceutical expenditures. Thus, when patients do not have to pay the full cost of treatment, they may be more likely to get involved in DS for the desired drugs, including both antibiotics and addictive drugs. This may be especially relevant for addictive drugs users because it is cheaper and less risky for them to obtain a prescribed drug than the street version.

Policy-makers widely use the organisation of the health care market as an instrument to achieve different goals by making providers and patients change their behaviour. Thus, to find the best incentives for minimising the prescription of antibiotics and addictive drugs, it is important to study the role of the health care market settings.

4 Aims

The main aim of our study is to test if the health care market settings may result in higher drug prescription rates. In order to achieve our goal, the study has the following objectives:

1) To determine the effect of private/public ownership of the health care centres on antibiotic prescription.
2) To test whether the competition between health care providers affects antibiotic prescription.
3) To find how a free choice of the provider may contribute to the suboptimal prescription of addictive drugs.

The first objective relates to how the financial incentives for the health care centre affect GPs' decision to prescribe antibiotics. We aim to study the difference in antibiotic prescription between private and public primary care centres. A potential mechanism by which type of ownership can affect prescription is that private health care centres are more reliant on profit-maximisation and patient satisfaction, and this may increase their willingness to attract patients by prescribing drugs.

The second objective is about the relationship of the level of competition between primary care providers and antibiotics prescription, given that payments for most providers are based on the number of visits and registered patients. We assume that competition may be an important determinant of antibiotic prescription and may contribute to the effect of the providers' reimbursement mechanisms on antibiotic prescription.

The third objective is to study how active the patients are in demanding drugs given a free choice of provider and how a strategy of switching providers (or DS) may contribute to the suboptimal addictive drugs prescription.

5 Institutional background and settings

We study the questions mentioned in the previous section in settings of the Scandinavian health care market. More specifically, we use examples of Sweden and Norway. The organisation of health care is similar in these countries, but the financial incentives and competition are slightly different. Health care in both countries is funded through national and local taxes, and the residents are covered by health care insurance. Patients have to cover parts of their health care cost up to a certain high-cost protection limit, which is about €240 in Norway [72] and €115 for outpatient care in Sweden [73].

There are some differences in the organisation of primary care in the two countries. In Sweden, counties and regions are responsible for the primary care, which is provided by team-based practices with GPs, gynaecologists, nurses, midwives, physiotherapists, psychologists, social workers, and behavioural therapists [74]. On average, there are about four GPs in such centres [75]. There are more than 1100 primary care units in Sweden, which are either public (owned by county councils) or private (owned by companies but financed by county councils) [76]. Payment to primary care providers varies among counties. GPs are salaried, while payment to the primary care centres is generally based on a mixture of CAP, FFS and performance-based payments [75].

In contrast to Sweden, most of the GPs in Norway are self-employed and get a mixture of FFS, CAP and payments from patients. About 5% of GPs are salaried physicians. All GPs sign a contract with municipalities, which are responsible for organising primary health care [77]. GPs play the role of gatekeepers in the Norwegian system. They prescribe drugs, provide preventive care, treat chronic and acute diseases, and make referrals to secondary care specialists. Patients are free to choose GP and can change their provider twice a year [78].

In Sweden, patients can switch providers as often as they want. However, the registration is done with a health care centre rather than a specific GP [74]. Compared to Norway, Swedish GPs have a weaker gatekeeping function. It is possible to visit specialists in the outpatient hospital departments without a referral from the GP. To decrease the use of specialist care, the patients co-payment rate for such consultations has been increased to a twice higher level than for a consultation with a GP. However, this may serve as a disincentive only for those who have not reached the high-cost protection limit of healthcare spending [75].

Out of regular working hours, patients in both countries are offered emergency primary care services [74, 77]. Once admitted to a hospital, treatment is arranged at no cost for the patient in Norway and the hospital care is organised at the regional level [77]. In Sweden, inpatient hospital care is provided by the counties and regions and implies small patient co-payment (about €9) per day with some exemptions [74].

It is also important to notice that the health care market in both countries is a market with fixed (regulated) prices, such that prices are not set by the providers or determined in the market.

6 Research design and methods

Although economic incentives in health care may significantly affect drug prescription, studying such effects has always been challenging due to the need for high-quality register data. Data from Scandinavian countries can serve as a good tool for such studies due to the following reasons. First, over-the-counter sales of the drugs are restricted, and all prescriptions are registered and monitored electronically. Moreover, there is a strict attitude towards antibiotic and addictive drugs consumption together with a relatively low prevalence of AR in Scandinavia [79]. Therefore it is interesting to know if the effects of economic factors on drug prescription are still present in such environment.

In order to answer the first research question about the effect of ownership type of health care centre on GPs' antibiotic prescription behaviour, we use prescription data for Västerbotten county of Sweden, provided by Västerbottens county board. The data contains information on the ownership type of primary health care centres (private or public) and all prescriptions made by the centres and distributed at pharmacies in Västerbotten for 2011-2016. The dataset includes a large number of variables, for example, the patient's age, gender, and area of residence, and patients are traceable over time. The information about the prescription contains the date it was prescribed, the workplace of the prescriber and his/her profession (e.g. physician, dentist) and the identification number of the prescribed drug. The dataset also includes information on the date the prescription was dispensed, information about the dispensed drug, the patient's co-payment and the total cost for the prescription. We also know if the physician, the pharmacy, or the patient opposed substitution and the additional cost in the latter case. For all drugs, the dataset also includes the Anatomical Therapeutic Chemical (ATC) Classification System code, number of defined daily doses per package, strength, and form.

To identify the effect of ownership type on the prescription of antibiotics, we would ideally use the information on tests and diagnoses in combination with information on antibiotic prescriptions. However, as information on tests and diagnoses is not available in our data, we rely on a different approach. Since we have data on all drugs prescribed at a health care centre, we can calculate the share of the prescriptions that are constituted by antibiotics and evaluate how these shares are affected by the ownership type of the centre. However, working with shares imply having too many zeroes in the outcome variable. Therefore, instead of calculating the shares, we measure the probability that a prescribed drug is an antibiotic and apply a discrete regression approach. Moreover, we evaluate if there is a systematic variation in the prescription of broad and narrow-spectrum antibiotics.

Since patients are free to choose a primary care centre, the characteristics of patients may vary systematically between centres. For example, if older and sicker patients are clustered in specific centres, this will create a selection bias in the results, as factors such as patient age and gender are likely to affect antibiotic prescription [80, 81] significantly. Moreover, observed geographical variations in antibiotic prescription might be affected by differences in demographic, geographic characteristics [82]. The above-mentioned factors constitute challenges for the empirical analysis. Since only about 30 per cent of patients choose a primary care centre, which is different to the one suggested by the county council [83], this reduces the problem of selection to some extent. However, to address the issue of a systematic variation in the needs of patients, we control for patient gender and age in our analysis.

This analysis does not detect if private health centres prescribe more antibiotics than public ones or if patients with infectious diseases are more likely to visit private clinics. Therefore, to get more insight into this, we conduct an additional analysis about the effect of the number of private clinics in a municipality on antibiotic prescription rates.

To answer the second research question, we use Norwegian data. The data about the levels of antibiotic prescription for Norwegian municipalities (426 municipalities on the period of study) is available at the Norwegian Public Health Institute webpage [84]. To measure competition between GPs in each municipality, we use the HELFO Database provided by the Norwegian Directorate of Health. The register contains the following monthly data for each individual GP: name, gender, length of the list, reimbursement type, municipality, workplace, and information about if the doctor is a specialist in general practice or not.

To see how competition affects antibiotic prescription, we combine the above-mentioned information with the data about prescription. We measure competition in several ways suggested the literature, such as the number of lists (the number of spots), the number of lists (the number of spots) per patient and the primary classical measure such as Herfindahl-Hirschman index (HHI), calculated as $HHI = \sum_{i=1}^{N} s_i^2$, where s_i - is the market share of GP i in the market of N GPs. We calculate the market share as the number of patients on the list divided by the total number of patients in a municipality. HHI varies in the interval between zero (perfect competition) and one (pure monopoly). We calculate HHI based on the municipality level because municipalities are responsible for the organisation of primary care in Norway.

It is important to notice that the Norwegian market is, to some extent, unique. For example, patients are able to choose only among available providers, while the providers can increase their list length only until some reasonable limit. To account for this, we use additional measures of competition previously used by Godager *et al.* [85] and Iversen and Ma [86], which are based on the number of available spots on the GPs' lists. In all models, we control for socioeconomic and socio-demographic municipality parameters as well as the availability of secondary care. The above-mentioned municipality characteristics have been retrieved from several publicly available sources, e.g. Statistics Norway [87], The Norwegian Directorate of Health webpage [88], and the Norwegian Public Health Institute webpage [84]. The analysis we use is quantitative based on the Ordinary Least Squares (OLS) method. In the empirical models, we also control for socio-demographic, socioeconomic characteristics of the municipalities, morbidity, availability of secondary care, and distance to the nearest pharmacy.

To answer the third research question about DS, we use the same Swedish data as used to answer the first research question. Due to changes in the patient ID system in 2013, it is impossible to follow the patients during the whole period between 2011 and 2016. Therefore, to identify the patients' behaviour consistently over time, we had to limit the study period to 2014-2016.

As mentioned earlier, DS is known as a strategy to switch providers during a single illness episode to get more drugs prescribed. DS may refer to different types of drugs, but most studies about DS focus on the addictive ones. There are two potential reasons for this. First, DS is more common among addictive drug users. The second reason is methodological. It is problematic to find switching episodes without data about visits. Most of the researchers do not have access to such information and have data about prescriptions only. Therefore, they are not able to identify switches when no drug has been prescribed. Such information is critical in the studies about DS for, e.g. antibiotics, because patients are interested just in the fact of antibiotic prescription. However, those who use addictive drugs may be interested in getting several prescriptions at the same time. This makes it possible to study DS using the data about prescriptions of addictive drugs by identifying the episodes with overlapping prescriptions in the data – prescriptions given by different providers but consumed simultaneously. Such overlapping prescriptions may serve as evidence of drug misuse.

In order to identify the overlaps, it is important to know the treatment duration. However, prescribed registers usually do not contain such information. In this thesis, we use a common proxy for it [89, 90] which is based on the Defined Daily Dose (DDD) – an average treatment dose for the main indication of the drug used in adults. Since the DDD may be not a perfect proxy and since some part of the overlaps caused by different prescribers may be legitimate (e.g. when a patient receives the next prescription a few days before the previous one expired), we compare the overlaps caused by the prescriptions given by different prescribers with the overlaps caused by the same provider. We control for the age, gender and municipality of the patient as well as for patient-specific effects.

We use the software "R" for the data analysis [91].

7 Results

7.1 **Paper 1:** Can Private Provision of Primary Care Contribute to the Spread of Antibiotic Resistance? A Study of Antibiotic Prescription in Sweden

Paper 1 investigates the link between the ownership type of primary health care centres in Västerbotten county of Sweden and prescriptions of antibiotics. To our knowledge, this is the first study that addresses this relationship. First, we test if privately owned but publicly funded primary care centres prescribe antibiotics more often than other drugs (compared to the public centres). Second, we study if private centres prescribe broad-spectrum antibiotics more often than narrow-spectrum. The first question is motivated by the hypothesis that private centres are maximising their profit by responding to the patients' demand for antibiotics since the ability to generate profit depends on the number of visits and listed patients. The motivation for the second research question is the following. Broad-spectrum antibiotics kill a wider range of bacteria and, therefore, contribute more to the AR compared to the narrow-spectrum ones. Due to the growth of AR rates, narrow-spectrum antibiotics may be less effective in treating infectious diseases. Therefore, GPs may be forced to prescribe broad-spectrum antibiotics more often. Prescription of the efficient treatment may also serve as quality of treatment mark for the patients. Thus, we hypothesised that private centres might be more willing to choose broad-spectrum antibiotics more often than public centres.

Using the data about prescriptions in primary care from Västerbotten and applying the research methods described in the previous section, we find that private health care centres were 6% more likely to prescribe an antibiotic and 9% more likely to choose the broad-spectrum one, holding other factors constant. Since we do not have complete information about visits and diagnoses, it is difficult to identify if the GPs at private centres prescribe antibiotics more often or if patients with infectious diseases are more likely to visit private centres than those with other types of diseases. In order to shed some light on it, we test the effect of the number of private health care centres on the number of prescriptions per inhabitant in the municipality and the share of broad-spectrum antibiotics. We find a positive and significant effect of the additional private centre on the prescriptions per capita and positive (but not significant effect) on the share of broad-spectrum antibiotics.

7.2 **Paper 2:** Competition in primary care and prescription of antibiotics in Norway

The second paper tests the relationship between competition in primary care in Norway and the prescription of antibiotics used for RTIs. We use municipality level data. Since there is no unique way to measure the competitiveness of the environment, we employ several proxies for competition defined in the literature. According to the standard prediction, the more providers are present in the market, the more competitive the environment is. We find a positive and statistically significant relationship between the number of providers and the prescription level. Since the number of providers does not account for their availability, we test other measures used in the literature: the number of providers per patient and the number of spots per capita. The effect of these variables on competition is also positive and significant. For example, a 1% increase in the number of providers may contribute to ten additional prescriptions per 1000 inhabitants per year, while one additional GP per 1000 patients may contribute to a three units increase in the prescription per capita.

Another classical measure of competition, such as HHI, shows that the closer the market is to perfect competition, the higher the levels of antibiotic prescription are. We find a difference in about 34 fewer yearly prescriptions of antibiotics for RTIs per 1000 inhabitants between municipalities with a monopoly (HHI = 1) and municipalities with almost perfect competition (HHI ≈ 0).

However, none of the measures mentioned above considers that in Norwegian settings, patients are not free to switch providers as often as they want and can choose only among the GPs that have available spots on the list. In order to account for this, we use two measures of competition suggested in the literature about competition in the Norwegian primary care market [85, 86], such as the number of open lists (spots) and the number of open lists (spots) per patient. We find a positive and significant effect of the number of open lists and the number of open spots on antibiotic prescription rates. Per capita measure of the number of open spots also suggests that the prescription rate increases with stronger competition. The effect of the number of open lists per capita is positive but not significant. This might happen because this measure does not account for how large the difference between the desired list length and the actual one is and if there is a sufficient amount of open spots for all patients willing to switch to a new provider.

In the case of pure monopoly (just one provider), 'per capita' competition measures may reveal stronger competition than in municipalities with many GPs. Moreover, there are some municipalities where most of the providers are salaried. Therefore, we further test the effect of the competition measure on antibiotic prescription, excluding the municipalities with one GP or 'low' share of FFS contracts, and find that our previous results are robust to the differences in the data.

7.3 **Paper 3:** Effects of 'doctor shopping' behaviour on prescription of addictive drugs in Västerbotten, Sweden

In Paper 3, we study how DS affects the prescription of addictive drugs in Västerbotten using the data about prescriptions from 2014 to 2016. To our knowledge, this is the first study in the Swedish market settings and using the methodological approach described in section 6. The advantages of the approach are the following. First, it allows us to better deal with the fact that DDD is not a perfect proxy for treatment duration. Next, it gives a possibility to better distinguish between drug abuse and medically legitimate prescriptions. Finally, we managed to take into analysis several types of drugs within a certain category defined by the treatment indication.

In this paper, we analyse three groups of addictive drugs, such as opioid painkillers, benzodiazepine anxiolytics, and z-hypnotic sleeping drugs. We find a relatively low prevalence of DS in Västerbotten. About 2-4 per cent (depending on the type of drug) of people exposed to addictive drugs have been involved in presumable shopping episodes. However, the effect of DS on drug consumption is high. The estimation results suggest that the number of DDDs per day grows with the number of providers in the overlap. Having two providers involved in the overlap may give patients 0.242, 0.429 and 0.153 additional DDDs per day of painkillers, anxiolytics and sleeping drugs, respectively. This corresponds to a 7%-18% increase in DDD per day compared to the doses given by the overlaps between prescriptions from the same provider. Having more than two providers in the overlap gives a disproportionally higher number of DDDs per day. The maximum number of unique providers of simultaneous prescriptions is four, and it is associated with 2.117 and 2.868 additional DDDs per day for painkillers and sleeping drugs, respectively (no cases with four prescribers for anxiolytics). Thus, multiple prescribers involved in the overlap may give patients up to three DDDs per day in addition to a standard treatment dose in adults of 1 DDD.

8 Discussion

Nowadays, policy-makers consider the growth of AR and abuse of addictive prescription drugs as substantial public-health problems worldwide. By manipulating market conditions, policy-makers aim to affect individual behaviour in order to achieve certain goals, e.g. better access to health care or its quality. However, these incentives may also have undesired effects, such as overprescription of drugs. Therefore, knowledge about how market-related factors affect drugs prescription is needed to design better incentives for the appropriate use of antibiotics and addictive drugs.

The literature on this topic confirms that economic incentives play an important role in many aspects of patients and physicians behaviour. For example, the way GPs are reimbursed and the level of competition in the market may affect medical decision-making, e.g. related to referrals to secondary care, long-term sickness certificates or generic reservation [62, 92, 93]. Moreover, market conditions and regulations may affect patients' use of services [94, 95]. However, there is a lack of studies about the effects of market conditions and economic incentives in outpatient care on the prescription of drugs, especially antibiotics and addictive drugs. The overall goal of the thesis was to fill this gap in the literature.

The first two research questions in the thesis focused on the behaviour of GPs towards antibiotic prescription and the financial incentives in primary care. When GPs are financed mainly through a mix of FFS and CAP, they may be willing to maximise their profit by attracting patients. In addition, they are motivated to have more and shorter consultations. One way to both please patients and keep consultation short is to prescribe the desired drug. On the one hand, prescription of drugs is an easy and quick way to please patients compared to, e.g. referrals to specialists. On the other hand, inappropriate use of antibiotics causes a substantial individual and societal cost in terms of growing AR rates. Thus, to create better and more targeted policy instruments for more appropriate drug use, it is important to know if (and to what extent) prescription of medications serves as a 'profit-maximisation tool' for physicians.

To our knowledge, there is just one study about the effects of FFS on antibiotic prescriptions [59]. The study is from Canada, and it found that FFS remuneration was associated with higher prescription levels. However, physicians are not always directly paid by CAP or FFS. These reimbursement mechanisms may apply to their employer. Therefore, it is important to know if there is an indirect effect of reimbursement on physicians' behaviour through the healthcare centres' ownership type. Paper 1 in the thesis investigates this effect. To our knowledge, there are no previous studies on it. We compared two types of primary care centres in Västerbotten county of Sweden: public and publicly-funded but privately-owned. The first type is prevailing. Even though GPs in both types of centres are salaried, private centres might be interested in profit-maximisation by increasing the number of visits and registered patients. We hypothesised that this profit-maximisation motivation might affect individual physician's decision-making. We found a significant difference in antibiotic prescription patterns between public and private primary care providers. Our results suggest that profit-maximisation is associated with higher antibiotic prescription rates.

Paper 2 complements Paper 1 in the following way. It focused on competition in the Norwegian primary care market and the prescription of antibiotics. In contrast to Sweden, most of the GPs in Norway are self-employed and are directly paid through the mix of CAP and FFS, which makes the Norwegian market more competitive. The reimbursement mechanism and the level of competition are closely related factors potentially contributing to overprescription. Hence, it is important to study their effects separately. We used several measures of competition used in the previous literature and found that the level of competition in terms of the number of providers increased antibiotic prescription rates. In addition, we tried to take into account specific properties of the Norwegian market. These properties are related to the possibility for patients to switch between providers. We found a link between a higher possibility of switching and a higher level of antibiotic prescription in a municipality.

Even though the first two research questions focused on antibiotics, the same studies might also be relevant for addictive drugs, which are discussed in Paper 3. This paper focused on switching providers (more specifically DS) and patients' demand for pharmaceuticals GPs face. There can be two ways of how patients switch providers. The first way is to register with a new provider until the best one has been found. Another way is to visit several providers without registration during a short time period to get as many drugs as possible. The first way is likely to be more common for patients who need antibiotics or other types of non-addictive drugs. In the case of addictive drugs, we expect that it may be difficult to receive more prescriptions than necessary in one clinic, and patients may be willing to switch clinics less systematically. They may visit several clinics at once to increase their chance of getting the prescription or increase the number of prescriptions. Without information about patient registration with the providers, we could not study the first way of switching. However, we found that the second way of DS in the market settings of Västerbotten may contribute to the overprescription of addictive drugs. It would also be interesting to study DS in Norwegian settings because the differences in market regulations may affect the possibility for DS. One of such regulations is how often patients may switch primary care providers. In Sweden, this possibility is unlimited, while in Norway, patients can do it only twice a year. Another difference is the gatekeeping function of primary care, which is very strong in Norway compared to Sweden. These factors affect competition between providers as well, and, therefore, it would be interesting to investigate them further.

In the thesis, we used data from Norway and Sweden – countries with a relatively low prevalence of drug abuse, strict attitude towards antibiotics and addictive drugs, as well as prescription monitoring programmes. Therefore, our results may shed some light on the severity of the problem, given that it has already been reasonably addressed. However, for more precise estimations, it would be beneficial to use individual prescription data together with the information about visits and diagnoses. Even though more studies are needed, we believe, that our findings hold the potential to facilitate policy-makers in designing policies for achieving more appropriate drug use in primary/outpatient care. For example, if more studies show that reducing competition in the market or reducing the effect of reimbursement on drug prescription is necessary, this can be done in several ways based on the incentives we have studied. First, if more salaried physicians are present in the market, the market becomes less competitive and fewer GPs would be motivated to please patients by frivolous prescriptions. However, this may lead to a lower quality of care. Another way of affecting competition is related to the number of providers. It could be possible to consider the Swedish example, where GPs are organised in health care centres, and patients register with health care centres rather than a specific GP. Such settings would decrease the number of competing providers and would potentially, to less extent, affect the health care provision and availability. Our results show that salaried GPs in private health care centres may still compete and, hence, may still be interested in providing better care for patients. Finally, the limit on the number of times patients can switch providers may affect competition in the market. However, we notice that in the Norwegian settings with a restricted possibility to switch providers, competition is still likely to have an effect on the prescriptions. Other policy instruments aimed to improve antibiotic use in primary care may be based on the antibiotic-related PFP indicators, which have previously been found to be an effective solution [52, 57]. One more possible instrument has been discussed in Paper 2. It is based on the practice of delayed antibiotic prescription and reduction in the patient co-payment for the 'control' visit in case of RTI. Finally, to reduce patient-induced demand and the possibility for DS, it is also important to consider if the free choice of provider should be limited and if the gatekeeping function of GPs is necessary. A more targeted policy instrument that could also be used to reduce the number of overlapping prescriptions caused by DS is electronic reminders or warning messages. Such messages may occur on the computer of physician when the prescription being dispensed overlaps with the previous one. Similar reminders may also be effective in improving antibiotic prescribing practices in primary care [96].

References

1. Gottlieb T, Nimmo GR. Antibiotic resistance is an emerging threat to public health: an urgent call to action at the Antimicrobial Resistance Summit 2011. Med J Aust. 2011;194(6):281-283. doi:10.5694/j.1326-5377.2011.tb02973.x
2. Fleming A. Penicillin. Nobel Lecture. December 11, 1945. Available from: https://www.nobelprize.org/uploads/2018/06/fleming-lecture.pdf [Accessed 03.08.2021]
3. Lobanovska M, Pilla G. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future?. Yale J Biol Med. 2017;90(1):135-145.
4. Coast J, Smith RD, Millar MR. Superbugs: should antimicrobial resistance be included as a cost in economic evaluation?. Health Econ. 1996;5(3):217-226. doi:10.1002/(SICI)1099-1050(199605)5:3<217::AID-HEC200>3.0.CO;2-S
5. Tackling Antimicrobial Resistance Ensuring Sustainable R&D. OECD, WHO, FAO, OIE. 2017; Available from: http://www.oecd.org/g20/summits/hamburg/Tackling-Antimicrobial-Resistance-Ensuring-Sustainable-RD.pdf [Accessed 03.08.2021]
6. Bush K, Courvalin P, Dantas G, et al. Tackling antibiotic resistance. Nat Rev Microbiol. 2011;9(12):894-896. doi:10.1038/nrmicro2693
7. Goossens H, Ferech M, Vander Stichele R, Elseviers M; ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet. 2005;365(9459):579-587. doi:10.1016/S0140-6736(05)17907-0
8. Facts about antibiotic resistance. The Infectious Diseases Society of America (IDSA). Available from: https://www.idsociety.org/public-health/antimicrobial-resistance/archive-antimicrobial-resistance/facts-about-antibiotic-resistance/. [Accessed 03.08.2021]
9. Strandberg EL, Brorsson A, Hagstam C, Troein M, Hedin K. "I'm Dr Jekyll and Mr Hyde": are GPs' antibiotic prescribing patterns contextually dependent? A qualitative focus group study. Scand J Prim Health Care. 2013;31(3):158-165. doi:10.3109/02813432.2013.824156
10. Das P, Horton R. Antibiotics: achieving the balance between access and excess. Lancet. 2016;387(10014):102-104. doi:10.1016/S0140-6736(15)00729-1
11. Lack of access to antibiotics is a major global health challenge. ScienceDaily 2019; Center for Disease Dynamics, Economics & Policy. Available from: www.sciencedaily.com/releases/2019/04/190409135849.htm. [Accessed 03.08.2021]
12. Harbarth S, Balkhy HH, Goossens H et al. Antimicrobial resistance: one world, one fight!. Antimicrob Resist Infect Control. 2015;4, 49. https://doi.org/10.1186/s13756-015-0091-2
13. Kusturica MP, Tomic Z, Bukumiric Z, et al. Home pharmacies in Serbia: an insight into self-medication practice. Int J Clin Pharm. 2015;37(2):373-378. doi:10.1007/s11096-015-0071-x
14. Şerban G, Buhaş SE. Study on self-medication: nonsteroidal antiinflammatory drugs. Analele Universităţii din Oradea, Fascicula: Ecotoxicologie, Zootehnie şi Tehnologii de Industrie Alimentară, 2014;13(A): 215-224.
15. Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: are patients more satisfied when expectations are met?. J Fam Pract. 1996;43(1):56-62.
16. Cadieux G, Abrahamowicz M, Dauphinee D, Tamblyn R. Are physicians with better clinical skills on licensing examinations less likely to prescribe antibiotics for viral respiratory infections in ambulatory care settings? [published correction appears in Med Care. 2011 May;49(5):527-8]. Med Care. 2011;49(2):156-165. doi:10.1097/MLR.0b013e3182028c1a

17. Rowbotham S, Chisholm A, Moschogianis S, et al. Challenges to nurse prescribers of a no-antibiotic prescribing strategy for managing self-limiting respiratory tract infections. J Adv Nurs. 2012;68(12):2622-2632. doi:10.1111/j.1365-2648.2012.05960.x
18. Van der Velden AW, Bell J, Sessa A, Duerden M, Altiner A. Sore throat: effective communication delivers improved diagnosis, enhanced self-care and more rational use of antibiotics. Int J Clin Pract Suppl. 2013;(180):10-16. doi:10.1111/ijcp.12336
19. Antibiotics resistance threats in the United States, 2013. Centers for Disease Control and Prevention (CDC). 2013; Available from: https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf. [Accessed 03.08.2021]
20. Roope LSJ, Smith RD, Pouwels KB, et al. The challenge of antimicrobial resistance: What economics can contribute. Science. 2019;364(6435):eaau4679. doi:10.1126/science.aau4679
21. O'Neill J. Review on antimicrobial resistance. Antimicrobial resistance: tackling a crisis for the Health and Wealth of Nations. 2014; Available from: https://amr-review.org/sites/default/files/AMR%20Review%20Paper%20-%20Tackling%20a%20crisis%20for%20the%20health%20and%20wealth%20of%20nations_1.pdf. [Accessed 03.08.2021]
22. Laxminarayan R, Brown GM. Economics of Antibiotic Resistance: A Theory of Optimal Use. Journal of Environmental Economics and Management. 2001;42(2): 183-206. https://doi.org/10.1006/jeem.2000.1156
23. Lloyd WF. Two lectures on the checks to population. The University of Oxford. 1833;77.
24. Laxminarayan R. How Broad Should the Scope of Antibiotics Patents Be? American Journal of Agricultural Economics. 2002;84(5):1287-1292.
25. Hollis A, Maybarduk P. Antibiotic Resistance Is a Tragedy of the Commons That Necessitates Global Cooperation. J Law Med Ethics. 2015;43 Suppl 3:33-37. doi:10.1111/jlme.12272
26. Littmann J, Buyx A, Cars O. Antibiotic resistance: An ethical challenge. Int J Antimicrob Agents. 2015;46(4):359-361. doi:10.1016/j.ijantimicag.2015.06.010
27. Littmann J, Viens AM. The Ethical Significance of Antimicrobial Resistance. Public Health Ethics. 2015;8(3):209-224. doi:10.1093/phe/phv025
28. Garau J. Impact of antibiotic restrictions: the ethical perspective. Clin Microbiol Infect. 2006;12 Suppl 5:16-24. doi:10.1111/j.1469-0691.2006.01527.x
29. Selgelid MJ. Ethics and drug resistance. Bioethics. 2007;21(4):218-229. doi:10.1111/j.1467-8519.2006.00542.x
30. The non-medical use of prescription drugs: policy direction issues. United Nations Office on Drugs and Crime 2011; Available from: https://www.unodc.org/documents/drug-prevention-and-treatment/nonmedical-use-prescription-drugs.pdf.
31. World drug report. United Nations Publications. 2010; United Nations Office on Drugs; Available from: https://www.unodc.org/documents/wdr/WDR_2010/World_Drug_Report_2010_lo-res.pdf. [Accessed 03.08.2021]
32. Under the counter: The diversion and abuse of controlled prescription drugs in the US. 2005, The National Center on Addiction and Substance Abuse (CASA) New York.
33. Edlund MJ, Martin BC, Fan MY, Devries A, Braden JB, Sullivan MD. Risks for opioid abuse and dependence among recipients of chronic opioid therapy: results from the TROUP study. Drug Alcohol Depend. 2010;112(1-2):90-98. doi:10.1016/j.drugalcdep.2010.05.017
34. Cutajar MC, Mullen PE, Ogloff JR, Thomas SD, Wells DL, Spataro J. Psychopathology in a large cohort of sexually abused children followed up to 43 years. Child Abuse Negl. 2010;34(11):813-822. doi:10.1016/j.chiabu.2010.04.004

35. Kreek MJ, Nielsen DA, Butelman ER, LaForge KS. Genetic influences on impulsivity, risk taking, stress responsivity and vulnerability to drug abuse and addiction. Nat Neurosci. 2005;8(11):1450-1457. doi:10.1038/nn1583
36. Compton WM, Volkow ND. Abuse of prescription drugs and the risk of addiction. Drug Alcohol Depend. 2006;83 Suppl 1:S4-S7. doi:10.1016/j.drugalcdep.2005.10.020
37. Partnership Attitude Tracking Study: Teens 2004. Partnership for a Drug-Free America, and United States of America. 2005; Available from: https://www.ojp.gov/ncjrs/virtual-library/abstracts/partnership-attitude-tracking-study-teens-2004.
38. National Survey on Drug Use and Health. Results from the 2008 National Survey on Drug Use and Health: Volume I. Summary of National Findings. 2008; Available from: https://dpft.org/resources/NSDUHresults2008.pdf [Accessed 03.08.2021]
39. Vadivelu N, Kai AM, Kodumudi V, Sramcik J, Kaye AD. The Opioid Crisis: a Comprehensive Overview. Curr Pain Headache Rep. 2018;22(3):16. Published 2018 Feb 23. doi:10.1007/s11916-018-0670-z
40. Crane EH. Highlights of the 2011 Drug Abuse Warning Network (DAWN) Findings on Drug-Related Emergency Department Visits. In: The CBHSQ Report. Rockville (MD): Substance Abuse and Mental Health Services Administration (US); February 22, 2013.1-9.
41. Birnbaum HG, White AG, Reynolds JL, et al. Estimated costs of prescription opioid analgesic abuse in the United States in 2001: a societal perspective. Clin J Pain. 2006;22(8):667-676. doi:10.1097/01.ajp.0000210915.80417.cf
42. Bruno R. Benzodiazepine and pharmaceutical opioid misuse and their relationship to crime: an examination of illicit prescription drug markets in Melbourne, Hobart and Darwin. National Drug Law Enforcement Research Fund. 2007.
43. West NA, Severtson SG, Green JL, Dart RC. Trends in abuse and misuse of prescription opioids among older adults. Drug Alcohol Depend. 2015;149:117-121. doi:10.1016/j.drugalcdep.2015.01.027
44. Pouwels KB, Dolk FCK, Smith DRM, Robotham JV, Smieszek T. Actual versus 'ideal' antibiotic prescribing for common conditions in English primary care. J Antimicrob Chemother. 2018; 73(suppl_2):19-26. doi:10.1093/jac/dkx502
45. The path of least resistance. Standing Medical Advisory Committee (Sub-Group on Antimicrobial Resistance). Department of Health. United Kingdom; 1998.
46. Nguyen H. The principal-agent problems in health care: evidence from prescribing patterns of private providers in Vietnam. Health Policy Plan. 2011;26 Suppl 1:i53-i62. doi:10.1093/heapol/czr028
47. Pauly MV. The rational nonpurchase of long-term-care insurance. Journal of Political Economy. 1990;98(1):153-168. https://doi.org/10.1086/261673
48. Vanden Eng J, Marcus R, Hadler JL, et al. Consumer attitudes and use of antibiotics. Emerg Infect Dis. 2003;9(9):1128-1135. doi:10.3201/eid0909.020591
49. Hoffmann K, Ristl R, Heschl L, Stelzer D, Maier M. Antibiotics and their effects: what do patients know and what is their source of information?. Eur J Public Health. 2014;24(3):502-507. doi:10.1093/eurpub/ckt112
50. Gualano MR, Gili R, Scaioli G, Bert F, Siliquini R. General population's knowledge and attitudes about antibiotics: a systematic review and meta-analysis. Pharmacoepidemiol Drug Saf. 2015;24(1):2-10. doi:10.1002/pds.3716
51. Mazińska B, Strużycka I, Hryniewicz W. Surveys of public knowledge and attitudes with regard to antibiotics in Poland: Did the European Antibiotic Awareness Day campaigns change attitudes?. PLoS One. 2017;12(2):e0172146. doi:10.1371/journal.pone.0172146

52. Ellegård LM, Dietrichson J, Anell A. Can pay-for-performance to primary care providers stimulate appropriate use of antibiotics?. Health Econ. 2018;27(1):e39-e54. doi:10.1002/hec.3535
53. Gosden T, Forland F, Kristiansen IS, et al. Capitation, salary, fee-for-service and mixed systems of payment: effects on the behaviour of primary care physicians. Cochrane Database Syst Rev. 2000;(3):CD002215. doi:10.1002/14651858.CD002215
54. Woodward RS, Warren-Boulton F. Considering the effects of financial incentives and professional ethics on 'appropriate' medical care. J Health Econ. 1984;3(3):223-237. doi:10.1016/0167-6296(84)90012-2
55. Evans RG. Supplier-Induced Demand: Some Empirical Evidence and Implications. The Economics of Health and Medical Care. International Economic Association Series. Palgrave Macmillan, London. 1974; 162-173 https://doi.org/10.1007/978-1-349-63660-0_10
56. DeWeerdt S. Tracing the US opioid crisis to its roots. Nature. 2019;573(7773):S10-S12. doi:10.1038/d41586-019-02686-2
57. Sun X, Liu X, Sun Q. The impact of a pay-for-performance scheme on prescription quality in rural China, in Health Care Policy in East Asia: A World Scientific Reference: Volume 1: Health Care System Reform and Policy Research in China. 2020; 195-227. doi:10.1142/9789813236134_0009
58. Lake TK, Rich EC, Valenzano CS, Maxfield MM. Paying more wisely: effects of payment reforms on evidence-based clinical decision-making. J Comp Eff Res. 2013;2(3):249-259. doi:10.2217/cer.13.27
59. Hutchinson J., Foley R. Method of physician remuneration and rates of antibiotic prescription-based study. Eur J Clin Pharmacol. 2001; 57: 159-65.
60. Silverman EM, Skinner JS, Fisher ES. The association between for-profit hospital ownership and increased Medicare spending. N Engl J Med. 1999; 341(6):420-426. doi:10.1056/NEJM199908053410606
61. Devereaux PJ, Schünemann HJ, Ravindran N, et al. Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis [published correction appears in JAMA. 2004 Jan 14;291(2):186]. JAMA. 2002;288(19):2449-2457. doi:10.1001/jama.288.19.2449
62. Granlund D. Are private physicians more likely to veto generic substitution of prescribed pharmaceuticals?. Soc Sci Med. 2009;69(11):1643-1650. doi:10.1016/j.socscimed.2009.09.016
63. Miani C; PitchforthE, Nolte E. Choice of primary care provider: a review of experiences in three countries. Technical Report. Policy Innovation and Research Unit (PIRU). 2013. DOI: https://doi.org/10.17037/PUBS.02478791
64. Cheraghi-Sohi S, Hole AR, Mead N, et al. What patients want from primary care consultations: a discrete choice experiment to identify patients' priorities. Ann Fam Med. 2008;6(2):107-115. doi:10.1370/afm.816
65. Beckman A, Anell A. Changes in health care utilisation following a reform involving choice and privatisation in Swedish primary care: a five-year follow-up of GP-visits. BMC Health Serv Res. 2013;13:452. doi:10.1186/1472-6963-13-452
66. Fletcher-Lartey S, Yee M, Gaarslev C, Khan R. Why do general practitioners prescribe antibiotics for upper respiratory tract infections to meet patient expectations: a mixed methods study. BMJ Open. 2016;6(10):e012244. Published 2016 Oct 24. doi:10.1136/bmjopen-2016-012244

67. Kohut MR, Keller SC, Linder JA, et al. The inconvincible patient: how clinicians perceive demand for antibiotics in the outpatient setting. Fam Pract. 2020;37(2):276-282. doi:10.1093/fampra/cmz066
68. Hansen GR. The drug-seeking patient in the emergency room. Emerg Med Clin North Am. 2005;23(2):349-365. doi:10.1016/j.emc.2004.12.006
69. Kann IC, Biørn E, Lurås H. Competition in general practice: prescriptions to the elderly in a list patient system. J Health Econ. 2010;29(5):751-764. doi:10.1016/j.jhealeco.2010.07.004
70. Sansone RA, Sansone LA. Doctor shopping: a phenomenon of many themes. Innov Clin Neurosci. 2012;9(11-12):42-46.
71. Gaynor M, Town RJ. Competition in health care markets. Handbook of health economics. 2011;2:499-637. https://doi.org/10.1016/B978-0-444-53592-4.00009-8
72. Frikort for helsetjenester [Exemption card for health services]. Helsenorge. 2021; (Norwegian) Available from: https://www.helsenorge.no/betaling-for-helsetjenester/frikort-for-helsetjenester/.
73. Högkostnadsskydd för öppenvård [High-cost protection for outpatient care]. 1177 Vårdguiden. 2021; (Swedish) Available from: https://www.1177.se/Vasterbotten/sa-fungerar-varden/kostnader-och-ersattningar/hogkostnadsskydd-for-oppenvard/. [Accessed 03.08.2021]
74. Anell A, Glenngård AH, Merkur S. Sweden health system review. Health Syst Transit. 2012;14(5):1-159.
75. Mossialos E, Wenzl M, Osborn R et al. 2015 international profiles of health care systems. 2016; Available from: https://www.commonwealthfund.org/sites/default/files/documents/___media_files_publications_fund_report_2016_jan_1857_mossialos_intl_profiles_2015_v7.pdf. [Accessed 03.08.2021]
76. Anell A. The public-private pendulum--patient choice and equity in Sweden. N Engl J Med. 2015;372(1):1-4. doi:10.1056/NEJMp1411430
77. Ringard Å, Sagan A, Sperre Saunes I, Lindahl AK. Norway: health system review. Health Syst Transit. 2013;15(8):1-162.
78. The Norwegian health care system and pharmaceutical system. Legemiddelverket. 2017; Available from: https://legemiddelverket.no/english/about-us/the-norwegian-health-care-system-and-pharmaceutical-system. [Accessed 03.08.2021]
79. Klein EY, Van Boeckel TP, Martinez EM, et al. Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proc Natl Acad Sci U S A. 2018;115(15):E3463-E3470. doi:10.1073/pnas.1717295115
80. Masiero G, Filippini M, Ferech M, Goossens H. Socioeconomic determinants of outpatient antibiotic use in Europe. Int J Public Health. 2010;55(5):469-478. doi:10.1007/s00038-010-0167-y
81. Filippini M, Masiero G, Moschetti K. Socioeconomic determinants of regional differences in outpatient antibiotic consumption: evidence from Switzerland. Health Policy. 2006;78(1):77-92. doi:10.1016/j.healthpol.2005.09.009
82. Piovani D, Clavenna A, Cartabia M, Bonati M; Antibiotic Collaborative Group. The regional profile of antibiotic prescriptions in Italian outpatient children. Eur J Clin Pharmacol. 2012;68(6):997-1005. doi:10.1007/s00228-011-1204-3
83. Nordqvist L, Jönsson S, Bern AB, et al. Etablering och konkurrens bland vårdcentraler – om kvalitetsdriven konkurrens och ekonomiska villkor [Establishment and competition among health centers – on quality-driven competition and economic conditions]. Konkurrensverkets rapportserie. Stockholm. 2014; (Swedish) Available from:

https://www.konkurrensverket.se/globalassets/publikationer/rapporter/rapport_2014-2.pdf. [Accessed 03.08.2021]
84. Kommunehelsa statistikkbank [Municipal Health Statistics Bank]. Norwegian Institute of Public Health. (Norwegian) Available from: http://khs.fhi.no/webview/. [Accessed 03.08.2021]
85. Godager G, Iversen T, Ma CT. Competition, gatekeeping, and health care access. J Health Econ. 2015;39:159-170. doi:10.1016/j.jhealeco.2014.11.005
86. Iversen T, Ma CT. Market conditions and general practitioners' referrals. Int J Health Care Finance Econ. 2011;11(4):245-265. doi:10.1007/s10754-011-9101-y
87. Statistisk sentralbyrå [Statistics Norway]. Available from: https://www.ssb.no/statbank/.
88. Reisetid – akuttjenester i Norge [Travel time – emergency services in Norway]. Helsedirektoratet. (Norwegian) Available from: https://reisetid.helsedirektoratet.no/felles#akuttutvalget. [Accessed 03.08.2021]
89. Sinnott SJ, Polinski JM, Byrne S, Gagne JJ. Measuring drug exposure: concordance between defined daily dose and days' supply depended on drug class. J Clin Epidemiol. 2016;69:107-113. doi:10.1016/j.jclinepi.2015.05.026
90. Merlo J, Wessling A, Melander A. Comparison of dose standard units for drug utilisation studies. Eur J Clin Pharmacol. 1996;50(1-2):27-30. doi:10.1007/s002280050064
91. The R Project for Statistical Computing. Available from: https://www.r-project.org/. [Accessed 03.08.2021]
92. Brekke KR, Holmås TH, Monstad K, Straume OR. Competition and physician behaviour: Does the competitive environment affect the propensity to issue sickness certificates?. J Health Econ. 2019;66:117-135. doi:10.1016/j.jhealeco.2019.05.007
93. Gosden T, Forland F, Kristiansen IS, et al. Capitation, salary, fee-for-service and mixed systems of payment: effects on the behaviour of primary care physicians. Cochrane Database Syst Rev. 2000;(3):CD002215. doi:10.1002/14651858.CD002215
94. Mykletun A, Torsvik G, Vaage K. Gatekeeping versus monitoring: Evidence from a case with extended selfreporting of sickness absence. Working Papers in Economics, Department of Economics, University of Bergen. 2014,
95. Yeung RY, Leung GM, McGhee SM, Johnston JM. Waiting time and doctor shopping in a mixed medical economy. Health Econ. 2004;13(11):1137-1144. doi:10.1002/hec.871
96. Høye S, Gjelstad S, Lindbæk M. Effects on antibiotic dispensing rates of interventions to promote delayed prescribing for respiratory tract infections in primary care. Br J Gen Pract. 2013;63(616):e777-e786. doi:10.3399/bjgp13X674468

Paper 1

PharmacoEconomics - Open (2021) 5:187–195
https://doi.org/10.1007/s41669-020-00234-7

ORIGINAL RESEARCH ARTICLE

Can Private Provision of Primary Care Contribute to the Spread of Antibiotic Resistance? A Study of Antibiotic Prescription in Sweden

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Accepted: 1 October 2020 / Published online: 23 October 2020

Abstract

Background Growing rates of antibiotic resistance, caused by increasing antibiotic use, pose a threat by making antibiotics less effective in treating infections.

Objective We aimed to study whether physicians working at privately and publicly owned health centres differed in the likelihood of prescribing antibiotics and choosing broad-spectrum over narrow-spectrum antibiotics.

Methods To estimate the effect of ownership on the probability of a prescribed drug being an antibiotic, we analysed all 4.5 million prescriptions issued from 2011 to 2015 at primary health centres in Västerbotten, Sweden. We controlled for patient age, sex, number of prescriptions per patient, and month of prescription, and used a maximum likelihood logit estimator. We then analysed how ownership affected the likelihood of a prescribed antibiotic being broad spectrum. We also used aggregated data to estimate the impact of the number of private health centres on the number of antibiotic prescriptions per inhabitant and the proportion of broad-spectrum antibiotics.

Results Holding other factors constant, private physicians were 6% more likely to prescribe antibiotics and 9% more likely to choose broad-spectrum antibiotics. An increase by one additional private health centre was positively associated with an increase in the number of antibiotic prescriptions per inhabitant and a higher proportion, although not significant, of broad-spectrum antibiotic prescriptions.

Conclusion Our findings suggest that private physicians prescribe more antibiotics, especially broad-spectrum antibiotics, than public physicians. Therefore, it is crucial to provide health centres with incentives to follow guidelines for antibiotic prescription, especially when the level of private provision of primary healthcare is high.

Key Points for Decision-Makers

We found that physicians working at privately owned health centres were 6% more likely to prescribe antibiotics than physicians at publicly owned health centres. In addition, the former were 9% more likely to choose a broad-spectrum antibiotic when prescribing any antibiotic. These results were obtained by controlling for other factors such as patient characteristics.

It may be especially important to monitor antibiotic prescription at private health centres and to give them economic incentives to adhere to guidelines for antibiotic prescription.

David Granlund and Yana V. Zykova contributed equally and share first authorship.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s41669-020-00234-7) contains supplementary material, which is available to authorized users.

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1 Introduction

Antibiotics introduced into a specific environment exert selective pressure on the bacterial populations inhabiting that environment. This gives an advantage to antibiotic-resistant bacteria which survive, reproduce, and can spread further. Antibiotic resistance (AR) is growing rapidly due to the intensive use of antibiotics, making these drugs increasingly less effective in treating infectious diseases. AR poses a significant threat to current and future generations [1].

The problem of inappropriate antibiotic prescription is especially relevant in primary care because the majority of antibiotic prescriptions are for respiratory tract infections (RTIs), which are frequent diagnoses in primary care; however, the cause of most RTIs is viruses, for which antibiotics are ineffective. Fleming-Dutra et al. [2] found that almost half of the antibiotic prescriptions for RTIs in the US were evaluated as inappropriate. There are many possible reasons why antibiotics are prescribed even when they are ineffective. For example, patients' impatience and limited knowledge may increase their readiness to receive antibiotic treatment. They may consider the doctor's willingness to prescribe antibiotics as a characteristic of quality and care [3, 4]. This is especially relevant for countries with restricted over-the-counter sales of these pharmaceuticals. If uninformed patients demand antibiotics for non-bacterial infections, and if the profitability of a healthcare centre depends on the number of patient visits, competition between these centres may create incentives to overprescribe antibiotics [5–7].

Previous research has shown that such economic incentives may play an important role in physicians' medical decision making [8]. However, there are not many studies on the effect of economic incentives on prescription of antibiotics. Notable exceptions are Hutchinson and Foley [9], Fogelberg [10], and Ellegård et al. [11]. Hutchinson and Foley found that physicians working under fee-for-service in Newfoundland, Canada, prescribed significantly more antibiotics than salaried physicians. Using aggregated Swedish data, Fogelberg found that stronger competition between healthcare providers significantly increased the number of antibiotic prescriptions as long as the provider was not required to pay for the prescribed drugs. Using yearly data on the consumption of pharmaceuticals by Swedish children, Ellegård et al. found that reimbursement schemes based on antibiotics-related pay-for-performance indicators stimulated more appropriate antibiotic prescription.

In this paper, we focus on the effect of type of ownership of healthcare centres on the prescription of antibiotics. Silverman et al. [12] and Devereaux et al. [13] found a significant positive correlation between the proportion of profit-driven hospitals and health expenditure, while Kessler and McClellan [14] found that private hospitals with profit incentives had significantly lower costs than non-profit hospitals for treating heart attack, controlling for treatment quality. The latter indicates that private provision of health care can increase efficiency. Granlund [15] found that private doctors were more likely to disallow generic substitution. More recently, Ellegård [16] studied how pay-for-performance incentives affected primary care providers' compliance with hypertension drug guidelines and found that private providers reacted more strongly to the economic incentives. To our knowledge, there are no studies to date addressing the impact of ownership of healthcare centres on the prescription of antibiotics.

The ability of private health centres to pay salaries and generate profits directly depend on the number of patients visits and patients listed at the health centre. We therefore hypothesised that private health centres have stronger incentives to please patients, and one way to do this can be to prescribe antibiotics to patients who ask for this.

The main aim of our study was to determine whether there is a significant difference between private and public primary healthcare centres in antibiotic prescription. To answer this question, we analysed prescriptions written at public and private primary healthcare centres in Västerbotten, Sweden, primarily in two ways. First, we investigated whether the probability of the prescribed drug being an antibiotic varies systematically across ownership type. Second, we tested whether there are systematic differences in the prescription of broad- versus narrow-spectrum antibiotics between private and public centres. The motivation for our second approach is that the rapid growth of AR has forced physicians to turn to more frequent prescription of broad-spectrum antibiotics. These antibiotics target a wider range of bacterial species, and hence contribute even more to the development of AR [17]. Thus, it is critical that inappropriate use of broad-spectrum antibiotics is reduced. However, patients may perceive prescription of a broad-spectrum antibiotic as a signal of high-quality healthcare because the probability of a patient being cured after the first prescription is higher in this case. Doctors' willingness to please patients based on economic incentives, together with other possible factors (e.g. diagnostic uncertainty), may motivate them to prescribe broad-spectrum antibiotics more frequently. We also analysed the impact of a new private health centre on the number of antibiotic prescriptions per capita and the share of broad-spectrum antibiotics.

2 Institutional Background and Incentives

Sweden is divided into 21 counties that are responsible for primary healthcare. Although most of the health centres are managed by the county councils, the operation of about 40% is outsourced to private providers contracted and financed by the counties [18]. Health centres are usually organised as team-based practices with general practitioners (GPs), nurses, midwives, gynaecologists, psychologists, social workers, behavioural therapists, and physiotherapists [19]. On average, there are four GPs in each health centre [18].

In 2010, Sweden implemented the System of Choice reform, aimed at increasing competition in primary healthcare by making entry to the market free for primary care providers fulfilling minimum requirements set by the county councils [20]. The System of Choice reform attracted new private providers to the market, and gave patients the free choice of registering with either a private or public provider. Patients register with a health centre rather than with a specific GP. Registration is obligatory for all residents except those from Stockholm County. If a patient does not make an active choice of provider, then he/she is listed in a public or private health centre suggested by the county council. The most common suggestion is the centre closest to the patient's residence. Although everyone in Sweden is free to choose a primary healthcare provider, only 30% choose a health centre different from the one suggested by the county [21].

Health centres should accept all new applicants and can pose only temporary restrictions on the number of patients. Patients registered at one centre can still visit GPs at other health centres [18]. Both public and private centres receive a mixture of capitation payment for registered patients (about 80%), fee-for-service (17–18%) and performance-based compensation (2–3%) for achieving different targets for quality [18]. In Västerbotten, capitation payments for registered patients constituted 87% of reimbursement to health centres.

Västerbotten County, located in the north of Sweden, is the second largest county, in terms of area, in the country, and consists of 15 municipalities. There are about 260,000 inhabitants in the county, 45% of whom live in the municipality of Umeå. At the beginning of our study period from 2011 to 2015, there were 6 private and 32 public health centres in Västerbotten, but in March 2014 a new private health centre opened in the municipality of Umeå. The proportion of private health centres in Västerbotten is much lower than that at the national level, which may partly be because the requirements that primary care providers have to fulfil to enter the market are higher in this county than in most other counties. For example, each health centre must offer its patients maternity care, children's care, and rehabilitation services [22, 23]. The high requirements also reduce the heterogeneity across health centres by restricting entry for health centres with limited services. Moreover, the listing system in Västerbotten has been criticised because, after the System of Choice reform was introduced in 2010, patients who did not make an active choice of provider stayed on the list of their previous health centre [24]. This principle created difficulties for new private providers because they had to start their practice with no patients on the list, and their ability to pay salaries and generate profits directly depend on capitation and payments for patient visits. Therefore, we hypothesised that private health centres have more incentives to attract new patients by pleasing them.

3 Methods

3.1 Data

To test our hypotheses, we used a dataset containing all fillings of prescriptions written at health centres in Västerbotten County from January 2011 through December 2015 and dispensed by Swedish pharmacies until April 2016. The dataset consists of approximately 11 million observations and includes a large number of variables, such as the patient's age at the time of drug prescription, sex, and area of residence. The information about each prescription includes the date of prescription and the workplace of the prescriber.

After excluding prescriptions written by health professionals other than physicians (e.g. nurses) and those with missing information, e.g. the Anatomical Therapeutic Classification (ATC) code, about 10 million observations remained. A large proportion of drugs was prescribed with an option for repeat purchases. As we were interested in analysing physicians' prescription decisions, we removed all repeat fillings and arrived at a dataset of 4,596,194 observations.

3.2 Empirical Models

3.2.1 Model 1 for the Effect of Ownership on Antibiotic Prescription

In the analysis of whether the type of health centre ownership affected the frequency of antibiotic prescription, we included all prescriptions (antibiotic and non-antibiotic) and estimated the effect of ownership on the probability of a prescribed drug being an antibiotic. The dummy variable Antibiotic was defined to equal one when the drug belonged to the 'J01—Antibacterial drugs' group according to the ATC classification, with methenamine (J01XX05) excluded. Methenamine is not considered an antibiotic but is rather an antiseptic substance that has no influence on AR [25]. Based on workplace information, we created the dummy variable Private, which indicates whether the primary centre was private or public. Health centres may significantly differ in the age and sex of patients, therefore we included in the analysis a dummy variable taking the value of 1 if the patient was a

Table 1 Classification of broad- and narrow-spectrum antibiotics

Narrow-spectrum antibiotics	Broad-spectrum antibiotics
PcV (phenoxymethylpenicillin) [J01CE02]	Amoxicillin [J01CA04]
Nitrofurantoin [J01XE01]	Amoxicillin and enzyme inhibitor [J01CR02]
Pivmecillinam [J01CA08]	Doxycycline [J01AA02]
Trimethoprim [J01EA01]	Cephalosporins [J01DB + J01DC + J01DD + J01DE]
	Erythromycin [J01FA01]
	Quinolones [J01MA02 + J01MA06]

The codes in square brackets are Anatomical Therapeutic Chemical classification codes assigned by the World Health Organization

women, as well as dummy variables for patients' age groups. We grouped patients into nine age groups: 0–2, 3–6, 7–12, 13–18, 19–25, 26–45, 46–65, 66–85 and ≥ 86 years of age. Controlling for the patient's age is important because, for example, the prescription of non-antibiotic drugs to children is substantially lower than for adults.

We defined the variable Prescriptions_per_patient for each health centre each year as the total number of prescriptions divided by the number of registered patients. We used this variable to control for the fact that some health centres may systematically prescribe more drugs per patient (antibiotic and non-antibiotic), for example due to treating patients with more severe diseases. If private and county-employed physicians prescribe the same number of antibiotics per patient, but private physicians prescribe fewer non-antibiotics, then the variable Prescriptions_per_patient prevents the estimate for Private from becoming positive just because a higher share of prescriptions written by private physicians are for antibiotics. We also controlled for the municipality where the health centre was located (Muni_centre), municipality-specific linear trends (Muni_centreTrend) and dummies for 59 of the 60 months studied (YearMonth). The equation for model 1 is (Eq. 1):

$$\Pr(\text{Antibiotic}_i = 1) = F\Bigg(\alpha + \beta_1 \text{Private}_i + \beta_2 \text{Women}_i + \sum_{a=2}^{9} \gamma_a \text{Age group}_{ai} + \beta_3 \text{Prescription\_per\_patient}_i + \sum_{m=2}^{15} \delta_m \text{Muni\_centre}_{mi} + \sum_{m=2}^{15} \eta_m \text{Muni\_centreTrend}_{mi} + \sum_{y=2}^{60} \theta_y \text{YearMonth}_{yi} + \varepsilon_i\Bigg). \tag{1}$$

3.2.2 Model 2 for Differences in the Prescription of Broad- and Narrow-Spectrum Antibiotics

With the second model, we examined whether there was a systematic difference in the prescription of broad- versus narrow-spectrum antibiotics between private and public health centres. Broad is a dummy variable with a value of 1 for the medications listed as broad-spectrum antibiotics in Table 1. Our selection of specific types of antibiotics was derived from Fogelberg [10] and recommended by medical experts at the Swedish Institute for Communicable Disease Control. Some antibiotic prescriptions (about 20%) from the original dataset belong to neither the narrow-spectrum nor broad-spectrum group (in the way we defined them).

We extracted all prescriptions for antibiotics that were classified as either broad- or narrow-spectrum antibiotics according to Table 1, which gave us 152,055 observations that we applied to the equation for model 2 (Eq. 2):

$$\Pr(\text{Broad}_i = 1) = F\Bigg(\alpha + \beta_1 \text{Private}_i + \beta_2 \text{Women}_i + \sum_{a=2}^{9} \gamma_a \text{Age group}_{ai} + \sum_{m=2}^{15} \delta_m \text{Muni\_centre}_{mi} + \sum_{m=2}^{15} \eta_m \text{Muni\_centreTrend}_{mi} + \sum_{y=2}^{60} \theta_y \text{YearMonth}_{yi} + \varepsilon_i\Bigg). \tag{2}$$

A maximum likelihood logit estimator was used to estimate models 1 and 2. To examine the robustness of the results, several other estimations were performed. These are presented and discussed in the online Appendix.

Table 2 presents descriptive statistics for the variables in models 1 and 2. It shows that the proportion of prescriptions for antibiotics, in particular broad-spectrum antibiotics, is higher for physicians working at private health centres. The descriptive statistics also show that 63% of antibiotics were prescribed to women.

3.2.3 Models 3 and 4 for the Impacts of a New Private Health Centre

Models 3 and 4 were used to assess whether the number of antibiotic prescriptions per inhabitant and the proportion of broad-spectrum antibiotics prescribed were affected by the number of private health centres in the patient's municipality of residence, N_Private. We consider this variable to be a proxy for the supply of private health centre services. As the variation in N_Private was limited to the opening of one new health centre, the estimates for this variable should be viewed as results from one case study. We lacked data for N_Private for the 1% of the prescriptions that were for

Table 2 Descriptive statistics for models 1 and 2

Variable	Model 1			Model 2		
	Sample	Antibiotic	Non-antibiotic	Sample	Broad-spectrum	Narrow-spectrum
Private	16.17	16.68	16.14	16.90	18.14	16.30
Women	57.99	63.39	57.76	66.41	51.21	73.84
Prescriptions_per_patient	3.77 ± 1.00	3.70 ± 0.99	3.77 ± 1.00			
Age group 0–2	0.66	3.52	0.53	3.96	2.97	4.45
Age group 3–6	0.69	4.35	0.53	4.80	2.95	5.70
Age group 7–12	0.73	3.67	0.60	3.83	2.18	4.64
Age group 13–18	1.12	5.41	0.94	4.61	3.37	5.22
Age group 19–25	2.66	8.60	2.40	7.93	6.57	8.59
Age group 26–45	11.51	18.37	11.22	17.88	17.74	17.95
Age group 46–65	30.39	22.71	30.72	22.47	27.97	19.78
Age group 66–85	42.72	26.79	43.40	27.78	29.92	26.72
Age group ≥ 86	9.53	6.58	9.65	6.74	6.33	6.93
Municipality of the health centre						
Nordmaling	2.89	2.28	2.91	2.44	1.91	2.70
Bjurholm	1.08	0.91	1.09	0.89	0.90	0.89
Vindeln	2.49	2.33	2.49	2.36	2.40	2.34
Robertsfors	2.96	2.48	2.98	2.48	2.80	2.33
Norsjö	2.10	2.17	2.09	2.27	2.27	2.27
Malå	1.96	1.97	1.96	1.98	1.99	1.98
Storuman	3.29	3.19	3.30	3.11	3.19	3.08
Sorsele	1.49	1.83	1.47	1.87	2.21	1.70
Dorotea	1.55	1.28	1.56	1.21	1.30	1.16
Vännäs	3.03	2.75	3.04	2.69	2.32	2.87
Vilhelmina	3.62	3.89	3.61	3.77	4.53	3.40
Åsele	1.70	1.56	1.71	1.56	1.66	1.51
Umeå	40.10	41.35	40.05	41.52	41.50	41.53
Lycksele	5.98	5.97	5.98	6.05	6.12	6.02
Skellefteå	25.77	26.05	25.76	25.81	24.91	26.24
Observations	4,596,194	189,579	4,406,615	152,055	49,940	102,115

Percentages are reported for discrete variables, and means and standard deviations are reported for continuous variables. Descriptive statistics for the municipality-specific time trends and the 60-month dummies are available upon request.

patients not living in Västerbotten, and therefore excluded these prescriptions when estimating models 3 and 4. The equation for model 3 is (Eq. 3).

$$\begin{aligned}\ln\text{N\_antibiotics}_{ryas} = {} & \beta_1 \text{N\_Private}_{ry} + \beta_2 \text{Women}_s + \sum_{a=2}^{9} \gamma_a \text{Age group}_a \\ & + \sum_{r=2}^{15} \delta_r \text{Muni\_patient}_r + \sum_{r=2}^{15} \delta_r \text{Muni\_patientTrend}_{ry} \\ & + \sum_{y=2}^{60} \eta_y \text{YearMonth}_y + \varepsilon_{ryas}. \end{aligned} \tag{3}$$

The dependent variable is the natural logarithm of the number of prescribed antibiotics per resident in municipality r in year–month y of age group a and sex s. Natural logarithms were used to allow N_Private to have the same percentage effect on the number of antibiotics prescribed in demographic groups with few antibiotic prescriptions per capita as in demographic groups with many antibiotic prescriptions per capita. For each municipality of residence and each year, we chose to have separate observations for each age group × sex combination to be able to control for differences in demographic composition across municipalities and time. We also controlled for municipality of residence of the patient (Muni_patient) and municipality-specific linear trends to avoid the coefficient for N_Private to be affected by differences in health between residents of Umeå (where the new health centre was opened) and residents of other municipalities. Muni_patient was identical to Muni_centre for 95% of the prescriptions, but we chose the former because it is less risk that patients' choices of place of residence are affected by preferences for antibiotics compared

Table 3 Descriptive statistics for models 3 and 4

Variable	Model 3	Model 4
N_antibiotics	0.012 ± 0.008	
lnN_antibiotics	− 4.595 ± 0.581	
Share_broad		0.329 ± 0.198
N_Private	2.352 ± 1.937	2.080 ± 1.921
Women	49.927	66.480
Observations	13,352	12,606

Percentages are reported for discrete variables, and means and standard deviations are reported for continuous variables. For model 3, the observations were weighted by the number of inhabitants, and for model 4, the weights were the number of prescriptions classified as either broad- or narrow-spectrum antibiotics. Descriptive statistics for age groups, municipality indicators, municipality-specific linear trends and the 60-month dummies are available upon request. For model 3, descriptive statistics are not reported for the weighted share of 2% of the observations for which N_antibiotics = 0 because the dependent variable was not defined for these observations. The online Appendix shows that nearly identical results were obtained when the dependent variable was transformed so that all observations could be used in the estimation. For model 4, the number of observations is for observations with a strictly positive weight, that is, for which at least one antibiotic classified as either broad- or narrow-spectrum was prescribed. There was no missing information for model 4

with Muni_centre. Lastly, we included dummies for year × month combinations.

Model 4 included the same explanatory variables as those in model 3, but its dependent variable was $Share\_broad_{ryas}$. For each municipality of residence × year × age group × sex combination, this variable equals the number of prescriptions of broad-spectrum antibiotics divided by the total number of prescriptions classified as either broad- or narrow-spectrum antibiotics. Models 3 and 4 were both estimated with ordinary least squares (OLS). In model 3, the observations were weighted using yearly data for the number of inhabitants in each municipality × age group × sex combination, whereas the number of prescriptions classified as either broad- or narrow-spectrum antibiotics for each observation was used as weights in model 4. Table 3 presents descriptive statistics for the dependent variables and some explanatory variables in models 3 and 4. The value for the weighted share of women in model 4 means that 66% of prescriptions classified as either broad- or narrow-spectrum antibiotics were for women.

4 Results

Table 4 presents the main results for the study. For model 1, the odds of prescribing an antibiotic were 1.06 higher for private health centres than for public centres, holding all other factors constant. This result can be interpreted in absolute terms using the fact that public physicians prescribed antibiotics in about 4.10% of cases, making the odds equal to 0.0428. Then, for private health centres, the odds increased by 6% to 0.0454, which means that the probability that a prescription was for an antibiotic was approximately 4.34%. This is 0.24 percentage points higher than the probability for public health centres. In relative terms, 4.34 is 6% higher than 4.10, meaning that the probability that a prescription was for an antibiotic was 6% higher for private health centres than for public centres, holding all other factors constant. Because the proportion of antibiotic prescriptions was very low, this increase in relative risk was approximately equal to the odds ratio minus one.

We also found significant effects of demographic variables on the probability that a prescription was for an antibiotic. According to the point estimates from the logistic regression of model 1, this probability was higher for women than for men and decreased with age up to the 66–85 years age group. The estimate for Prescriptions_per_patient showed that the probability of a prescription being for an antibiotic was not significantly related to the average number of prescriptions per patient listed at the health centre.

The results for model 2 show that the odds of prescribing broad-spectrum antibiotics (versus narrow-spectrum antibiotics) were 1.14 higher for private health centres than for public centres. Public physicians prescribed broad-spectrum antibiotics in about 32.35% of the cases, making the odds approximately equal to 0.4782. Hence, the model predicted the odds for private health centres to be about 0.5451 if they had prescribed to patients with the same demographics as the patients of county-employed physicians. This means that the probability of a broad-spectrum antibiotic being prescribed was approximately 35.28%, which was 3 percentage points higher than the probability for public health centres. In relative terms, physicians in private centres were 9% more likely to choose a broad-spectrum antibiotic when prescribing any antibiotic than county-employed physicians, holding all other factors constant. The results for model 2 also showed that the probability of prescribing broad-spectrum antibiotics was lower for women and increased with age up to the 46–65 years age group.

In the online Appendix, we show that the results for models 1 and 2 are robust to using probit instead of logit estimation, to controlling for age by using the continuous variables age and age^2 instead of indicators for age groups, and to excluding municipality-specific linear trends.

Because the dependent variable in model 3 was in natural logarithms and the model was estimated with OLS, the coefficient estimates show the approximate[1] percentage impact

[1] The estimated percentage effect of a variable can be calculated using the formula $100 * [e^{B_i} - 1]$, where B_i is the coefficient estimate for the variable. For example, the estimated effect of a unit increase of *N_Private* on *N_antibiotics* is $100 * \left[e^{0.037} - 1\right] \approx 3.8$.

Table 4 Results of estimation, odds ratios for models 1 and 2, and coefficient estimates for models 3 and 4

Model	1	2	3	4
Private	1.060*** (0.008)	1.140*** (0.019)		
N_Private			0.037* (0.021)	0.013 (0.010)
Women	1.297*** (0.006)	0.337*** (0.004)	0.573*** (0.006)	− 0.236*** (0.003)
Age group 3–6	1.232*** (0.023)	0.817*** (0.035)	− 0.101*** (0.021)	− 0.031*** (0.009)
Age group 7–12	0.917* (0.018)	0.762*** (0.035)	− 0.603*** (0.020)	− 0.040*** (0.009)
Age group 13–18	0.825*** (0.015)	1.193*** (0.051)	− 0.283*** (0.020)	0.040*** (0.009)
Age group 19–25	0.516*** (0.008)	1.572*** (0.059)	− 0.430*** (0.018)	0.091*** (0.008)
Age group 26–45	0.236*** (0.004)	1.913*** (0.065)	− 0.425*** (0.017)	0.130*** (0.007)
Age group 46–65	0.108*** (0.002)	2.845*** (0.095)	− 0.223*** (0.017)	0.216*** (0.007)
Age group 66–85	0.089*** (0.001)	2.260*** (0.074)	0.338*** (0.017)	0.161*** (0.007)
Age group ≥ 86	0.095*** (0.002)	1.955*** (0.075)	0.856*** (0.025)	0.131*** (0.008)
Prescriptions_per_patient	0.997 (0.004)			
Year × Month FE	Yes	Yes	Yes	Yes
Muni_centre FE	Yes	Yes		
Muni_centre linear trends	Yes	Yes		
Muni_patient FE			Yes	Yes
Muni_patient linear trends			Yes	Yes
Observations	4,596,194	152,055	13,352	12,606
Log likelihood	− 790,026	− 89,700	− 3680	6550
R^2			0.699	0.473

The dependent variables are as follows: model 1, an indicator for the prescribed drug being an antibiotic; model 2, an indicator for the prescribed antibiotic being broad-spectrum; model 3, the natural logarithm of the number of prescribed antibiotics per resident; model 4, the proportion of antibiotic prescriptions that are broad-spectrum. Standard errors derived from asymptotic theory under the assumption of independence between observations are shown in parentheses. Estimation results for year × month dummies, fixed effects and separate linear trends for the municipality where the health centre was located (Muni_centre), and fixed effects and the separate linear trend for the municipality of residence (Muni_patient) are omitted to save space and are available upon request. *FE* fixed effects, *$p < 0.1$, **$p < 0.05$, ***$p < 0.01$

of the explanatory variables on the number of antibiotic prescriptions per capita. Hence, the estimate for N_Private indicates that one additional private health centre increased the number of antibiotic prescriptions in the municipality by nearly 4%. It should however be noted that the effect of N_Private is estimated imprecisely because of the small variation in this variable and the estimate is only significantly different from zero at the 10% significance level. The results for model 3 also show that women and the elderly received more antibiotic prescriptions than men and younger individuals.

The point estimate for N_Private for model 4 is consistent with the presence of a higher number of private health centres leading to a larger proportion of broad-spectrum antibiotic prescriptions. However, the estimate is not statistically significant, which prevents us from concluding that this is indeed the case. In the online Appendix, we show that the estimate is significant at the 10% level if the natural logarithm of $\text{Share\_broad}_{ryas}$ is used as the dependent variable instead of $\text{Share\_broad}_{ryas}$. The result for model 4 confirms the result for model 2 that women and children were less likely to be prescribed a broad-spectrum antibiotic than men and older age groups.

5 Discussion and Conclusions

Growing rates of AR, caused by increasing antibiotic use, pose a threat to current and future generations due to antibiotic drugs becoming less effective in treating infectious diseases. Therefore, it is crucial to discover the factors affecting antibiotic use. Our results are consistent with the hypothesis that the incentives for private health centres to please patients may result in more prescription of antibiotics, and, in particular, broad-spectrum antibiotics.

The results of our first model show that physicians working at private health centres were 6% more likely to prescribe antibiotics than non-antibiotic drugs compared with county-employed physicians working in non-profit health centres. This result alone does not prove that private physicians are more likely to prescribe antibiotics than county-employed physicians for similar patients because unobserved characteristics can differ systematically between patients seeking care at private health centres and those seeking care at public centres. For example, it cannot be ruled out that patients with infectious diseases are more likely, for some reason, to visit private health centres.

However, the results of model 3 show that the number of prescriptions for antibiotics increased with the number of private health centres in the municipality. This indicates that the result for model 1 is not entirely caused by patients needing antibiotic prescriptions to a greater extent choosing to visit private health centres. Instead, the results of models 1 and 3 are both consistent with physicians working at private health centres being more likely to prescribe antibiotics, all else being equal, so that an increase in the number of private health centres leads to more antibiotic prescriptions. However, other interpretations of the effects of a new private health centre are also possible. For example, a new private health centre increases competition for patients, which can affect the prescription behaviour of both public and private health centres. It can also increase access to primary care and therefore reduce the possibility that some patients refrain from seeking care.

The results from the second model show that private physicians, in addition to being more likely to prescribe antibiotics, were 9% more likely than county-employed physicians to choose broad-spectrum antibiotics. Even though a systematic variation in diagnoses between different health centres may also affect this result, we believe that the second model is much less vulnerable to these potential differences since it considers infectious diseases only. Thus, the result from the second model strengthens the support for our hypothesis that antibiotic prescription at private centres is affected by their stronger incentives to please patients.

The results also show significant difference in antibiotic prescriptions across demographic groups. Women are prescribed more antibiotics than men and this might be partly explained by women having a higher frequency of urinary tract infections, a common reason for antibiotic use [26]. In addition, according to model 3, elderly patients are prescribed more antibiotics but, according to model 1, the likelihood that a prescription is for an antibiotic is lower for elderly patients compared with younger patients. Together, these results suggest that elderly patients are prescribed more antibiotics per person, but are prescribed even more other drugs, making the proportion of antibiotic prescriptions lower for the elderly than for younger individuals.

An important limitation of this study is the lack of diagnostic information. This prevents us from drawing conclusions about the appropriateness of the antibiotic prescriptions made by county and privately employed physicians. In addition, the results of model 3 and 4 do not allow us to exclude the possibility that at least part of the differences across physician groups observed in models 1 and 2 are caused by the selection of patients. For this reason, future research should preferably be based on individual-level data on visits that includes diagnostic information, and the diagnoses should preferably be set by another physician than the prescribing physician to reduce the risk that the diagnoses set are adjusted to better motivate the prescriptions. Another limitation is that we do not have information about the prescribers' age, sex, or type of employment contract (e.g. permanent or temporary), therefore we cannot study if these factors dampen or increase the differences in prescription behaviour between private and public physicians.

The high use of antibiotics, especially broad-spectrum antibiotics, imposes a cost for society in terms of growing rates of AR. Privatisation can improve efficiency in healthcare provision. However, our results suggest that it may be especially important to monitor antibiotic prescription at private health centres, and to give these centres economic incentives to adhere to guidelines for antibiotic prescription.

Acknowledgements The authors are grateful to the County Council in Västerbotten for supplying the data used in this article, and to Øystein Myrland, Andrea Mannberg and Ilya Zykov for their helpful comments and suggestions.

Declarations

Funding Granlund acknowledges support from the Jan Wallander and Tom Hedelius Foundation and the Tore Browaldhs Foundation (Grant number P2016-0113:1). The publication charges for this article have been funded by a grant from the publication fund of UiT The Arctic University of Norway

Conflict of interest None

Ethics approval The regional ethical review board of Umeå declared that they found no ethical problem with this research project.

Consent to participate Not applicable.

Consent for publication Not applicable.

Data availability statement Subject to the appropriate ethics clearance, the dataset generated for the study is available from the authors on reasonable request.

Code availability The code is available from the authors on reasonable request.

Author contributions Both authors contributed equally to analysing the data and writing the manuscript.

References

1. Abadi ATB, Rizvanov AA, Haertlé T, Blatt NL. World Health Organization Report: current crisis of antibiotic resistance. BioNanoScience. 2019;9(4):778–88. https://doi.org/10.1007/s12668-019-00658-4.
2. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010–2011. JAMA. 2016;315(17):1864–73. https://doi.org/10.1001/jama.2016.4151.
3. Avorn J, Solomon DH. Cultural and economic factors that (mis) shape antibiotic use: the nonpharmacologic basis of therapeutics. Ann Intern Med. 2000;133(2):128–35. https://doi.org/10.7326/0003-4819-133-2-200007180-00012.
4. Ashworth M, White P, Jongsma H, Schofield P, Armstrong D. Antibiotic prescribing and patient satisfaction in primary care in England: cross-sectional analysis of national patient survey data and prescribing data. Br J Gen Pract. 2016;66(642):e40–6. https://doi.org/10.3399/bjgp15X688105.
5. Butler CC, Rollnick S, Pill R, Maggs-Rapport F, Stott N. Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. BMJ. 1998;317(7159):637–42. https://doi.org/10.1136/bmj.317.7159.637.
6. Hamm RM, Hicks RJ, Bemben D. Antibiotics and respiratory infections: are patients more satisfied when expectations are met? J Fam Pract. 1996;43(1):56–62.
7. Zgierska A, Rabago D, Miller MM. Impact of patient satisfaction ratings on physicians and clinical care. Patient Prefer Adherence. 2014;8:437. https://doi.org/10.2147/PPA.S59077.
8. Gosden T, Forland F, Kristiansen I, Sutton M, Leese B, Giuffrida A, et al. Capitation, salary, fee-for-service and mixed systems of payment: effects on the behaviour of primary care physicians. Cochrane Syst Rev. 2000. https://doi.org/10.1002/14651858.
9. Hutchinson J, Foley R. Method of physician remuneration and rates of antibiotic prescription. Can Med Assoc J. 1999;160(7):1013–7.
10. Fogelberg S. Effects of competition between healthcare providers on prescription of antibiotics. IFN Working Paper 949: Research Institute of Industrial Economics; 2013. https://www.ifn.se/wfiles/wp/wp949.pdf. Accessed 18 Sept 2018.
11. Ellegård LM, Dietrichson J, Anell A. Can pay-for-performance to primary care providers stimulate appropriate use of antibiotics? Health Econ. 2018;27(1):e39–54. https://doi.org/10.1002/hec.3535.
12. Silverman EM, Skinner JS, Fisher ES. The association between for-profit hospital ownership and increased Medicare spending. N Engl J Med. 1999;341(6):420–6. https://doi.org/10.1056/NEJM199908053410606.
13. Devereaux P, Schünemann HJ, Ravindran N, Bhandari M, Garg AX, Choi PT-L, et al. Comparison of mortality between private for-profit and private not-for-profit hemodialysis centers: a systematic review and meta-analysis. JAMA. 2002;288(19):2449–57. https://doi.org/10.1001/jama.288.19.2449.
14. Kessler DP, McClellan MB. The effects of hospital ownership on medical productivity. RAND J Econ. 2002;33(3):488–506.
15. Granlund D. Are private physicians more likely to veto generic substitution of prescribed pharmaceuticals? Soc Sci Med. 2009;69(11):1643–50. https://doi.org/10.1016/j.socscimed.2009.09.016.
16. Ellegård LM. Effects of pay-for-performance on prescription of hypertension drugs among public and private primary care providers in Sweden. Int J Health Econ Manag. 2020;20:215–28. https://doi.org/10.1007/s10754-020-09278-y.
17. Kaier K, Moog S. Economic consequences of the demography of MRSA patients and the impact of broad-spectrum antimicrobials. Appl Health Econ Health Policy. 2012;10(4):227–34. https://doi.org/10.2165/11631350-000000000-00000.
18. Mossialos E, Wenzl M, Osborn R, Sarnak D. 2015 International profiles of health care systems. The Commonwealth Fund; 2016. https://www.commonwealthfund.org/sites/default/files/documents/___media_files_publications_fund_report_2016_jan_1857_mossialos_intl_profiles_2015_v7.pdf. Accessed 18 Sept 2018.
19. Anell A, Glenngard AH, Merkur SM. Sweden: Health system review. Health Syst Trans. 2012;14(5):1–159.
20. Anell A. Choice and privatisation in Swedish primary care. Health Econ Policy Law. 2011;6(4):549–69. https://doi.org/10.1017/S1744133110000216.
21. Nordqvist L, Jönsson S, Bern A, Larsson K, Lind H. Etablering och konkurrens bland vårdcentraler—om kvalitetsdriven konkurrens och ekonomiska villkor. Konkurrensverkets rapportserie. Stockholm. 2014. https://www.konkurrensverket.se/globalassets/publikationer/rapporter/rapport_2014-2.pdf. Accessed 18 Sept 2018.
22. Anell A, Nylinder P, Glenngård A. Vårdval i primärvården: jämförelse av uppdrag, ersättningsprinciper och kostnadsansvar: Stockholm: Sveriges Kommuner och Landsting; 2012. https://lup.lub.lu.se/record/3357756. Accessed 18 Sept 2018.
23. Lundvall K, Öhlin J, Stefansdotter A. Inträdeshinder för privata vårdcentraler: Erfarenheter från valfrihetsreformen inom primärvård. Uppdragsforskningsrapport, Konkurrensverket, Stockholm. 2011. https://www.konkurrensverket.se/globalassets/publikationer/uppdragsforskning/forsk_rap_2011-4.pdf. Accessed 18 Sept 2018.
24. Uhlin G. Landstingsstyrelsens styrning, uppföljning och kontroll av primärvården inom hälsoval Västerbotten. Landstingsrevisionen Västerbottens Läns Landsting, Earnst & Young; 2011.
25. Sundvall P-D, Stuart B, Davis M, Roderick P, Moore M. Antibiotic use in the care home setting: a retrospective cohort study analysing routine data. BMC Geriatr. 2015;15(1):71. https://doi.org/10.1186/s12877-015-0073-5.
26. Smith DRM, Dolk FCK, Smieszek T, Robotham JV, Pouwels KB. Understanding the gender gap in antibiotic prescribing: a cross-sectional analysis of English primary care. BMJ Open. 2018;8(2):e020203. https://doi.org/10.1136/bmjopen-2017-020203.

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Online appendix for "Can private provision of primary care contribute to the spread of antibiotic resistance? A study of antibiotic prescription in Sweden"

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This appendix includes robustness analyses of the four models presented in the main text. The first two columns of Table A1, probit 1 and probit 2, present the results when equations 1 and 2 are estimated with a probit instead of a logit estimator. Because the logistic distribution has a variance of $\pi^2/3$, we expect the coefficient obtained using logistic regression, which is the natural logarithm of the odds ratio, to be about $\pi/\sqrt{3} \approx 1.8$ as large as the coefficient obtained using probit [1]. This is also what we see when we compare the results of models 1 and 2, reported in Table 4, with those of probit A1 and A2. For example, in the comparison of the coefficient for *Private*, we find that for model 1, it is $\ln(1.060) \approx 0.058$, which is twice as high as the coefficient for probit A1 of 0.029.

The comparison of results for model 1 (Table 4) with those for logistic A1a (Table A1) shows that the estimated odds ratio for *Private* is about one standard error larger when we control for age using *age* and age^2 instead of using the age-group indicators. However, according to model 2 (Table 4) and logistic A2a, the choice of control variable for age has nearly no effect on the estimate of *Private* for the probability of a broad-spectrum antibiotic being prescribed.

Table A1. Robustness analysis of models 1 and 2.

Model	Probit A1	Probit 2	Logistic A1a	Logistic A2a	Logistic A1b	Logistic A2b
Private	0.029***	0.078***	1.071***	1.138***	1.059***	1.136***
	(0.0)	(0.010)	(0.008)	(0.019)	(0.008)	(0.019)
Women	0.122***	-0.655***	1.323***	0.337***	1.297***	0.337***
	(0.002)	(0.007)	(0.007)	(0.004)	(0.006)	(0.004)
Age group 3–6	0.122***	-0.125***			1.232***	0.816***
	(0.011)	(0.025)			(0.023)	(0.035)
Age group 7–12	-0.050***	-0.158***			0.917***	0.764***
	(0.011)	(0.026)			(0.018)	(0.035)
Age group 13–18	-0.104***	0.095***			0.826***	1.196***
	(0.010)	(0.025)			(0.015)	(0.051)
Age group 19–25	-0.366***	0.249***			0.516***	1.577***
	(0.009)	(0.022)			(0.008)	(0.059)
Age group 26–45	-0.763***	0.372***			0.236***	1.931***
	(0.009)	(0.020)			(0.004)	(0.065)
Age group 46–65	-1.120***	0.614***			0.108***	2.878***
	(0.008)	(0.019)			(0.002)	(0.096)
Age group 66–85	-1.200***	0.466***			0.089***	2.263***
	(0.008)	(0.019)			(0.001)	(0.074)
Age group ≥ 86	-1.176***	0.378***			0.095***	1.951***
	(0.009)	(0.022)			(0.002)	(0.075)
Prescriptions_ per_patient	-0.001		0.998		0.992**	
	(0.002)		(0.004)		(0.004)	
Age			0.931***	1.047***		
			(0.000)	(0.001)		
Age^2			1.0004***	0.9996***		
			(0.000)	(0.000)		
Year × Month FE	Yes	Yes	Yes	Yes	Yes	Yes
Muni_centre FE	Yes	Yes	Yes	Yes	Yes	Yes
Muni_centre time trends	Yes	Yes	Yes	Yes		
Observations	4,596,194	152,055	4,596,194	152,055	4,596,194	152,055
Log Likelihood	-733,755	-89,772	-733,721	-89,742	-733,918	-89,785

Notes*:* Coefficient estimates are reported for the probit estimations, and odds ratios are reported for the logistic estimations. The dependent variable in Probit A1, Logistic A1a and Logistic A1b is an indicator of the prescribed drug being an antibiotic. In the other three estimations, the dependent variable is an indicator of the prescribed antibiotic being broad spectrum. See also the notes to Table 4.

According to the point estimates for *age* and *age*^{2}, the probability of a prescription being an antibiotic is lowest at age 83, whereas the probability of an antibiotic prescription being for a broad-spectrum antibiotic is highest at age 60. Both these results are consistent with the estimates obtained using age-group indicators.

The results for model A1b show that excluding municipality-specific time trends makes the odds ratio for *Prescriptions_per_patient* lower and significantly different from one. In contrast, the comparison of the estimates for models 1 and 2 with those for models A1b and A2b shows that nearly identical results are obtained with and without municipality-specific time trends.

Tables A2 and A3 present robustness analyses of models 3 and 4. First, model lnN_antibioticsSV differs from model 3 by its dependent variable being $lnN\_antibioticsSV_{ryas} = \ln[N\_antibiotics_{ryas} * (\mathrm{N}_{ryas} - 1) + 0.5)/\mathrm{N}_{ryas}]$, where N_{ryas} denotes the number of inhabitants in municipality *r*, year *y*, age group *a*, and sex *s*. This is a transformation suggested by Smithson and Verkuilen [2] which avoids the problem of excluding a weighted share of 2% of the observations, for which *N_antibiotics* = 0, from the regression when *lnN_antibiotics* is used as the dependent variable. The results for model lnN_antibioticsSM are very similar to the results for model 3.

Model lnShare_broad differs from model 4 in using the natural logarithm of *Share_broad* (instead of *Share_broad* itself) as the dependent variable. With this dependent variable, *N_Private* is allowed to have the same percentage effect on *Share_broad* for all municipality × year × month × age group × sex combination. On the other hand, when *Share_broad* is used as the dependent variable, *N_Private* is restricted to have the same effect in percentage points on *Share_broad* for all observations, for example, to increase *Share_broad* by 0.04 both for age × sex groups that are almost never prescribed broad-spectrum antibiotics and for age × sex groups for which *Share_broad* often exceeds 0.5. For this reason, it is advantageous to use *lnShare_broad* as the dependent variable. A disadvantage in using *lnShare_broad* is that it is undefined for the weighted share of 6% of the observations in which *Share_broad* = 0. Because of this, we also present the results for model lnShare_broadSV, where the dependent variable is $lnShare\_broadSV_{ryas} = \ln\left[Share\_broad_{ryas} * (NA_{ryas} - 1) + 0.5)/NA_{ryas}\right]$. Here, NA_{ryas} is the number of prescriptions for antibiotics classified as either broad or narrow spectrum.

The estimate for *N_Private* for models lnShare_broad and lnShare_broadSV is significant at the 5 and 10% level, respectively, and shows that one more private health centre is associated with a 6% increase in the proportion of broad-spectrum antibiotics. The latter can be compared to the point estimate from model 4 of 0.013 which is 4% of the mean *Share_broad* of 0.329. That is, using *lnShare_broad* or *lnShare_broadSV*, instead of *Share_broad*, as the dependent variable results in a slightly larger predicted effect of *N_Private*, but it does not change the sign of the estimate for this or other variables reported in the tables. Using $lnShare\_broadSV_{ryas}$ instead of $lnShare\_broad_{ryas}$ decreases the standard error and reduces the coefficient estimate for *Age group 13–18*, but has only a small effect on other estimates.

Because *Share_broad* and *Share_broadSV* are fractional variables, a fractional logit estimator and a maximum likelihood estimator for a beta distribution, respectively, can also be used. In terms of marginal effects, the estimates for *N_Private* are 0.013 (SE = 0.011) and 0.014 (SE = 0.008), where the latter is significantly different from zero at the 10% level. That is, these estimators give results for marginal effects nearly identical to those from the OLS estimation of model 4. Because the coefficients for these estimators are not as easy to interpret as OLS results, they are not presented in tables but are available on request.

Models Reg_private 3 and 4 differ from models 3 and 4 in including *Reg_private* instead of *N_Private* as explanatory variable. *Reg_private* is defined as the number of patients registered at private health centres within the municipality divided by the number of patients registered at all health centres within the municipality. Similar to *N_Private*, we consider *Reg_private* to be a measure of the supply of private primary care services. *Reg_private* increases when *N_Private* increases, but *Reg_private* can also be affected by the size of private and public health centres, for example, the size in terms of the number of physicians. For a given supply, *Reg_private* is also affected by patients' choices of health centres, which makes it potentially more endogenous than *N_Private*. We only have yearly information for *Reg_private* and, therefore, aggregate the data into the municipality × year × age group × sex combination before estimating these models. At this aggregation level, *lnShare_broad* is only undefined for a weighted share of 0.5% of the observations, and we therefore use this as the dependent variable in model Reg_private 4. In model Reg_private 3, the dependent variable is the natural logarithm of the number of prescribed antibiotics per resident. The results show that the impacts of *Reg_private* are imprecisely estimated, but the estimates are positive and significantly different from zero at the 5 and 10% significance level, respectively. This indicates that different proxies for the supply of private healthcare services points in the same direction.

In model lnbroad, presented in Table A3, the natural logarithm of the number of broad-spectrum antibiotics per resident, *lnbroad*, is used as the dependent variable, and the observations are weighted by the number of inhabitants. This model estimates the total impact of *N_Private* on the number of prescriptions for broad-spectrum antibiotics – both the impact on prescription of any antibiotic and the impact on the choice of broad-spectrum drugs when prescribing antibiotics. The variable *lnbroad* is undefined for nearly half of the 16,200 observations, but the weight of these observations is only 9% because it is mainly observations with few inhabitants that have no prescription of broad-spectrum antibiotics. Still, to investigate the importance of excluding these observations, we also report the result of model lnbroadSV, where the dependent variable is $lnbroadSV_{ryas} = \ln[broad_{ryas} * (N_{ryas} - 1) + 0.5)/N_{ryas}]$. The results indicate than one additional private health centre increases prescriptions for broad-spectrum antibiotics by 10%. This estimate is expected because a unit increase in *N_Private* increases antibiotic prescriptions by 4% according to model 3 and the proportion of broad-spectrum antibiotics by 6% according to model lnShare_broad. The choice of dependent variable is found to affect the estimate for the 46–65-year age group, but to have little effect on the other estimates.

Lastly, Logistic A3 and Logistic A4 report the results obtained from logistic regressions of the same observations as analysed in models 1 and 2, but when *N_Private_centre* is used as explanatory variable instead of *Private*. An advantage with these models is that they can be estimated using all relevant prescriptions without having to transform the dependent variable. The variable *N_Private_centre* is defined as the number of private health centres in the municipality where the health centre the patient visits is located (as compared to the municipality of residence of the patient). We used this variable in Logistic A3 and Logistic A4 so that we could estimate the models also using prescriptions written in Västerbotten County for patients living outside the county. The results confirm that the supply of private primary care increases the probability that an antibiotic is prescribed and the probability that the prescribed antibiotic is broad spectrum.

Table A2. Robustness analysis of models 3 and 4.

Model	lnN_antibiotics SV	lnShare_broad	lnShare_broad SV	Reg_private 3	Reg_private 4
N_Private	0.034*	0.057*	0.056**		
	(0.020)	(0.032)	(0.027)		
Reg_private				3.479**	3.499*
				(1.578)	(1.843)
Women	0.567***	-0.641***	-0.599***	0.567***	-0.639***
	(0.005)	(0.009)	(0.007)	(0.010)	(0.013)
Age group 3–6	-0.111***	-0.179***	-0.162***	-0.118***	-0.173***
	(0.020)	(0.029)	(0.023)	(0.035)	(0.043)
Age group 7–12	-0.604***	-0.234***	-0.217***	-0.644***	-0.263***
	(0.019)	(0.032)	(0.025)	(0.033)	(0.045)
Age group 13–18	-0.286***	0.085***	0.025	-0.312***	0.047
	(0.018)	(0.030)	(0.024)	(0.033)	(0.043)
Age group 19–25	-0.422***	0.186***	0.136***	-0.446***	0.190***
	(0.017)	(0.027)	(0.021)	(0.031)	(0.039)
Age group 26–45	-0.417***	0.298***	0.239***	-0.427***	0.355***
	(0.016)	(0.024)	(0.019)	(0.029)	(0.035)
Age group 46–65	-0.214***	0.507***	0.463***	-0.226***	0.602***
	(0.016)	(0.023)	(0.019)	(0.029)	(0.035)
Age group 66–85	0.345***	0.320***	0.285***	0.335***	0.428***
	(0.017)	(0.023)	(0.019)	(0.029)	(0.034)
Age group ≥ 86	0.875***	0.294***	0.220***	0.856***	0.314***
	(0.024)	(0.027)	(0.022)	(0.042)	(0.040)
Year × Month FE	Yes	Yes	Yes		
Year FE				Yes	Yes
Muni_centre FE					
Muni_centre time trends					
Muni_patient FE	Yes	Yes	Yes	Yes	Yes
Muni_patient time trends	Yes	Yes	Yes	Yes	Yes
Observations	16,200	8,395	12,606	1,350	1,234
R^2	0.669	0.512	0.463	0.883	0.768

Note*:* Coefficient estimates are reported for all five models. For the first three models, the name of the model indicates which dependent variable is used. For the last two models, the dependent variables are *lnN_antibiotics* and *Share_broad*. See also the note to Table 4.

Table A3. Further robustness analysis of the impact of the number of private health centres.

Model	lnbroad	lnbroadSV	Logistic A3	Logistic A4
N_Private	0.092**	0.098***		
	(0.036)	(0.029)		
N_Private_centre			1.061***	1.077*
			(0.020)	(0.049)
Women	0.093***	0.084***	1.298***	0.337***
	(0.010)	(0.008)	(0.006)	(0.004)
Age group 3–6	-0.335***	-0.315***	1.232***	0.817***
	(0.038)	(0.028)	(0.023)	(0.035)
Age group 7–12	-1.025***	-0.944***	0.917***	0.762***
	(0.037)	(0.027)	(0.018)	(0.035)
Age group 13–18	-0.624***	-0.664***	0.827***	1.202***
	(0.036)	(0.027)	(0.015)	(0.051)
Age group 19–25	-0.541***	-0.576***	0.518***	1.588***
	(0.033)	(0.025)	(0.008)	(0.060)
Age group 26–45	-0.318***	-0.439***	0.236***	1.943***
	(0.031)	(0.023)	(0.004)	(0.066)
Age group 46–65	0.073**	-0.028	0.108***	2.904***
	(0.031)	(0.023)	(0.002)	(0.096)
Age group 66–85	0.520***	0.426***	0.090***	2.279***
	(0.032)	(0.024)	(0.001)	(0.075)
Age group ≥ 86	1.026***	0.907***	0.095***	1.970***
	(0.045)	(0.034)	(0.002)	(0.076)
Prescriptions_ per_patient			1.003	
			(0.004)	
Year × Month FE	Yes	Yes	Yes	Yes
Year FE				
Muni_centre FE			Yes	Yes
Muni_centre time trends			Yes	Yes
Muni_patient FE	Yes	Yes		
Muni_patient time trends	Yes	Yes		
Observations	8,395	16,200	4,596,194	152,055
Log Likelihood			-733,802	-89,728
R^2	0.638	0.574		

Note*:* Coefficient estimates are reported for the first two models and odds ratios are reported for the logistic models. The dependent variables are *lnbroad* and *lnbroadSV*, an indicator for the prescribed drug being an antibiotic and an indicator for the prescribed antibiotic being broad spectrum, respectively. See also the note to Table 4.

References

1. Verbeek, M. (2008). *A guide to modern econometrics*: John Wiley & Sons.

2. Smithson, M., & Verkuilen, J. (2006). A better lemon squeezer? Maximum-likelihood regression with beta-distributed dependent variables. Psychological methods, 11(1), 54–71. doi: 10.1037/1082-989X.11.1.54

Paper 2

Competition in primary care and prescription of antibiotics in Norway.

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Abstract

Appropriate use of antibiotics is an important strategy to combat the problem of growing antibiotic resistance rates. In order to follow this strategy, it is important to understand the determinants of antibiotic use. We analyse the potential link between competition among general practitioners (GPs) and regional antibiotic consumption in Norway in 2015 and 2016. We use the data about antibiotic consumption expressed by the number of prescriptions of antibiotics for respiratory tract infections (phenoxymethylpenicillin (J01CE02), doxycycline (J01AA02), amoxicillin (J01CA04) and macrolides (J01FA)) per 1000 inhabitants. We apply several measures of competition previously used in the literature. Among the main measures used in the paper are the Herfindahl-Hirshman index (HHI), and the following proxies for competition applied both with and without correction for the municipality size: the number of practices, the number of available spots, the number of open lists and the number of open spots. We apply multiple regression analysis to the data mentioned above and control for socioeconomic characteristics of the municipalities. Our findings suggest a positive relationship between the number of antibiotic prescriptions and competition in the municipality according to the majority of competition measures. According to HHI, a 'perfect' competition may contribute to 34 additional antibiotic prescriptions per 1000 inhabitants compared to a monopoly. Moreover, our estimations suggest that antibiotic prescription is significantly related to the average number of consultations per patient, travel time to a pharmacy, travel time to a nearest hospital, income, and the share of women.

Keywords

Antibiotic resistance, economic incentives, salary, fee-for-service, capitation, Herfindahl-Hirschman Index (HHI)

1. Introduction

Antibiotic resistance (AR) rates have increased significantly during the last 50 years, making antibiotics less and less effective in treating infectious diseases. Widespread use of antibiotics is the main reason for such growth. Antibiotics constitute an important cure for a range of, sometimes life-threatening, diseases. However, in many cases, antibiotics are prescribed when the treatment has very little or even no effect. This is especially common in primary care in the case of Respiratory Tract Infections (RTIs). According to Fleming-Dutra *et al.* [1], almost half of antibiotics prescriptions for RTIs in the US are inappropriate. A decrease in antibiotic misuse may slow down the growing rates of AR. To accomplish a reduction in inappropriate prescriptions of antibiotics, it is important to analyse drivers of antibiotics use.

This paper tests if competition between primary care providers, more specifically, general practitioners (GPs), affects antibiotic prescription. According to economic theory, 'perfect' market competition leads to the most efficient outcomes for both buyers and sellers. However, the health market is associated with asymmetric information and could hardly be called 'perfect'. Patients usually have limited knowledge about their health condition and the potential effect of treatment. Therefore, the role of competition versus regulation for the efficiency of the health care market has always been a subject of debate. Previous research shows that competition may affect physicians' medical decision-making and their gatekeeping function [2-4]. In the case of antibiotics, competition may affect doctor's prescription behaviour in the following ways. Patients may have limited knowledge about the problem of AR or about the effectiveness of antibiotics and do not carry the full cost of their antibiotic use. Therefore, they may consider the doctor's decision to prescribe an antibiotic as a quality of care mark [5, 6]. At the same time, if doctors' reimbursements depend on the number of patients, and if the environment is competitive, willingness to attract patients may cause over-prescription of antibiotics [7-9].

To the best of our knowledge, there are only a few studies about competition and antibiotic use. Fogelberg [10] studied the effect of a competition-inducing reform implemented in Sweden, in a period between 2007 and 2010, on the prescription of antibiotics. The reform allowed patients to choose their primary care providers, increased the number of primary clinics by attracting new private providers to the market, and changed the compensation rules. Because the reform took place in different municipalities at different dates, Fogelberg conducted the difference-in-difference analysis using municipality level data. According to the study results, the competition-inducing reform increased prescriptions of antibiotics in the areas where providers did not have to pay for the prescribed pharmaceuticals. Fogelberg's study provides important insights, and the difference-in-difference approach makes it possible to identify the causal effect of the reform on antibiotics prescriptions. However, this approach does not allow measuring the relationship between market concentration and antibiotics use. In another paper, Kwon and Jun [11] studied the effect of the information disclosure policy on antibiotic prescription rates in Korea. The policy forced clinics and hospitals with more than one hundred antibiotic prescriptions for the common cold per quarter to disclose their antibiotic prescription rates. Kwon and Jun found that competition between clinics affected the policy effect size: the average prescription rates declined less in the markets with stronger competition. Kwon and Jun measured competition by the number of clinics per 1000 inhabitants. However, the number of clinics may grow proportionally with population size, i.e., areas with few clinics can have the same or even higher number of clinics per person than areas with many clinics. Therefore, it is important to account for how great is the selection of providers for the patients and, hence, how easy is it to switch from one provider to another. Bennett *et al.* [12] used the Herfindahl-Hirschman index (HHI) to study the link between competition and antibiotic use in Taiwan from 1997 to 2005 using a sample of 200,000 patients. The HHI takes into account the market share of each specific provider and shows how concentrated the market is, rather than the number of providers per consumer. The results of the study by Bennett *et al.* suggest that antibiotic use is positively correlated with the level of competition in the market. However, the study treated clinics and hospitals with the median size of 25 physicians, rather than GPs, as competitors.

In this paper, we test if competition between primary care providers affects prescriptions of antibiotics in Norway. In contrast to Bennett *et al.* [12], we measure competitions not between clinics but between GPs. This allows us to take into account both how great the selection of providers for the patients is and how homogeneous the providers are in terms of market share. We use data on antibiotic prescriptions in primary care for Norwegian municipalities in 2015 and 2016, along with data on the level of competition and other socioeconomic characteristics. In contrast to Bennett *et al.* [12], we use aggregated information about all prescriptions of antibiotic used for RTIs dispensed by the pharmacies in Norway (which reflects the residential location of the patients) and account for the availability of the health services in different municipalities. Another advantage of our approach is that nearly all antibiotics prescribed by GPs and all antibiotics dispensed by pharmacies in Norway are registered electronically, as well as over-the-counter sales of antibiotics are restricted. Moreover, Norway has a strict attitude towards antibiotic consumption, high public awareness about the AR problem, and a relatively low prevalence of AR [13, 14]. This can diminish the effect of the associated confounders in the analysis.

3. Primary health care in Norway

Municipalities are responsible for the organisation of primary care in Norway. All Norwegian residents are covered by the National Insurance Scheme (Folketrygden). GPs play a very important role in Norwegian health care system due to their gatekeeping function. They may work individually or in a primary health care centre and do nearly all initial assessments, treatment, and referrals to secondary care [4]. According to the data from Norwegian Health Economics Administration (HELFO), in July 2017, there were 4787 GPs in Norway.

In 2001, Norway implemented a reform called The Regular General Practitioners Scheme (also called the 'list-patient' system). The reform made it possible for patients to choose a personal GP and change GP twice per year. Almost all registered users (99%) actively choose a GP. The reform also allowed GPs to set the maximum length of their patient list. On average, each GP has about 1200 patients on the list [15].

The implementation of the 'list-patient' system in 2001 also changed the way GPs are reimbursed [16]. Although primary health care is still primarily funded and regulated by the central government, the 2001 reform has made the market substantially more competitive [4]. Besides the free choice of GP, another reason for the increase in competition is that most of GPs in Norway are self-employed and get a mixture of fee-for-service (FFS), capitation (CAP), and co-payments from patients. Only about 5% of GPs are salaried physicians.

The patient co-payment rate is about 15%. In 2014 the average consultation fee was 172 NOK. After reaching a certain ceiling (2185NOK (230 euro) in 2015), the patient is exempted from co-payments for the rest of the year. In 2014 the average consultation fee was 172NOK. Some groups of patients are exempted from this fee, e.g., children under 16, visits related to prenatal care, visits related to transmittable diseases that are a threat to public health [17].

4. Empirical approach

Measures of competition

Even though it is possible to choose GP at the different to the patient residence municipality, it is not common to do this [18]. Since municipalities are responsible for the organisation of primary care in Norway, we treat each municipality as a separate market. Measuring competition in primary care is challenging because there is no unique definition of competition. In the paper, we use measures of competition at the regional level suggested in the previous research on this topic.

A common measure of competition used in the literature is the number of providers [19]. Intuitively, the more providers are presented in the market – the more competitive is the environment. However, since the number of providers is a function of the population size, the number of providers says little about the supply of health services for an individual patient. Some studies, therefore, use the number of providers per capita as the measure of competition [11]. This allows to accounts for the availability of care, but a disadvantage of it is that municipalities with a small population and a single GP may appear more competitive than municipalities with a large population and many GPs. A third option is to use another classical measure of competition – the Herfindahl Index (HHI) [18]. This index considers both the size of the market in terms of the number of providers and the number of patients on a GP’s list in relation to the total number of listed patients in a municipality. HHI is defined by the formula $HHI = \sum_{i=1}^{N} s_i^2$, where s_i is the market share of GP i in a market of N GPs. In our case, the market share is calculated as the number of patients on the list divided by the total number of listed patients in each municipality. HHI varies in the interval between $\frac{1}{N}$ (when there are N equal-sized providers in the market) and one. The higher the value of HHI is, the lower is the level of competition between GPs in a municipality. In a very competitive environment, HHI is close to zero. HHI accounts both for the number of providers in the market and for how patients are distributed across them. This measure of competition provides some insight into the actual behaviour of the GPs in the municipality because equal list lengths may sign that all providers are equally involved in competing for the patients.

A common problem with all measures mentioned above is that they fail to account for the special characteristics of the Norwegian health market. In Norway, patients may not freely switch between GPs – the choice is limited by the number of providers who accept new patients (GPs with open lists). To account for this, several measures have been suggested in the literature. One of them is the macro indicator SUPPLY, previously used by Kann et al. [20], which is a dummy variable equal to one if the sum of the preferred list length of each GP in the municipality divided by the number of inhabitants is more than 1.3 and equal zero elsewhere. As in Kann et al. [20], the cut-off is based on the average supply of GPs in different municipalities, which is equal to 1.2. Since the estimation results may depend on the cut-off value, we use the number of spots per capita as an additional measure of competition. This measure and the SUPPLY account for the availability of GPs in terms of the sum of filled and open spots. Open spots on the list of GP may sign competition in the following ways. First, open spots mean that patients are able to switch between GPs. Second, the excess capacity of the list means that the GP has not reached the desired number of registered patients and, therefore, is likely willing to compete. Thus, the information about excess capacity may provide additional knowledge about actual preferences of GPs.

Other measures of cometition which account for this are the number of open spots in the municipality and the number of open spots per capita. They have previously been used by Iversen and Ma [21] to study the effects of market conditions on referrals to specialists. However, it is important to know how the available spots are distributed across GPs. To account for this, the following measures have previously been used in the literature [18, 21]: the number of open practices and the number of open practices per capita.

Data and variables

To identify the effect of competition on antibiotic consumption, we use yearly data on prescriptions of antibiotics used for RTI (phenoxymethylpenicillin (J01CE02), doxycycline (J01AA02), amoxicillin (J01CA04) and macrolides (J01FA)) processed at Norwegian pharmacies. The data covers the years 2015 and 2016 and includes patients up to the age of 79 years. Our data is on the municipality level, and we have retrieved it from the Norwegian Public Health Institute webpage [22]. During the study period, there were 428 municipalities in Norway. The data for 3 of them is missing. With 425 municipalities and two years, we have access to 850 unique observations. Prescriptions of antibiotics for patients in the inpatient settings (hospitals or nursing homes) are not included in the data.

To measure competition among GPs in each municipality, we use the data from HELFO register provided by the Norwegian Directorate of Health (Helsedirektoratet). The register contains monthly data on patient lists (number of patients on the list, maximal expected length of the list) and GP's characteristics (name, gender, municipality, reimbursement type, if the doctor is a specialist in general practice or not).

Identifying the link between competition and antibiotic prescriptions is challenging for a number of reasons. One such reason is that a range of socioeconomic, cultural, and regulatory factors may also affect antibiotic prescription rates. Norway has a homogenous regulatory system for prescriptions of antibiotics. However, the patient population differs between municipalities. We control for sociodemographic and socioeconomic characteristics of the patient population in each municipality, which are important according to the literature [23-25], such as age and gender balance, education, income, and the level of immigrants. We have collected the above-mentioned data from the Norwegian Public Health Institute webpage [22] and Statistics Norway[1].

Another challenge is that the number of antibiotic prescriptions in the data may be underestimated for municipalities with low pharmacy density [22]. In such areas, the percentage of drug delivery (including antibiotics) for acute treatment directly from a doctor's office or emergency service may be higher than in other areas (these types of deliveries are not a part of the statistics on antibiotic prescriptions). Similarly, the availability of secondary care may play an important role. On the one hand, because secondary care can sometimes serve as a substitute for primary care, the number of antibiotic prescriptions at municipalities with hospitals can be lower in the data. On the other hand, antibiotic prescriptions at the municipalities with hospitals can be higher due to better access to health care and due to after discharge prescriptions. The problems mentioned above are to some extent solved by the fact that the prescriptions are aggregated by the patient municipality of residence. However, to account for the potential differences in antibiotic prescriptions, we use travel time to the nearest hospital as a control variable. Both estimated travel time to hospital and travel time to the nearest pharmacy in different municipalities were retrieved from the Norwegian Directorate of Health webpage [26]. The data on travel time is missing for 32 (of 425) municipalities.

We also include regional fixed effects to our model to control for cultural, regulatory or other unobserved differences across the regions (there are five geographical regions in Norway: Nord-Norge,

[1] One observation is missing and therefore we had to exclude it from the analysis.

Sørlandet, Trøndelag, Vestlandet, Østlandet). We present the description of the variables (yearly municipality characteristics) included in the analysis and the descriptive statistics in Table 1.

Table 1 Description of the variables and descriptive statistics

Variable	Description	mean	SD	min	max
Antibiotics	the number of prescriptions of antibiotics used for RTIs (phenoxymethylpenicillin (J01CE02), doxycycline (J01AA02), amoxicillin (J01CA04) and macrolides (J01FA)) per 1000 inhabitants	181.078	51.302	40.203	378.267
Competition					
N providers	the number of GPs' lists in the municipality	12.747	40.052	1	523.700
N providers per capita	the number of GPs' lists in a municipality per 1000 inhabitants	1.239	1.404	0.538	19.231
HHI	Herfindahl-Hirschman Index	0.269	0.223	0.002	1
N spots per capita	the total number of spots on the GPs' lists in a municipality per inhabitant	1.188	1.167	0.707	16.304
SUPPLY	dummy variable equal to one if N spots per capita is more than 1.3 and equal zero elsewhere			762[1]	55[1]
N open spots	the total number of open spots on the GPs' lists in a municipality	823.181	2685.397	1	38319.080
N open spots per capita	the total number of open spots on the GPs' lists in a municipality per 1000 inhabitants	125.701	162.135	0.361	1175.568
N open practices	the total number of open GPs' lists in a municipality	6.480	20.942	0.083	319.200
N open practices per capita	the total number of open GPs' lists in a municipality per 10000 inhabitants	7.816	5.850	0.373	55.860
Women	percent of women	48.459	1.054	42.960	50.846
Age 0_15	percent of people of age from 0 to 4	19.605	2.386	12.173	25.786
Age16_34	percent of people of age from 16 to 34	23.759	2.344	18.026	33.111
Age35_54	percent of people of age from 35 to 54	27.804	1.748	22.459	33.612
Low_income	per cent of people in households with income below 60% of national median income, calculated by EU scale	9.170	2.058	3.900	19.700
Immigrants	percent of immigrants	9.540	3.584	1.717	25.461
Education	per cent of people over 16 with higher education	19.082	3.6284	9.900	31.500
Time to pharmacy	estimated median travel time to pharmacy in minutes	21.228	30.326	0.000	216.000
Time to hospital	estimated median travel time to hospital in minutes	59.501	51.410	2	262

Notes: 1. The number of observations is presented.

Estimation results

We present estimation results of the regression analysis in Table 2. The table includes nine specifications of the same model using different measures of competition discussed above. The results suggest that the number of antibiotic prescriptions increases with higher competition according to all competition measures. However, the link between antibiotic prescriptions and the number of open practices per capita is not statistically significant (specification 9). Specification 3 suggests that there are about 34 fewer yearly prescriptions of antibiotics for RTIs per 1000 inhabitants in municipalities with a monopoly for primary care (HHI = 1) than in municipalities with the highest level of competition (HHI $\approx$ 0). The average number of antibiotic prescriptions in municipalities with just one GP is about

145 prescriptions per 1000 inhabitants per year. Thus, with moving to the almost pure competition, this number increases by about 24 per cent.

Table 2 Estimation results of the regression model

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
ln (N providers)	9.625*** (2.128)								
N providers per capita		2.523** (1.081)							
HHI			-34.465*** (8.476)						
N spots per capita				3.973*** (1.247)					
SUPPLY					16.976*** (5.065)				
ln (N open spots)						3.279*** (1.063)			
N open spots per capita							0.033*** (0.010)		
ln (N open practices)								4.568** (2.113)	
N open practices per capita									0.020 (0.312)
Women	4.711***	6.975***	5.253***	6.844***	7.033***	6.290***	7.274***	6.138***	6.987***
	(1.727)	(1.668)	(1.710)	(1.664)	(1.662)	(1.679)	(1.664)	(1.714)	(1.680)
Age 0_15	0.182	-0.051	-0.155	-0.070	0.105	0.093	0.192	0.142	-0.031
	(0.778)	(0.783)	(0.779)	(0.781)	(0.782)	(0.782)	(0.783)	(0.788)	(0.788)
Age16_34	-1.447*	0.052	-1.032	0.040	0.081	-0.398	0.188	-0.654	-0.101
	(0.851)	(0.809)	(0.832)	(0.805)	(0.805)	(0.809)	(0.807)	(0.844)	(0.822)
Age35_54	3.501***	4.963***	3.576***	5.094***	5.295***	4.537***	5.298***	4.178***	4.568***
	(1.164)	(1.165)	(1.168)	(1.161)	(1.169)	(1.149)	(1.168)	(1.165)	(1.187)
Low_income	1.615*	1.525*	1.725**	1.545*	1.774**	1.778**	1.819**	1.601*	1.606*
	(0.823)	(0.832)	(0.826)	(0.829)	(0.829)	(0.831)	(0.830)	(0.831)	(0.834)
Immigrants	-0.547	-0.420	-0.266	-0.514	-0.322	-0.360	-0.271	-0.353	-0.212
	(0.568)	(0.576)	(0.565)	(0.575)	(0.568)	(0.569)	(0.567)	(0.573)	(0.575)
Education	-3.066***	-2.508***	-2.640***	-2.466***	-2.544***	-2.725***	-2.616***	-2.770***	-2.555***
	(0.507)	(0.499)	(0.496)	(0.498)	(0.497)	(0.501)	(0.497)	(0.509)	(0.501)
Time to pharmacy	-0.550***	-0.606***	-0.527***	-0.602***	-0.632***	-0.631***	-0.668***	-0.604***	-0.613***
	(0.064)	(0.063)	(0.066)	(0.063)	(0.063)	(0.063)	(0.065)	(0.063)	(0.065)
Time to hospital	-0.147***	-0.175***	-0.176***	-0.174***	-0.158***	-0.151***	-0.155***	-0.154***	-0.159***
	(0.038)	(0.039)	(0.038)	(0.038)	(0.038)	(0.038)	(0.038)	(0.038)	(0.039)
Year FE	yes	yes	yes	yes	yes	yes	yes	yes	yes
Region FE	yes	yes	yes	yes	yes	yes	yes	yes	yes
Year*Region FE	yes	yes	yes	yes	yes	yes	yes	yes	yes
Constant	-56.792	-232.395***	-72.850	-230.960***	-250.075***	-195.958**	-267.682***	-156.938*	-218.554**
	(94.199)	(88.309)	(94.407)	(87.918)	(88.299)	(88.120)	(88.965)	(92.429)	(90.538)
Observations	817	817	817	817	817	817	817	817	817
R^2	0.439	0.428	0.436	0.432	0.432	0.431	0.433	0.428	0.424
Adjusted R^2	0.425	0.415	0.423	0.418	0.419	0.418	0.419	0.414	0.411
Residual Std. Error (df = 797)	38.890	39.252	38.983	39.137	39.111	39.153	39.101	39.271	39.386
F Statistic (df = 19; 797)	32.789***	31.416***	32.431***	31.848***	31.946***	31.789***	31.985***	31.346***	30.919***

Notes: *p<0.1; **p<0.05; ***p<0.01. Standard errors are shown in parentheses. Estimation results for time- and region-specific fixed effects are available upon request.

With an increase in the number of providers by 1%, the number of prescriptions per 1000 inhabitants per year increases by ten units (specification 1). One additional GP per 1000 patients is associated with a three units' increase in the dependant variable (specification 2). The number of spots per capita and SUPPLY (specifications 4 and 5) is also positively associated with the antibiotic prescription rate. More specifically, we find that the number of antibiotic prescriptions per 1000 inhabitants is 17 units higher in municipalities where the number of spots per person is above 1.3 than in the rest of municipalities (specification 5). A one per cent increase in the number of open spots and the number of open practices may give up to about 3 and 5 additional prescriptions per 1000 inhabitants, respectively (specifications 6 and 8). Finally, the number of open spots per 1000 inhabitants has a positive association with the outcome variable. For example, according to the prediction in specification 7, 100 additional open spots per 1000 patients may increase the number of prescriptions per 1000 patients by three units.

Our results also suggest a significant effect of regional and other socioeconomic characteristics. A higher share of women in the region is associated with a higher level of antibiotic consumption. We do not find any significant relationship between the share of children and antibiotic prescriptions. However, all specifications predict the use of more antibiotics by people age 35 to 54 compared to the age group of 55 to 79. Previous research suggests that a higher education level is associated with a more responsible use of antibiotics [27, 28]. In accordance with this, we find that the total use of antibiotics decreases with a higher percentage of educated people in a municipality. The level of income may also serve as an indicator of patient knowledge adequacy [29]. Our results are consistent with this: we find a significant and positive relationship between the share of low-income households and antibiotic consumption in all specifications. Immigration is another important factor to consider due to various attitudes towards antibiotics among different cultures. However, we do not find any significant relationship between the share of immigrants and the use of antibiotics.

According to our estimation results, the longer it takes to travel to the pharmacy, the lower is the antibiotic prescription rate in the municipality. This result is consistent with the presumption that a higher percentage of drug delivery for acute treatment directly from a doctor's office or emergency service in municipalities with low drugstore density. However, it is also possible that patients who got an antibiotic prescription for self-limiting infections (which do not require antibiotic therapy) choose not to utilise the drug if the travel time to the pharmacy is too long. Time to hospital is also negatively associated with antibiotic prescriptions. This result does not support an assumption about hospitals being a substitute for GPs.

5. Robustness analysis

The above results may have a bias caused by the fact that some municipalities in Norway have very few or just a single provider (monopoly). In a large part of these municipalities, the providers are salaried and work for the municipality. Services provided by salaried physicians serve as a substitute to those provided by GPs with FFS contract. However, salaried GPs have no incentives to take part in the competition. Therefore, we identify the municipalities without competition (or with a weak competition) by creating a dummy variable for no competition. These are the municipalities with just one GP, municipalities with only salaried GPs or municipalities where the share of FFS contracts is meagre. As the cut-off point for the low share of FFS contracts, we choose 40 per cent. According to the data in the municipalities with the share of FFS providers less than 40 per cent, there is not more than one provider reimbursed with FFS. The analysis presented in the appendix (Table A1) shows that a difference in antibiotic prescription between municipalities without competition (according to the definition above) and the rest of the municipalities is 11 prescriptions per 1000 inhabitants per year.

However, it is further plausible that the observed effect of competition on antibiotics prescriptions is caused by FFS, rather than by GPs desire to attract patients. To see this, note that it may be time-consuming to convince patients with viral infections that they do not need antibiotics. FFS pays GPs per service and therefore incentivises doctors to provide many short consultations instead of few and lengthy consultations. Finally, some of the measures used (e.g., N providers per capita, N open practices per capita) may inflate competition in municipalities with a monopoly. To check if the results are robust, we re-run the main model (Table 2) using the data, excluding municipalities without competition (the mean share of FFS contracts in the new data is 94). We present the new results in the appendix (Table A2). When we exclude municipalities without competition from the analysis, the effect size of most competition measures increases (Table A2). For example, according to the new results, there are about 50 (instead of 34) fewer yearly prescriptions of antibiotics for RTIs per 1000 inhabitants in municipalities with a monopoly for primary care (HHI = 1) than in municipalities with the highest level of competition (HHI $\approx$ 0), while the coefficient in front of SUPPLY becomes 37 instead of 17. Thus, results from Table A2 support the hypothesis about less responsible antibiotic prescription in a more competitive environment.

In the online appendix, we also address potential collinearity problems (Tables A3 - A5). In Table A3 and Table A4, we present a correlation matrix for the specifications in the main text and a correlation matrix for specifications in Table A2, respectively. From Table A3 and Table A4, we may notice a moderate correlation between *Time to pharmacy* and *Time to hospital* and between *ln(N providers)* and *Education*. Therefore, in Table A5 we present variance inflation factors measures, which do not exceed five for the model in the main text. These measures may serve as evidence of the absence of serious collinearity problem requiring correction[2] [31].

5. Discussion and conclusions

Growing rates of AR are one of the major public health problems worldwide. Reduction in inappropriate use of antibiotics is an important strategy to tackle this problem. Therefore, the analysis of the driving forces of antibiotic misuse is critical. However, there is a lack of empirical evidence about the possible determinants of antibiotic consumption.

This paper considered an important factor from an economic perspective – competition between health care providers. It is essential to know in what way it can be beneficial or harmful for health care. Competition in a 'perfect' market should make producers more sensitive to consumers' needs and preferences. However, the health care market is characterised by asymmetric information and knowledge. Consequently, increased competition may make GPs more inclined to please patients via frivolous prescription of antibiotics, as this can increase the chance to keep existing and attract new patients. This may result in inappropriate antibiotic prescriptions.

A challenge for all studies about competition in the health care market is how to define competition accurately. We, therefore, tested our hypothesis using a wide range of proxies for competition used in the literature, such as the number of providers, the number of providers per capita, and HHI, together with other measures which take into account the Norwegian primary care market settings and are based on the number of open spots on the GPs' lists. Our findings lend some support to the hypothesis about higher antibiotic prescription rates in the municipalities with stronger competition and are consistent with the previous literature on this topic [10-12]. We found that antibiotic prescription rates are significantly higher in municipalities with stronger competition according to all measures except one, which did not show any significant effect. According to our results, the antibiotic prescription rate increases with the number of providers and their availability in terms of the number of providers per capita and the number of spots per capita. The effects of the measures mentioned above remain positive and significant if we remove from the analysis municipalities with salaried providers or a monopoly on primary care. However, none of the measures above reflects the actual behaviour of GPs and their willingness to compete. We, therefore, show that antibiotic prescription rates are likely to be higher in the markets with more equal market shares (lower HHI). Equal market shares may be a sign that all GPs put equal effort into attracting patients. On the one hand, equal effort does not necessarily mean that it is high. On the other hand, it is unlikely that everyone would put low effort in competing for the patients in an environment with many GPs (lower HHI).

[2] The variance inflation factors analysis for the models in Table A2 does not differ significantly from Table A5 and is available upon request.

Measures based on the open spots on the lists also attempt to reflect the actual behaviour or preferences of the providers because the difference between the actual and the desired list length likely means that the GP is willing to attract new patients and, therefore, to compete. Moreover, a stronger competition may be stimulated by a better possibility for the patients to switch providers, i.e. a sufficient amount of open spots in the municipality. We show that the antibiotic prescription rate increases both with the higher number of open spots and the number of open spots per capita in the municipality. It has been argued by Godager et al. [18] that it does not matter for a patient how many open spots the provider has on the list, but the fact of the availability of the GP is important. Our results show that the antibiotic prescription rate increases with the higher number of open practices (disregarding the number of open spots), while the number of open practices per capita does not significantly affect the prescriptions according to the model. However, the number of open practices per capita may not indicate the actual possibility to switch providers. For example, this possibility may be poor if there are many available providers in the municipality per capita, but they all have very few open spots.

Moreover, the number of open practices per capita does not indicate the number of providers with a list length far below the desired one, while higher excess capacity may imply higher willingness to attract patients and compete. Thus, to measure providers' actual behaviour, access to individual prescription data is preferable. It may also allow capturing the effects of changes in the excess capacity on prescriptions and account for individual characteristics of GPs (e.g. reimbursement type, age, gender) and patients (e.g. age, gender, health condition). Access to individual prescription data may also allow measuring competition based on the available providers in a certain proximity, rather than defining each municipality as a separate market. This is important to account for, given that patients can potentially choose GPs outside the municipality of residence. Such distance-based measure of competition has previously been used by Godager et al. [18] to study the effect of competition on referrals to speciality care. They defined HHI for each specific GP in the following way. For each GP a geographical area with a radius of 10 km has been defined (a GP's circle). A GP is supposed to compete only with the GPs whose circles overlap with this GP's circle.

As discussed above, measures based on the number of open spots/lists are challenging to use on the aggregated level. In addition, the lack of open spots in the municipality does not guarantee a full list for each specific provider and does not prevent them from losing patients because patients are allowed to choose a GP outside the municipality of residence, and since new practices can be established to meet patients' demand for health care. Therefore, we believe that measures based on the number of providers (including HHI) are more reliable in measuring competition at the aggregated level. These measures do not indicate the real effort of GPs, but they show how favourable the conditions for the competition are. Even though the use of individual prescription data along with the diagnostic information would be beneficial, we believe that a considerable difference in antibiotic consumption between the municipalities found using aggregated data along with a relatively low level of antibiotic consumption (including misuse) in Norway may still serve as an argument in favour of competition being an important determinant of antibiotic consumption.

Thus, our results suggest that competition in primary care may indeed be one of the factors contributing to the problem of growing AR rates and antibiotic misuse, and that policies aimed to improve antibiotic prescription in primary care may be needed. The design of such policies may be, to some extent, based on our findings. It could be important to consider increasing the share of contracts with fixed salaries and limiting the maximum list length. Another way of approaching the problem is by implementing antibiotic-related pay-for-performance indicators in general practice. Moreover, policies should target not only GPs, but patients as well. There is a need for educational campaigns among patients about the indications for antibiotic treatment and both individual and societal effects of antibiotic use. Another thing that may be important to consider is reducing the co-payment rates for the follow-up appointment for infectious diseases, especially RTIs. In this case, patients would not feel left without attention if an antibiotic is not prescribed immediately, and GPs would have more room for control over the patient's condition.

References

1. Fleming-Dutra, K.E., Hersh, A.L., Shapiro, D.J., Bartoces, M., Enns, E.A., File, T.M., et al.: Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010-2011. Jama, 315(17), 1864–1873 (2016). doi:10.1001/jama.2016.4151.

2. Kann, I. C., Bjørn, E., Lurås, H.: Competition in general practice: prescriptions to the elderly in a list patient system. Journal of health economics, 29(5), 751-764 (2010). https://doi.org/10.1016/j.jhealeco.2010.07.004

3. Scott, A., Shiell, A.: Analysing the effect of competition on general practitioners' behaviour using a multilevel modelling framework. Health economics, 6(6), 577-588 (1997). https://doi.org/10.1002/(SICI)1099-1050(199711)6:6<577::AID-HEC291>3.0.CO;2-Y

4. Brekke, K. R., Holmås, T. H., Monstad, K., Straume, O. R.: Competition and physician behaviour: Does the competitive environment affect the propensity to issue sickness certificates?. Journal of health economics, 66, 117-135 (2019). https://doi.org/10.1016/j.jhealeco.2019.05.007

5. Avorn, J., Solomon, D.H.: Cultural and economic factors that (mis) shape antibiotic use: the nonpharmacologic basis of therapeutics. Annals of Internal Medicine, 133(2), 128-135 (2000). doi:10.7326/0003-4819-133-2-200007180-00012.

6. Ashworth, M., White, P., Jongsma, H., Schofield, P., Armstrong, D.: Antibiotic prescribing and patient satisfaction in primary care in England: cross-sectional analysis of national patient survey data and prescribing data. British Journal of General Practice, 66(642), e40-e46 (2016). https://doi.org/10.3399/bjgp15X688105.

7. Butler, C.C., Rollnick, S., Pill, R., Maggs-Rapport, F., Stott, N.: Understanding the culture of prescribing: qualitative study of general practitioners' and patients' perceptions of antibiotics for sore throats. Bmj, 317(7159), 637-642 (1998). https://doi.org/10.1136/bmj.317.7159.637.

8. Hamm, R.M., Hicks, R.J., Bemben, D.: Antibiotics and respiratory infections: are patients more satisfied when expectations are met? Journal of Family Practice, 43(1), 56–62 (1996).

9. Zgierska, A., Rabago, D., Miller, M.M.: Impact of patient satisfaction ratings on physicians and clinical care. Patient preference and adherence, 8, 437 (2014). doi:10.2147/PPA.S59077.

10. Fogelberg, S.: Effects of competition between healthcare providers on prescription of antibiotics. IFN Working Paper 949: Research Institute of Industrial Economics. (2013). http://www.ifn.se/wfiles/wp/wp949.pdf. Accessed 18 Nov 2020

11. Kwon, I., Jun, D.: Information disclosure and peer effects in the use of antibiotics. Journal of health economics, 42, 1-16 (2015). https://doi.org/10.1016/j.jhealeco.2014.10.008

12. Bennett D, Hung C-L, Lauderdale T-L.: Health Care Competition and Antibiotic Use in Taiwan. The Journal of Industrial Economics, 63, 371– 393 (2015). https://doi.org/10.1111/joie.12075

13. Klein, E. Y., Van Boeckel, T. P., Martinez, E. M., Pant, S., Gandra, S., Levin, S. A., Gossens, H., Laxminarayan, R.: Global increase and geographic convergence in antibiotic consumption between 2000 and 2015. Proceedings of the National Academy of Sciences, 115(15), E3463-E3470 (2018). https://doi.org/10.1073/pnas.1717295115

14. European centre for disease prevention and control, https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-surveillance-europe-2016. Accessed 18 Nov 2020

15. The Norwegian Medicines Agency (Legemiddelverket), https://legemiddelverket.no/english/about-us/the-norwegian-health-care-system-and-pharmaceutical-system. Accessed 18 Nov 2020

16. Aasland, O. G., Rosta, J., Nylenna, M.: Healthcare reforms and job satisfaction among doctors in Norway. Scandinavian journal of public health, 38(3), 253-258 (2010). https://doi.org/10.1177/1403494810364559

17. Ringard, A., Sagan, A., Sperre Saunes, I., Lindahl, A. K.: Norway: Health system review. Health Systems in Transition, 15(8), 1-162 (2013). Retrieved from https://apps.who.int/iris/bitstream/handle/10665/330299/HiT-15-8-2013-eng.pdf?sequence=5&isAllowed=y (accessed 18 November 2020).

18. Godager, G., Iversen, T., Ma, C. A.: Competition, gatekeeping, and health care access. Journal of Health Economics, 39, 159-170 (2015). https://doi.org/10.1016/j.jhealeco.2014.11.005

19. Brekke, K. R., Gravelle, H., Siciliani, L., Straume, O. R.: Patient choice, mobility and competition among health care providers. Health care provision and patient mobility, 1-26 (2014). https://doi.org/10.1007/978-88-470-5480-6_1

20. Kann, I. C., Biørn, E., Lurås, H.: Competition in general practice: prescriptions to the elderly in a list patient system. Journal of health economics, 29(5), 751-764 (2010). https://doi.org/10.1016/j.jhealeco.2010.07.004

21. Iversen, T., Ma, C. A.: Market conditions and general practitioners' referrals. International journal of health care finance and economics, 11(4), 245 (2011). DOI 10.1007/s10754-011-9101-y

22. Norwegian Institute of Public Health, http://khs.fhi.no/webview/. Accessed 18 Nov 2020

23. Filippini, M., Masiero, G., Moschetti, K.: Socioeconomic determinants of regional differences in outpatient antibiotic consumption: evidence from Switzerland. Health policy, 78(1), 77-92 (2006). https://doi.org/10.1016/j.healthpol.2005.09.009

24. Masiero, G., Filippini, M., Ferech, M., Goossens, H.: Socioeconomic determinants of outpatient antibiotic use in Europe. International journal of public health, 55(5), 469-478 (2010). https://doi.org/10.1007/s00038-010-0167-y

25. Matuz, M., Benko, R., Doro, P., Hajdu, E., Nagy, G., Nagy, E.,Monnet, D. L., Soos, G.: Regional variations in community consumption of antibiotics in Hungary, 1996–2003. British journal of clinical pharmacology, 61(1), 96-100 (2006). https://doi.org/10.1111/j.1365-2125.2005.02525.x

26. Norwegian Directorate of Health (Helsedirektoratet), https://reisetid.helsedirektoratet.no/felles#akuttutvalget. Accessed 18 Nov 2020.

27. Wilson, A. A., Crane, L. A., Barrett, P. H., Gonzales, R.: Public beliefs and use of antibiotics for acute respiratory illness. Journal of general internal medicine, 14(11), 658-662 (1999). https://doi.org/10.1046/j.1525-1497.1999.08118.x

28. Faber, M. S., Heckenbach, K., Velasco, E., Eckmanns, T.: Antibiotics for the common cold: expectations of Germany's general population. Eurosurveillance, 15(35), 19655 (2010). https://doi.org/10.2807/ese.15.35.19655-en

29. You, J. H. S., Yau, B., Choi, K. C., Chau, C. T. S., Huang, Q. R., Lee, S. S.: Public knowledge, attitudes and behavior on antibiotic use: a telephone survey in Hong Kong. Infection, 36(2), 153-157 (2008). 10.1007/s15010-007-7214-5

30. Gjelstad, S., Straand, J., Dalen, I., Fetveit, A., Strøm, H., Lindbæk, M.: Do general practitioners' consultation rates influence their prescribing patterns of antibiotics for acute respiratory tract infections? Journal of antimicrobial chemotherapy, 66(10), 2425-2433 (2011). https://doi.org/10.1093/jac/dkr295

31. Gareth J, Daniela W, Trevor H, Robert T. An introduction to statistical learning: with applications in R. Spinger. (2013). https://doi.org/10.1111/insr.12051_19

Appendix

Robustness analysis

Table A1 Estimation results of the model comparing municipalities without competition (municipalities with only one provider, or less than two GPs reimbursed with FFS and the share of FFS providers less than 40 per cent) and the rest of the municipalities

	Dependent variable: Antibiotics
No competition	-11.458** (5.067)
Women	6.415*** (1.687)
Age 0_15	-0.130 (0.785)
Age16_34	-0.204 (0.807)
Age35_54	4.235*** (1.160)
Low_income	1.504* (0.832)
Immigrants	-0.204 (0.569)
Education	-2.485*** (0.500)
Time to pharmacy	-0.606*** (0.063)
Time to hospital	-0.153*** (0.038)
Year FE	Yes
Region FE	Yes
Year*Region FE	Yes
Constant	-187.986** (89.038)
Observations	817
R^2	0.428
Adjusted R^2	0.414
Residual Std. Error	39.260 (df = 797)
F Statistic	31.386*** (df = 19; 797)

Notes: *p<0.1; **p<0.05; ***p<0.01. Standard errors are shown in parentheses. Estimation results for time- and region-specific fixed effects are available upon request.

Table A2 Estimation results of the main model excluding the municipalities with less than 1 GP reimbursed with FFS and the share of FFS providers less than 40 per cent

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
ln (N providers)	9.665*** (2.345)								
N providers per capita		2.282** (1.104)							
HHI			- 50.443*** (12.430)						
N spots per capita				3.734*** (1.264)					
SUPPLY					36.994*** (6.607)				
ln (N open spots)						3.632*** (1.165)			
N open spots per capita							0.040*** (0.011)		
ln (N open practices)								4.917** (2.337)	
N open practices per capita									0.024 (0.335)
Women	5.240**	7.589***	5.424***	7.441***	7.441***	6.950***	7.823***	6.827***	7.629***
	(2.035)	(1.969)	(2.026)	(1.964)	(1.964)	(1.973)	(1.958)	(2.004)	(1.986)
Age 0_15	0.411	0.041	0.160	0.013	0.013	0.250	0.307	0.352	0.057
	(0.839)	(0.842)	(0.836)	(0.840)	(0.840)	(0.841)	(0.840)	(0.854)	(0.850)
Age16_34	-1.890**	-0.496	-1.696*	-0.488	-0.488	-0.848	-0.128	-1.169	-0.634
	(0.893)	(0.850)	(0.879)	(0.846)	(0.846)	(0.847)	(0.854)	(0.883)	(0.865)
Age35_54	3.168**	4.600***	2.884**	4.732***	4.732***	4.058***	4.892***	3.738***	4.155***
	(1.271)	(1.280)	(1.287)	(1.273)	(1.273)	(1.255)	(1.269)	(1.274)	(1.312)
Low_income	1.702*	1.696*	1.988**	1.706*	1.706*	1.957**	2.038**	1.749*	1.755*
	(0.886)	(0.894)	(0.888)	(0.891)	(0.891)	(0.893)	(0.892)	(0.894)	(0.897)
Immigrants	-0.614	-0.417	-0.383	-0.518	-0.518	-0.415	-0.326	-0.392	-0.202
	(0.600)	(0.606)	(0.593)	(0.604)	(0.604)	(0.598)	(0.594)	(0.604)	(0.607)
Education	-2.760***	-2.199***	-2.369***	-2.157***	-2.157***	-2.384***	-2.249***	-2.472***	-2.240***
	(0.536)	(0.526)	(0.522)	(0.524)	(0.524)	(0.525)	(0.522)	(0.537)	(0.527)
Time to pharmacy	-0.545***	-0.595***	-0.501***	-0.591***	-0.591***	-0.626***	-0.670***	-0.594***	-0.601***
	(0.069)	(0.069)	(0.072)	(0.068)	(0.068)	(0.069)	(0.071)	(0.069)	(0.070)
Time to hospital	-0.120***	-0.153***	-0.149***	-0.154***	-0.154***	-0.119***	-0.122***	-0.126***	-0.137***
	(0.041)	(0.042)	(0.041)	(0.041)	(0.041)	(0.041)	(0.041)	(0.041)	(0.041)
Year FE	yes	yes	yes	yes	yes	yes	yes	yes	yes
Region FE	yes	yes	yes	yes	yes	yes	yes	yes	yes
Year*Region FE	yes	yes	yes	yes	yes	yes	yes	yes	yes
Constant	-73.697	-248.377**	-10.000	-246.258**	-266.683**	-217.222**	-286.929***	-177.582	-234.972**
	(111.829)	(106.103)	(103.710)	(105.617)	(104.101)	(105.573)	(106.207)	(109.073)	(109.480)
Observations	743	743	743	743	743	0.398	0.401	0.393	0.390
R^2	0.404	0.393	0.403	743	0.415	0.382	0.385	0.377	0.373
Adjusted R^2	0.388	0.377	0.387	0.397	0.399	39.248	39.150	39.391	39.511
Residual Std. Error (df = 751)	39.055	39.395	39.069	0.381	38.682	25.116***	25.435***	24.659***	24.278***
F Statistic (df = 19; 751)	25.743***	24.646***	25.698***	39.275	26.980***	0.398	0.401	0.393	0.390

Notes: $^{*}p<0.1$; $^{**}p<0.05$; $^{***}p<0.01$. Standard errors are shown in parentheses. Estimation results for time- and region-specific fixed effects are available upon request.

Table A3 Correlation matrix for specifications in the main text

	ln (N providers)	N providers per capita	HHI	N spots per capita	SUPPLY	ln (N open spots)	N open spots per capita	ln (N open practices)	N open practices per capita	Women	Age 0_15	Age16_34	Age35_54	Low_income	Immigrants	Education	Time to pharmacy	Time to hospital
Women	0.45	-0.20	-0.42	-0.13	-0.14	0.22	-0.25	0.37	-0.38	1								
Age 0_15	0.27	-0.20	-0.29	-0.15	-0.17	0.06	-0.26	0.16	-0.37	0.27	1							
Age16_34	0.51	-0.09	-0.40	-0.04	-0.13	0.20	-0.22	0.45	-0.27	0.10	0.36	1						
Age35_54	0.39	-0.21	-0.38	-0.16	-0.24	0.17	-0.30	0.34	-0.36	0.22	0.20	0.04	1					
Low_income	0.02	0.15	0.03	0.13	0.03	0.00	0.00	0.06	0.13	-0.02	-0.20	0.06	-0.06	1				
Immigrants	0.40	0.05	-0.26	0.08	-0.08	0.23	-0.12	0.40	-0.07	-0.02	0.08	0.43	0.43	0.28	1			
Education	0.57	-0.18	-0.40	-0.13	-0.12	0.29	-0.20	0.51	-0.31	0.40	0.33	0.45	0.26	-0.04	0.36	1		
Time to pharmacy	-0.48	0.23	0.50	0.15	0.24	-0.09	0.42	-0.33	0.53	-0.48	-0.36	-0.25	-0.26	0.08	-0.01	-0.34	1	
Time to hospital	-0.42	0.34	0.31	0.24	0.18	-0.18	0.26	-0.33	0.51	-0.43	-0.40	-0.25	-0.26	0.11	-0.10	-0.41	0.61	1

Table A4 Correlation matrix for specifications in Table A2

	ln (N providers)	N providers per capita	HHI	N spots per capita	SUPPLY	ln (N open spots)	N open spots per capita	ln (N open practices)	N open practices per capita	Women	Age 0_15	Age16_34	Age35_54	Low_income	Immigrants	Education	Time to pharmacy	Time to hospital
Women	0.45	-0.20	-0.42	-0.13	-0.14	0.21	-0.25	0.34	-0.38	1								
Age 0_15	0.23	-0.20	-0.29	-0.15	-0.17	0.06	-0.26	0.13	-0.37	0.27	1							
Age16_34	0.52	-0.09	-0.40	-0.04	-0.13	0.18	-0.22	0.44	-0.27	0.10	0.36	1						
Age35_54	0.37	-0.21	-0.38	-0.16	-0.24	0.20	-0.30	0.33	-0.36	0.22	0.20	0.04	1					
Low_income	0.00	0.15	0.03	0.13	0.03	-0.03	0.00	0.03	0.13	-0.02	-0.20	0.06	-0.06	1				
Immigrants	0.41	0.05	-0.26	0.08	-0.08	0.24	-0.12	0.42	-0.07	-0.02	0.08	0.43	0.43	0.28	1			
Education	0.59	-0.18	-0.40	-0.13	-0.12	0.28	-0.20	0.52	-0.31	0.40	0.33	0.45	0.26	-0.04	0.36	1		
Time to pharmacy	-0.46	0.23	0.50	0.15	0.24	-0.09	0.42	-0.32	0.53	-0.48	-0.36	-0.25	-0.26	0.08	-0.01	-0.34	1	
Time to hospital	-0.44	0.34	0.31	0.24	0.18	-0.24	0.26	-0.36	0.51	-0.43	-0.40	-0.25	-0.26	0.11	-0.10	-0.41	0.61	1

Table A5 Estimation of variance inflation factors for specifications in the main text

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
ln (N providers)	2.53								
	(0.40)								
N providers per capita		1.22							
		(0.82)							
HHI			1.91						
			(0.52)						
N spots per capita				1.13					
				(0.89)					
SUPPLY					1.13				
					(0.89)				
ln (N open spots)						1.77			
						(0.85)			
N open spots per capita							1.33		
							(0.75)		
ln (N open practices)								1.89	
								(0.53)	
N open practices per capita									1.76
									(0.57)
Women	1.79	1.64	1.75	1.64	1.64	1.67	1.64	1.73	1.65
	(0.56)	(0.61)	(0.57)	(0.61)	(0.61)	(0.60)	(0.61)	(0.58)	(0.61)
Age 0_15	1.86	1.85	1.85	1.85	1.85	1.86	1.86	1.87	1.86
	(0.54)	(0.54)	(0.54)	(0.54)	(0.54)	(0.54)	(0.54)	(0.53)	(0.54)
Age16_34	2.14	1.90	2.04	1.90	1.90	1.91	1.91	2.07	1.95
	(0.47)	(0.53)	(0.49)	(0.63)	(0.53)	(0.52)	(0.52)	(0.48)	(0.51)
Age35_54	2.23	2.19	2.04	2.19	2.20	2.14	2.22	2.19	2.26
	(0.45)	(0.46)	(0.45)	(0.46)	(0.45)	(0.47)	(0.45)	(0.46)	(0.44)
Low_income	1.55	1.55	1.55	1.55	1.55	1.56	1.56	1.55	1.55
	(0.65)	(0.64)	(0.64)	(0.65)	(0.65)	(0.64)	(0.64)	(0.65)	(0.64)
Immigrants	2.24	2.26	2.20	2.26	2.21	2.22	2.20	2.23	2.23
	(0.45)	(0.44)	(0.45)	(.044)	(0.45)	(0.45)	(0.45)	(0.45)	(0.45)
Education	1.83	1.74	1.74	1.74	1.74	1.76	1.74	1.80	1.74
	(0.55)	(0.58)	(0.58)	(0.57)	(0.58)	(0.57)	(0.58)	(0.55)	(0.58)
Time to pharmacy	2.03	1.94	2.15	1.93	1.96	1.95	2.07	1.94	2.02
	(0.49)	(0.52)	(0.47)	(0.52)	(0.51)	(0.51)	(0.48)	(0.52)	(0.49)
Time to hospital	2.02	2.08	2.04	2.05	2.01	2.02	2.01	2.01	2.08
	(0.49)	(0.48)	(0.49)	(0.49)	(0.50)	(0.50)	(0.50)	(0.50)	(0.48)
Year FE	2.97	2.97	2.97	2.97	2.97	2.97	2.97	3.00	2.97
	(0.34)	(0.34)	(0.34)	(0.34)	(0.34)	(0.34)	(0.34)	(0.33)	(0.34)
Region FE	<4.15	<4.15	<4.15	<4.15	<4.15	<4.17	<4.15	<4.16	<4.15
Year*Region FE	<3.14	<3.14	<3.14	<3.14	<3.14	<3.14	<3.14	<3.14	<3.14

Notes: Tolerance is shown in parentheses. Estimation results for time- and region-specific fixed effects are available upon request.

Paper 3

Effects of 'doctor shopping' behaviour on prescription of addictive drugs in Västerbotten, Sweden

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Abstract

Free choice of health care providers is aimed to improve the quality of health care by increasing both access to it and the competition between providers. However, it may also give patients possibilities for doctor shopping (DS) behaviour, i.e., visiting different providers to receive illicit drug prescriptions. Abuse of prescribed addictive drugs is a growing problem worldwide and is associated with increased mortality, lower quality of life and other problems on both the individual and societal level. We study DS behaviour for three types of addictive drugs - opioid painkillers, benzodiazepine anxiolytics, and z-hypnotic sleeping drugs, in the outpatient care sector in Västerbotten County, Sweden. Our dataset contains all drug prescriptions purchased by the residents of Västerbotten in the period from January 2014 to April 2016 (approximately 160 thousand observations). To identify signs of addictive prescription drugs abuse by DS, we analyse overlapping prescriptions. We use Defined Daily Doses (DDDs), which is the average treatment dose of a specific drug per day for adults, as a proxy for the treatment duration. To control for medically legitimate overlaps, we compare overlapping prescriptions within a clinic with overlapping prescriptions between different clinics. Our empirical results suggest that there is a significant and positive relationship between the number of overlapping doses and the number of unique providers in the overlap. More specifically, we find that visiting different providers on average gives patients up to three additional DDDs per day. This is three times higher than the standard treatment dose. We discuss policy implications in the concluding discussion.

Keywords

Outpatient care, free choice of health care provider, switching provider, opioids, benzodiazepines, addictive prescription drugs abuse.

Declarations of interest: None

Acknowledgements

We are grateful to the County Council of Västerbotten and David Granlund for supplying the data used in this article.

1. Introduction

Addictive drugs are used to treat various health conditions, e.g. pain, sleeping disorder, panic, stress, anxiety and attention deficit disorder. Abuse of such drugs is a growing problem for both developed and developing countries and may be associated with job loss, lower productivity, reduced life quality and life expectancy, risky behaviour, domestic violence and crime [1-3]. People misuse and become addicted to drugs for several reasons. For example, inadequate knowledge may lead people to believe that medically prescribed drugs are safer and less addictive than drugs acquired on the street [4]. Moreover, patients may self-increase the dose prescribed by a doctor or start medication by using left-overs from previous prescriptions. They may also share their drugs with others or even sell them [5].

It may be challenging to detect misuse of prescription drugs and to prevent it. One way of doing this is based on the analysis of prescription register data. The aim of such analysis is to identify 'doctor shopping' (DS) behaviour. The definition of DS varies among studies and health care settings, but generally, it refers to visiting multiple health care providers to get more help or prescriptions of drugs during a specific illness episode [6]. This is a type of behaviour that patients with the demand for addictive drugs are likely to be involved in. Even though DS most often refers to addictive drugs, this phenomenon is also observed for other conditions and drug types. For example, Wang and Lin [7] defined DS as visiting multiple providers during a single treatment episode and found the DS rate to be 6.3 per cent for patients with upper respiratory infections. In a Canadian study by Macpherson *et al.* [8], the DS (visiting at least three providers) rate was estimated as 18 per cent for children with various acute symptoms.

The level of DS is closely related to the structure of the health care market. One reason for this is that the health care market is characterised by both incomplete and asymmetrically distributed information. Patients often have incomplete information about the addictiveness and the effectiveness of drugs, while doctors may find it difficult to understand how addicted the patient is or how severe the associated condition (e.g., pain, anxiety or sleeping disorder) is. This means that patients can use DS as a strategy to get more drugs to satisfy an addiction, but also that there is a risk that uninformed patients become addicted if they use DS as a strategy to get more help. Another important issue is the moral hazard, which arises when a patient's expenses are covered by insurance (public or private). When the competition between providers is high, and their income depends on the number of visits and registered patients, providers may be willing to comply with patients' demand for drugs. Moreover, when the choice of provider is unrestricted, and there is no gatekeeping function of primary care, it is easier for patients to get involved in shopping behaviour. All the problems mentioned above are exacerbated when physicians have incomplete information about the patient's prescription history or when acquiring such information is costly.

In order to find better incentives aimed to limit drug abuse by DS, it is important to study DS in different market settings. Most previous studies on DS and misuse of addictive drugs on prescription register data are from the US and focus on estimating the frequency of DS [9-12]. A few studies have also been done in France [13, 14], Australia [15] and Norway [16]. These studies have contributed with important insights on DS behaviour. For example, according to one of the studies on the US data [10], 0.3% of subjects exposed to opioids exhibited shopping behaviour. In other studies from the US, it was found that the risk of DS was higher for oxycodone than tapentadol (which has lower abuse potential) [17] and that shoppers had longer travel distances and higher opioid consumption rates compared to nonshoppers [18-20]. The studies on French data [13, 14] focused on single drug consumption and characterised shoppers by their socio-demographic characteristics. For example, they found that the number of shoppers for oxycodone has increased from 2010 to 2016 [14] and that subjects with heavy shopping behaviour for methylphenidate were significantly older than subjects with light shopping behaviour [13]. The study from Australia [15] found that patients with higher opioid consumption are more likely to visit several prescribers during a certain period of time. The Norwegian study [16] compared addictive to non-addictive drugs users and found that the latter use multiple providers less frequently.

In this study, we measure the relationship between DS behaviour and the amount of addictive drugs consumed by patients using data on outpatient prescriptions from Västerbotten County, Sweden. Our analysis is based on the three most significant categories of addictive drugs by their treatment indication: opioid painkillers, benzodiazepine anxiolytics, and z-hypnotic sleeping drugs. Most previous research on the relationship between DS and drug use to a large extent rely on the use of descriptive statistics to identify individuals with signs of DS behaviour in order to find the frequency of DS. We make use of the panel structure in the data and estimate multivariate regression models to measure the effect of the number of providers involved in DS and the amount of drugs used by shoppers, where we control for unobserved individual effects.

To the best of our knowledge, there is only one study by Schneberk *et al.* [20] using a similar approach. This study found that shoppers had higher aggregated opioid consumption than nonshoppers. However, nonshoppers may systematically differ from shoppers due to less severe diseases/conditions and hence have lower demand for drugs and, by default, lower consumption level. To solve this problem, Schneberk *et al.* used a sub-sample of patients with consumption above a certain level in the group of nonshoppers. However, there are no formal criteria for choosing this level. As a consequence, the selection can create a bias which leads to inaccurate and misleading estimations. Moreover, Schneberk *et al.* do not make full use of the information in register data and define DS as having prescriptions from different providers during a certain period. However, visiting different providers to get a prescription of addictive drugs is not necessarily a sign of drug abuse and may be legitimate, e.g. if a permanent prescriber is currently unavailable. The use of prescription databases allows, to some extent, distinguishing between the legitimate use of drugs from DS. To do this, we base our study on identifying overlapping prescriptions in the data. This approach allows finding if drugs supplied by different prescribers have been consumed simultaneously. Usually, having overlapping prescriptions from at least two different prescribers is considered to be a sign of DS behaviour [21].

A common problem for studies using register data on prescriptions is that these registers rarely include information about the intended treatment duration or the length of the supply period for a specific prescription. This makes it difficult to identify overlapping prescriptions. To overcome this problem, researchers have to make assumptions about a prescription length based on the type and amount of drug as well as on treatment guidelines [22]. The most used [23] and preferred [24] proxy for treatment duration is based on the number of defined daily doses (DDDs).

The DDD has been established in order to compare the consumption of different drugs from the same therapeutic class and is an average maintenance dose for adults when used for the main indication of the drug [25]. However, the use of DDDs to calculate treatment duration has limitations. For example, according to Nielsen *et al.* [26], DDD does not accurately reflect the actual consumption of opioids in the treatment of chronic pain. The use of DDDs may be especially problematic when there is a high variation in diagnoses, weight, type of drug used, and other individual patient-prescriber characteristics. This may result in an inaccurate estimation of the overlaps, especially if there is a high variation in diagnoses, weight, type of drug used, and other individual patient-prescriber characteristics. Moreover, some overlaps may occur when a patient change provider or visit a new provider to renew a prescription a few days prior to the expiration of the old one given by a temporary unavailable permanent prescriber. Therefore, even when prescriptions from different providers overlap, this overlap may be medically legitimate. To overcome this problem, we focus solely on episodes when an overlap occurred and test if individuals with overlapping prescriptions from different providers have access to more addictive drugs than individuals with overlapping prescriptions from the same provider.

Thus, the main difference of our study from previous research is that we do not give patients initial attributes based on their participation in DS (which may be inaccurately defined) but attempt to distinguish between legitimate use of drugs and DS. We analyse only events when an overlap happened, which allows us to exclude cases when patients consume drugs sporadically and in low or standard doses. Moreover, we analyse the effect of DS on drug consumption at every single day of the overlap, rather than on aggregated consumption level.

Another important contribution of our study is that we analyse all types of drugs within a given drug category together. According to medical guidelines [27, 28], different types of drugs within a given category of opioid painkillers, benzodiazepine anxiolytics, and z-hypnotic sleeping drugs should not be used together. However, overlaps between different drugs do occur. In some cases, overlaps within a drug category can indicate legitimate use, e.g. if one type of opioid has been substituted by another in a treatment regimen. However, within-category overlaps can also indicate drug abuse. All previous studies analyse DS behaviour mainly for a single drug. Our approach allows us to retrieve more information that may indicate drug abuse.

Finally, Sweden represents an interesting case itself. All prescriptions of addictive drugs purchased by patients are included in the data, while, for example, in the US, there is no universal electronic registration system and mandatory registration of prescriptions, and where many physicians are unwilling to spend extra time and effort checking the history of drug overuse by a patient [29]. No studies with similar methodology and research question have been done for the countries with health care settings similar to the Swedish. On the one hand, it is a relatively regulated health market in terms of rules for drug prescriptions and health care services. On the other hand, the Swedish health care market is relatively liberal because patients can freely choose and switch between different healthcare providers.

2. The Swedish health care setting

In Sweden, patients can get prescriptions for addictive drugs via three channels in the outpatient care sector: primary care, outpatient specialist care and after-hours care [30]. Electronic records about prescriptions are held in both inpatient and outpatient care, and medical practitioners may see the prescriptions made by other prescribers [30]. The electronic registration of all prescriptions is unified and mandatory all over the country.

The primary care sector is coordinated on the municipal level and is provided by health care centres. These centres are team-based practices, including general practitioners (GPs), nurses, gynaecologists, midwives, psychologists, social workers, and physiotherapists [31]. On average, there are 4-5 GPs in a primary care centre [30]. GPs are paid a salary that depends on the region, provider, experience and professional abilities [32]. Centres are reimbursed with a mixture of capitation (60-95%), fee-for-service (5%–38%) and performance-based payments (0-3%) [30].

The Swedish primary care market is relatively competitive [30]. Although all primary health care centres are publicly funded, they can be both publicly and privately owned. Patients are free to choose their primary care provider and can change it as often as they want. There is no registration required in order to visit a specific provider [33]. Patients register with a specific centre rather than a GP, and the centres should accept all new patients but may pose temporary restrictions on their number. There is no regulation prohibiting medical practitioners from having a private practice outside the primary care centre or public hospitals (for those who are specialists) unless the employer has established such rules [30].

All Swedish residents are covered by mandatory and uniform health insurance, which includes pharmaceutical insurance. Those who are over 20 have to pay a consultation fee (co-payment) which is about €20 in Västerbotten [34]. Patients are required to cover parts of their health care costs up to a limit of out-pocket payments, which is about €115 for outpatient care [35] and €200 for prescribed medications [36] in Västerbotten per year. After the limit has been reached, all further costs are covered by the health insurance with some exceptions. For example, specific drugs may not be included in the benefit scheme, while some drugs may always be free of charge for the patient [37].

GPs are usually the first point of contact, but they do not have a formal gatekeeping function. Patients may visit outpatient specialist care without any referral and are free to choose a specialist. These departments are usually located at the hospitals, and the physicians are salaried. To limit overuse of outpatient specialist care, patients have to pay a fee that is three times higher than for visiting a GP at a health care centre. However, this rule is valid only until a patient has reached the annual limit of out-pocket payments [30]. Specialist care visits with the referral from a GP are free of charge.

After-hours care is provided by primary care providers. Primary care centres collaborate with each other in order to organise such services. The co-payment rate for such consultations is the same as for visits to primary care centres during regular hours. To reduce the load on emergency care in hospitals, urgent care centres may be open during the day time as well [30].

3. Empirical approach

3.1. Data

We use data about prescriptions made by Swedish health care providers to the residents of Västerbotten County from August 2012, purchased by them in Swedish pharmacies and billed[1] in a period from

[1] We have access to the prescriptions made from 2010. However, due to an inconsistency with IDs of the patients we had to shorten the time period where we can follow all the patients. This issue with patient ID relates to the billing date (when the county got the datafiles) rather than purchase date, which is highly correlated with the purchase date.

January 2014 to April 2016. The dataset consists of approximately 160 thousand observations. Prescriptions made at the inpatient setting of hospitals and nursing homes are not included in the data [38]. Each line in the data contains information about the date of prescription and purchase, ID and name of the prescriber's workplace (at the department level for outpatient specialist care within hospitals), and ID of the patient (anonymised), age, gender. Finally, we have information about the prescribed drug, such as the Anatomical Therapeutic Chemical (ATC) classification code and the number of DDDs prescribed. The data does not contain information on the dispensing pharmacy or information about diagnoses.

In the data about prescriptions, we have removed prescriptions without ATC code and prescriptions without patient ID. We have created three datasets according to the type of addictive drug by its treatment indication and according to the ATC code. Table 1 presents addictive drugs used in outpatient care in Sweden, which we have taken to the analysis divided by their medical indication, such as painkillers (opioids), sleeping medicine and central nervous system (CNS) depressants/anxiolytics.

Table 1. Classification of the drugs included in the analysis

Indication	ATC (Anatomical Therapeutic Chemical) classification
Painkillers	Opioids, N02A (all, excluding Oripavine derivatives, N02AE and Diphenylpropylamide derivatives, N02AC)
Sleeping medicines	Hypnotics and sedatives, N05C (Benzodiazepine related drugs, N05CF)
Anxiolytics	Anxiolytics, N05B (Benzodiazepine derivatives, N05BA)

3.2. Calculation of the overlaps

We identify the overlaps between prescriptions in the following steps. First, we use the date of purchase in combination with the number of DDDs in a prescription to calculate the periods of consumption/supply for each prescription. We thereafter create a panel dataset for each drug category, where each observation represents one day of supply of a specific drug by ATC5[2] for a single patient

[2] ATC5 refers to the last level of the ATC classification, where the ATC code contains 7 digits.

and single clinic. For each day of supply, the number of DDDs given by one prescription is 1. In the third step, we aggregate the data over each consumption day for each patient to calculate the total number of DDDs and the number of unique providers in an overlap. We combine this data with patient information, such as gender, age and municipality. We also include information about the number of unique drug types according to the ATC5 code for each consumption day because patients might consume different types of drugs in each category from Table1 simultaneously or switch drugs in time. These drugs types are presented further in the descriptive statistics. This procedure gives us three datasets: 1) painkillers, 2) anxiolytics, and 3) sleeping drugs. Each dataset only contains days with overlaps between different prescriptions (DDDs > 1). The illustration of the overlaps and an example of data modifications are presented in Figure 1.

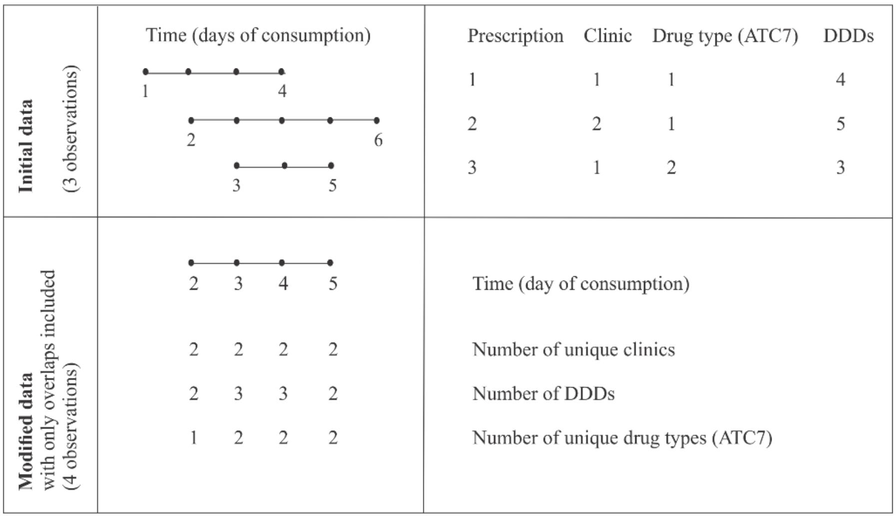

Figure1. Calculation of the overlaps (example). Three prescriptions (1, 2, and 3) for the same individual from the initial dataset have purchase dates 1, 2 and 3, respectively. Given the number of DDDs prescribed (4, 5 and 3, respectively), the consumption period has been calculated for each of the prescriptions, such that the end of consumption dates are equal to and 4, 6 and 5, for prescriptions 1, 2 and 3, respectively. The modified dataset consists of information about four days of consumption (2, 3, 4 and 5) – days when at least two prescriptions overlap.

It should be noted that some of the prescriptions in the original dataset (prescriptions of a single drug (based on ATC5) made on the same day in the same clinic for the same patient) are represented by several transactions. These repeated transactions constitute 4.7%, 1.5% and 0.2% of all observations for opioid painkillers, anxiolytics and sleeping drugs, respectively, and might happen due to, e.g. different formulations prescribed, brand names of the purchased packages, prices or co-payment rates. However, according to the personal communication with GPs in Västerbotten, this is unlikely to happen due to visiting multiple prescribers in the same clinic. We treat such repeated observations as one and use the sum of the DDDs to calculate the length of the prescription.

3.3. Empirical specification

Our aim is to test if DS behaviour is associated with drug misuse, i.e. if overlapping prescriptions to the same person from different health prescribers result in a higher number of DDDs than overlaps within one prescriber. To do this, we estimate a model where we regress the number of unique prescribers (starting from one) in an overlap on the number of DDDs consumed on a single day. We carry out our analysis on each drug category separately. Since the number of DDDs consumed may vary systematically with age and gender, we include controls for these characteristics. We also include patient municipality in the model because the choice of and access to health care providers may depend on patient location. To control for potential differences between different types of drugs within an ATC5 drug category and other non-observable confounders, we estimate the model using individual-specific effects and year fixed effects. In addition, to deal with the fact that some drugs within a group (according to their treatment indication) may be used simultaneously, we include the number of unique drugs by ATC5 in the overlap as an explanatory variable. Our estimation model is represented by equation (1).

$$\begin{aligned} DDDs_i = F(\alpha &+ \sum_{n=2}^{N} \gamma_n Number\ of\ unique\ prescribers\ involved_{ni} \\ &+ \sum_{l=2}^{L} \delta_l Number\ of\ unique\ drugs\ by\ ATC5_{li} + \beta_1 Age_i + \beta_2 Age^2{}_i \\ &+ \beta_3 Women_i + \sum_{m=2}^{15} \theta_m Municipality_{mi} + \sum_{y=2}^{3} \mu_y Year_{yi} + \varepsilon_i). \end{aligned} \qquad (1).$$

4. Results

4.1. Descriptive statistics

We present the incidence of shopping behaviour, measured as the frequency of overlaps caused by multiple prescribers (more than one), in Table 2.

Table 2. Incidence of shopping behaviour.

	(1) Number of subjects exposed to the drug			(2) Number (%) of subjects with shopping behaviour[4]			(3) Percentage of days with shopping behaviour for shoppers		
	P[1]	A[2]	S[3]	P	A	S	P	A	S
Total	20473	4503	14586	777 (3.8)	94 (2.09)	623 (4.27)	7.93	14.30	10.59
Gender									
Men	9207	1684	5126	361 (3.9)	43 (2.6)	266 (5.2)	8.16	12.10	8.16
Women	11266	2819	9460	416 (3.7)	51 (1.8)	357 (3.8)	7.74	16.80	7.74
Age									
<18	220	82	35	1(0.45)	1 (1.22)	1 (2.86)	15.20	6.94	15.20
18-25	1349	177	563	21(1.56)	4 (2.26)	13 (2.31)	6.04	11.00	6.04
26-35	1941	358	1141	71(3.36)	11 (3.07)	29 (2.54)	6.88	27.40	6.88
36-45	2371	416	1459	83 (3.50)	10 (2.40)	58 (3.98)	5.02	13.60	5.02
46-55	3319	541	2067	130 (3.92)	15 (2.77)	81 (3.92)	7.87	19.40	7.87
56-65	3698	674	2714	145 (3.92)	11 (1.63)	130 (4.79)	8.25	11.60	8.25
66-75	3846	857	3289	174 (4.52)	20 (2.23)	173 (5.26)	9.19	7.93	9.19
76-85	2910	926	3040	115 (3.95)	14 (1.51)	114 (3.75)	9.96	12.30	9.96
86+	1583	656	1477	50 (3.16)	8 (1.22)	32 (2.17)	4.70	13.40	4.70
Municipality									
Nordmaling	654	119	427	31 (4.74)	4 (3.36)	13 (3.04)	7.02	15.30	7.02
Bjurholm	214	63	153	9 (4.21)	1 (1.59)	9 (5.88)	8.41	14.30	8.41
Vindeln	480	104	404	17 (3.54)	4 (3.85)	17 (4.21)	8.55	7.88	8.55
Robertsfors	595	90	377	21 (3.53)	0 (0.00)	13 (3.45)	9.30	-	9.30
Norsjö	360	90	255	12 (3.33)	1 (1.11)	8 (3.14)	7.25	12.90	7.25
Malå	400	67	234	18 (4.50)	1 (1.49)	11 (4.70)	6.62	2.87	6.62
Storuman	689	128	319	32 (4.64)	5 (3.91)	15 (4.70)	7.29	23.80	7.29
Sorsele	340	75	204	11 (3.24)	3 (4.00)	10 (4.90)	7.43	25.80	7.43
Vilhelmina	739	181	431	28 (3.79)	3 (1.66)	20 (4.64)	9.01	29.30	9.01
Dorotea	300	71	153	15 (5.00)	1 (1.41)	6 (3.92)	9.95	5.88	9.95
Vännäs	700	111	425	23 (3.29)	0 (0.00)	14 (3.29)	7.15	-	7.15
Åsele	285	81	171	16 (5.61)	2 (2.47)	2 (1.17)	4.13	1.96	4.13
Umeå	7652	1805	6230	261 (3.41)	41 (2.27)	283 (4.54)	6.65	8.43	6.65
Lycksele	1282	289	689	56 (4.37)	4 (1.38)	24 (3.48)	9.19	28.50	9.19
Skellefteå	5876	1253	4209	229 (3.90)	24 (1.92)	178 (4.23)	9.36	18.40	9.36

Notes: 1 – P refers to pain killers, 2 – A refers to anxiolytics, 3 – S refers to sleeping drugs. 4 – shopping behaviour is defined as having overlapping prescriptions from at least two different prescribers.

As can be seen in the table, shoppers constitute between 2 and 4 per cent of people exposed to addictive drugs, depending on the type of drug (first row, panel 2). More women than men consume addictive drugs, but a lower share of these women are shoppers in comparison to men. The number of subjects using addictive drugs increases with age up to a certain limit from 66 to 85 (depending on the type of drug) and thereafter decreases. The number of shoppers displays a similar pattern. However, the age pattern for the share of individuals with shopping behaviour is less clear. For individuals using anxiolytics, shopping behaviour is most common among relatively young people (age group from 26 to

35). The incidence of shopping behaviour varies across municipalities. However, these differences do not appear to be systematically related to how urban or rural the municipality is or the number of providers in a municipality.

Table 3 shows the types of drugs by ATC5 classification present in the data and the incidence of their use. Oxycodone and Tramadol are the most prescribed opioid painkillers in the general population and among shoppers, while Ketobemidone and Tapentadol are rarely used. However, strong opioids such as Fentanyl and Oxycodone are more frequently associated with shopping compared to weak opioids such as Tramadol and Codeine (column 2).

Table 3. Drugs used by shoppers and non-shoppers.

Drug (ATC5)	(1) Number of subjects exposed to the drug	(2) Number (%) of subjects exposed[1] to the drug with shopping behaviour[2] observed	(3) Number (%) of subjects exposed[3] to the drug with the overlapping prescriptions from the same prescriber
Pain-killers	20473	456 (2.23)	1316 (6.43)
Ketobemidone (N02AB01)	76	0 (0.00)	2 (2.63)
Fentanyl (N02AB03)	929	55 (5.92)	254 (27.34)
Morphine (N02AA01)	1841	30 (1.63)	117 (6.36)
Morphine + antispasmodics (N02AG01)	111	0 (0.00)	1 (0.90)
Tramadol (N02AX02)	7060	104 (1.47)	463 (6.56)
Tapentadol (N02AX06)	10	0 (0.00)	0 (0.00)
Oxycodone (N02AA05)	7561	225 (2.98)	383 (5.07)
Oxycodone + naloxone (N02AA55)	105	3 (2.86)	8 (7.62)
Codeine (N02AA59)	6164	90 (1.46)	380 (6.16)
Anxyolitics	4503	40 (0.89)	271 (6.02)
Diazepam (N05BA01)	876	10 (1.14)	64 (7.31)
Oxazepam (N05BA04)	3142	16 (0.51)	80 (2.55)
Lorazepam (N05BA06)	131	2 (1.53)	9 (6.87)
Alprazolam (N05BA12)	564	16 (2.84)	139 (24.65)
Sleeping drugs	14586	272 (1.86)	1317 (9.03)
Zopiklon (N05CF01)	8551	122 (1.43)	659 (7.71)
Zolpidem (N05CF02)	6952	162 (2.33)	737 (10.60)

Notes: 1 – exposure during shopping; 2 – shopping behaviour is defined as having overlapping prescriptions from at least two different prescribers; 3 – exposure during the overlap between prescriptions from the same prescriber.

For anxiolytics drugs, Table 3 shows that Diazepam and Oxazepam are most used in the general population, while Alprazolam and Lorazepam, which have the highest abuse potential [39], are to a greater extent associated with shopping behaviour. Column 2 and 3 show the numbers and percentage of patients who have overlaps between prescriptions. As shown in the two columns, it is more common to have overlapping prescriptions from the same provider (column 3) than to have overlapping prescriptions from different providers (column 2), regardless of the prescribed drug. Although the distribution of drugs is not identical between shoppers and patients with overlapping prescriptions from the same provider, there does not appear to be a systematic difference in the type of drugs used.

In Table 4, we present the descriptive statistics for datasets 1, 2 and 3. As shown in the table, the mean number of overlapping DDDs in our data is 2.33 for opioid painkillers, 2.79 for anxiolytics, and 2.2 for sleeping drugs (panel 3). The mean number of overlapping doses grows with the number of unique drugs in the overlap for opioid painkillers and sleeping drugs. The maximum number of overlapping DDDs are 15, 14, and 12 for painkillers, anxiolytics and sleeping drugs, respectively (panel 4). Patients may have up to four unique prescribers in an overlap. There appears to be a positive correlation between the number of unique prescribers and the mean number of overlapping DDDs. Overlaps between prescriptions from the same prescriber constitute a majority of observations, and the number of overlapping days decreases significantly with the number of providers involved. Most patients consume just one type of drug at a specific point in time. Simultaneous consumption of different types of drugs within an ATC5 category constitutes about 5-11 per cent of the observations (panel 1).

The distribution of the overlapping DDDs varies slightly between gender, age and municipalities. Women, in general, have a slightly higher number of overlapping doses for all groups of drugs. Age groups 36-45 and 46-55 on average have more overlapping doses of opioids than the general population, while for anxiolytics, these age groups 26-45 and 66-75. Age group 26-35 has the highest mean number of overlapping doses of sleeping drugs. This number for the age groups 36-55 and 86+ is also higher than average. Åsele, Lycksele and Storuman, which are all sparsely populated inland municipalities, have the highest mean number of overlapping DDDs for painkillers, anxiolytics and sleeping drugs, respectively. However, most of the overlapping consumption days occur in the most populated and urban municipalities, Umeå and Skellefteå.

Table 4. Descriptive statistics for datasets 1, 2 and 3.

	(1) Number of observations			(2) Min number of DDDs per day with the overlap			(3) Mean (SD) number of DDDs per day with the overlap			(4) Max number of DDDs per day with the overlap		
	P[1]	A[2]	S[3]	P	A	S	P	A	S	P	A	S
Total	146091	72205	296211	2	2	2	2.33 (0.81)	2.79 (1.40)	2.20 (0.61)	15	14	12
Gender												
Men	66329	33075	113450	2	2	2	2.31 (0.72)	2.84 (1.42)	2.16 (0.45)	9	12	7
Women	79699	39130	182761	2	2	2	2.34 (0.89)	2.76 (1.39)	2.22 (0.70)	15	14	12
Age												
<18	20	36	98	2	2	2	2.00 (0.00)	2.00 (0.00)	2.00 (0.00)	2	2	2
18-25	1308	1857	3950	2	2	2	2.12 (0.38)	2.55 (0.62)	2.16 (0.50)	5	4	5
26-35	7616	9979	15482	2	2	2	2.22 (0.56)	2.97 (1.45)	2.38 (0.89)	10	10	8
36-45	22349	10520	22841	2	2	2	2.44 (0.83)	3.02 (1.56)	2.23 (0.85)	8	10	12
46-55	32558	14874	42422	2	2	2	2.45 (1.17)	2.70 (1.20)	2.21 (0.62)	15	12	12
56-65	30950	15713	67835	2	2	2	2.29 (0.65)	2.79 (1.61)	2.20 (0.61)	7	14	8
66-75	26791	11673	69350	2	2	2	2.25 (0.65)	2.94 (1.51)	2.19 (0.56)	9	10	8
76-85	15434	6016	51082	2	2	2	2.23 (0.58)	2.29 (0.72)	2.10 (0.34)	7	6	5
86+	9065	1537	23151	2	2	2	2.25 (0.58)	2.15 (0.36)	2.25 (0.719)	5	4	9
Municipality												
Nordmaling	3914	2060	10723	2	2	2	2.15 (0.42)	2.40 (0.83)	2.14 (0.42)	6	7	6
Bjurholm	703	260	1951	2	2	2	2.07 (0.26)	2.00 (0.00)	2.01 (0.10)	4	2	3
Vindeln	1918	1595	8795	2	2	2	2.09 (0.31)	2.82 (1.04)	2.13 (0.40)	4	7	4
Robertsfors	3376	410	7200	2	2	2	2.18 (0.52)	2.02 (0.15)	2.15 (0.40)	6	3	4
Norsjö	3601	171	4657	2	2	2	2.27 (0.65)	2.00 (0.00)	2.11 (0.58)	6	2	7
Malå	4272	103	3113	2	2	2	2.14 (0.41)	2.00 (0.00)	2.06 (0.25)	5	2	4
Storuman	8221	1607	5251	2	2	2	2.34 (0.71)	3.31 (2.34)	2.20 (0.47)	6	12	5
Sorsele	1979	484	3457	2	2	2	2.24 (0.57)	2.66 (1.00)	2.06 (0.25)	5	5	3
Vilhelmina	6177	2586	10318	2	2	2	2.21 (0.53)	3.05 (1.26)	2.09 (0.33)	6	7	5
Dorotea	2201	323	1911	2	2	2	2.44 (0.78)	2.07 (0.26)	2.12 (0.37)	6	3	4
Vännäs	3959	2621	7510	2	2	2	2.12 (0.25)	3.11 (1.96)	2.05 (0.21)	5	10	4
Åsele	3322	595	3085	2	2	2	2.80 (2.13)	2.39 (0.52)	2.25 (0.43)	14	4	3
Umeå	49316	39739	144227	2	2	2	2.35 (0.86)	2.72 (1.38)	2.20 (0.60)	15	14	9
Lycksele	15250	5685	14042	2	2	2	2.58 (0.94)	3.38 (1.49)	2.37 (1.00)	10	9	8
Skellefteå	37882	13966	69971	2	2	2	2.26 (0.66)	2.74 (1.27)	2.22 (0.72)	9	10	12
Number of unique drugs by ATC5 involved												
1	131714	69712	282441	2	2	2	2.29 (0.78)	2.80 (1.42)	2.19 (0.61)	15	14	12
2	14256	2446	13770	2	2	2	2.63 (0.99)	2.76 (1.02)	2.31 (0.65)	12	7	6
3	121	47	-	3	3	-	3.24 (0.48)	3.79 (0.95)	-	5	5	-
Nr of unique prescribers involved												
1	132124	68575	266540	2	2	2	2.31 (0.79)	2.74 (1.34)	2.17 (0.56)	15	14	12
2	13779	3510	28511	2	2	2	2.48 (0.93)	2.71 (2.07)	2.41 (0.89)	9	12	8
3	174	120	1138	3	3	3	4.62 (1.39)	4.47 (1.24)	3.95 (0.90)	8	6	7
4	14	-	22	4	-	4	4.07 (0.27)	-	5.41 (0.59)	5	-	6

Notes: 1 – P refers to painkillers, 2 – A refers to anxiolytics, 3 – S refers to sleeping drugs.

4.2. Model estimation

We present the main results of our empirical analysis in Table 5. Column 1 presents the estimated coefficients and standard errors emanating from a Generalised Least Square (GLS) regression with random patient effects for opioid painkillers. Column 2 and 3 present the corresponding results for anxiolytics and sleeping drugs, respectively. According to the Hausman test, a fixed-effects model is preferable to a random-effects approach. However, the results for time-variant explanatory variables are robust to the difference in the estimation method. Therefore, since the fixed-effect model does not estimate the effect of the time-invariant control variables, we only present the results for the random-effects model here. The estimation results for models with patient fixed effects are available in Table A1 in the appendix.

Table 5 shows that the number of DDDs per day increases significantly with the number of unique prescribers involved in the overlap for all types of addictive drugs. Overlaps in prescriptions from the same prescriber are associated with on average 1.31 (painkillers), 2.74 (anxiolytics) and 2.17 (sleeping drugs) DDDs per day[3]. Having two providers involved in the overlap (compared to the overlap between prescriptions made by the same prescriber) is associated with an increase in DDDs by 0.242, 0.429 and 0.153 units for painkillers, anxiolytics and sleeping drugs, respectively, which corresponds to a percentage increase of 7% –18% depending on the drug category. A relatively small increase in the number of DDDs when two unique providers are involved in the overlap may sign that most of the overlaps with just one additional provider are legitimate and do not relate to DS.

However, if more than two unique prescribers are involved in the overlap, the differences are disproportionally higher. With three different providers, patients have access to about 1.197 to 1.593 more DDDs. When four different providers are involved, this number increases to 2.117 for painkillers and 2.868 for sleeping drugs (there are no cases with four providers for anxiolytics). Thus, depending on the type of drugs, the increase in the number of DDDs corresponds to a percentage increase of 44% – 122%, 132% – 161% for two and three additional providers, respectively. However, according to

[3] Unconditional means, calculated form the data.

Table 4, the number of overlapping events with more than two providers involved is relatively small for all drugs.

Table 5. Model (1) estimation results. GLS with random patient effects.

	Dependent variable: DDDs		
	Painkillers (1)	Anxiolytics (2)	Sleeping drugs (3)
Number of unique prescribers involved			
2	0.242*** (0.007)	0.429*** (0.026)	0.153*** (0.004)
3	1.593*** (0.047)	1.197*** (0.097)	1.314*** (0.016)
4	2.117*** (0.161)		2.868*** (0.090)
Number of unique drugs by ATC5			
2	0.390*** (0.008)	0.225*** (0.031)	0.201*** (0.006)
3	1.300*** (0.064)	0.792*** (0.159)	
Age	-0.0004 (0.003)	-0.091*** (0.010)	0.003 (0.002)
Age²	-0.00001 (0.00003)	0.001*** (0.0001)	-0.00004** (0.00002)
Women	0.003 (0.021)	-0.127* (0.071)	0.011 (0.014)
Municipality			
Bjurholm	0.014 (0.132)	0.167 (0.388)	-0.095* (0.057)
Vindeln	0.026 (0.091)	0.261 (0.278)	0.012 (0.050)
Robertsfors	0.005 (0.083)	0.141 (0.325)	0.099** (0.050)
Norsjö	-0.108 (0.079)	0.050 (0.395)	0.089* (0.051)
Malå	0.195** (0.078)	-0.074 (0.451)	-0.002 (0.067)
Storuman	0.089 (0.069)	2.306*** (0.224)	0.007 (0.057)
Sorsele	0.091 (0.085)	0.298 (0.388)	0.013 (0.060)
Vilhelmina	0.087 (0.069)	0.066 (0.256)	0.017 (0.049)
Dorotea	0.050 (0.095)	-0.122 (0.333)	0.032 (0.081)
Vännäs	0.033 (0.072)	0.463* (0.273)	-0.003 (0.050)
Åsele	0.131 (0.085)	0.255 (0.343)	0.076 (0.079)
Umeå	0.013 (0.056)	0.203 (0.177)	0.017 (0.037)
Lycksele	0.132** (0.063)	-0.621*** (0.211)	0.032 (0.044)
Skellefteå	0.060 (0.057)	0.219 (0.191)	-0.002 (0.038)
Year			
2015	0.021*** (0.004)	0.159*** (0.010)	0.021*** (0.002)
2016	0.001 (0.006)	0.565*** (0.014)	0.061*** (0.003)
2017		-1.443*** (0.037)	
Constant	1.969*** (0.109)	4.658*** (0.332)	1.952*** (0.075)
Observations	146,091	72,205	296,211
R^2	0.115	0.080	0.110
Adjusted R^2	0.115	0.080	0.109
F Statistic	5,885.604***	5,380.405***	12,144.660***

Notes: *p<0.1; **p<0.05; ***p<0.01; Numbers in parentheses are standard errors.

Similarly to the results above, the number of DDDs per day grows with the number of unique drugs by ATC5 in the overlap. Age does not appear to have a significant effect on the number of DDDs for painkillers and sleeping drugs. For anxiolytics, the number of DDDs increases slightly up to the age of 91 and decreases thereafter. The estimation results do not show any significant difference between men and women in the number of DDDs per day for painkillers and sleeping drugs.

5. Discussion and conclusions

Abuse of addictive prescription drugs is a growing problem worldwide. The structure of the health care market, such as the degree of competition, the way providers are compensated, and access to the free choice of provider, can facilitate drug abuse via increased possibilities for DS. Both informed and uninformed patients may engage in shopping behaviour. Some patients may already be addicted, while others may seek help and be unaware of the effects of drugs and the consequences of consumption. If patients are free to choose their provider and if the providers are uninformed about patients' needs or addiction and have financial incentives to please patients, the problem of drug misuse by DS may be exaggerated.

This paper analyses shopping behaviour in the Västerbotten County of Sweden for the time period 2014-2016. The main difference between our study and previous research is that we test the effects of DS on drug consumption by identifying overlapping prescriptions, which may be a sign of drug misuse. We identify overlaps between prescriptions from three major groups of addictive drugs (opioid pain-killers benzodiazepine anxiolytics, and z-hypnotic sleeping drugs) and test if the number of different providers affects the DDDs available to the patient. This approach allows us to, at least to some extent, differentiate between DS and medically legitimate overlaps.

To the best of our knowledge, this is the first study on prescription drug abuse in Sweden. Sweden is known for having a fairly regulated health care market. Most of the prescribers are salaried, while the choice of the provider is limited by the small number of providers. For example, most of the municipalities in Västerbotten have one or two primary care centres (with 4-5 GPs on average), while the largest municipality Umeå has 13. All drug prescriptions are monitored and registered electronically all over the country. However, potential DS events (overlapping prescriptions from at least two different providers) still occur. The share of people involved in such events was about 2 to 4 per cent, depending on the type of drug. Although the prevalence of DS is relatively low, the results of our study show that the problem of DS for addictive drugs may still be relevant in this setting. Our estimation results suggest that the number of overlapping prescriptions grows with the number of unique prescribers in the overlap.

Having different providers involved in the overlap may increase the number of DDDs by up to three units, which is three times higher than the standard treatment dose of one DDD in adults.

A common limitation for the studies on prescribed drug registers is that is it problematic to distinguish between drug abuse by DS and medically legitimate use. Our approach attempts to address this problem by comparing the overlaps where several prescribers are involved with overlaps between prescriptions by the same prescriber. The model for painkillers is most vulnerable to the issue mentioned above. Opioids may be prescribed for treatment of pain associated with different diagnoses and manipulations, e.g. cancer, injuries, surgery. Therefore, the type of opioid, treatment regimen, form of the substance and doses may differ a lot from prescription to prescription. Our results may, therefore, partly be caused by legitimate use of opioid painkillers. However, we find very similar results for anxiolytics and sleeping drugs. The medically prescribed dose and usage of these drugs are much more homogenous, and it is therefore unlikely that we falsely interpret DS as a sign of misuse.

On many markets, increased competition improves efficiency by reducing prices and increasing the availability and quality of valued services. However, in the health care market, increased competition in terms of free choice of health care providers can potentially lead to increased DS. Our analysis suggests that it can. One way to reduce drug abuse caused by DS is to set an upper limit on how many times patients can switch between different providers. Some countries have introduced such measures. For example, in Norway, patients may only change their GP twice per year [40]. Another important issue to consider is the gatekeeping function of primary care. More possibilities for DS are available when patients are allowed to visit specialists without a referral from a GP. Moreover, to avoid the over-prescription of drugs, it may be important to rely on more targeted policy mechanisms. One of them is electronic monitoring of the prescriptions when a prescriber has control over prescriptions made by others. For example, such monitoring programs have become an efficient policy solution to the opioid epidemic in the US [41]. However, our analysis suggests that electronic monitoring systems may not be enough. The prescribers in our dataset have access to such systems but still hand out overlapping prescriptions. For future research, it would be interesting to compare DS between countries with different market structures and to evaluate policy interventions.

References

1. UNODC, World Drug Report 2010 (United Nations Publication, Sales No. E.10.XI.13); https://www.unodc.org/documents/wdr/WDR_2010/World_Drug_Report_2010_lo-res.pdf. Accessed 19 April 2021.
2. Bhatt, R. Domestic violence and substance abuse. International Journal of Gynecology & Obstetrics. 1998; 63: S25-S31. https://doi.org/10.1016/S0020-7292(98)00181-7
3. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in Drug and Opioid Overdose Deaths - United States, 2000-2014. MMWR Morb Mortal Wkly Rep. 2016; 64(50-51):1378-82. doi: 10.15585/mmwr.mm6450a3.
4. Abraham O, Szela L, Thakur T, Brasel K, Brown R. Adolescents' Perspectives on Prescription Opioid Misuse and Medication Safety. J Pediatr Pharmacol Ther. 2021; 26(2):133-143. doi:10.5863/1551-6776-26.2.133.
5. Garnier LM, Arria AM, Caldeira KM, Vincent KB, O'Grady KE, Wish ED. Sharing and selling of prescription medications in a college student sample. J Clin Psychiatry. 2010; 71(3):262-269. doi:10.4088/JCP.09m05189ecr.
6. Sansone, R. A., & Sansone, L. A. Doctor shopping: a phenomenon of many themes. Innovations in clinical neuroscience. 2012; 9(11-12), 42.
7. Wang, M. J., & Lin, S. P. Study on doctor shopping behavior: insight from patients with upper respiratory tract infection in Taiwan. Health policy. 2010; 94(1), 61-67. https://doi.org/10.1016/j.healthpol.2009.08.009.
8. Macpherson, A. K., Kramer, M. S., Ducharme, F. M., Yang, H., & Bélanger, F. P. Doctor shopping before and after a visit to a paediatric emergency department. Paediatrics & child health. 2001; 6(6), 341–346. https://doi.org/10.1093/pch/6.6.341.
9. Cepeda MS, Fife D, Chow W, Mastrogiovanni G, Henderson SC. Assessing opioid shopping behaviour: a large cohort study from a medication dispensing database in the US. Drug Safety. 2012; 35(4):325-334. DOI: 10.2165/11596600-000000000-00000.

10. Cepeda MS, Fife D, Chow W, Mastrogiovanni G, Henderson SC. Opioid shopping behavior: how often, how soon, which drugs, and what payment method. J Clin Pharmacol. 2013; 53(1):112-7. doi: 10.1177/0091270012436561.

11. Simeone R. Doctor Shopping Behavior and the Diversion of Prescription Opioids. Substance abuse : research and treatment. 2017; 11, 1178221817696077. https://doi.org/10.1177/1178221817696077.

12. McDonald DC, Carlson KE. Estimating the prevalence of opioid diversion by "doctor shoppers" in the United States. PLoS One. 2013; 8(7):e69241. doi: 10.1371/journal.pone.0069241.

13. Soeiro T, Frauger É, Pradel V, Micallef J. Doctor shopping for methylphenidate as a proxy for misuse and potential abuse in the 67 million inhabitants in France. Fundam Clin Pharmacol. 2020; doi: 10.1111/fcp.12612.

14. Soeiro T, Pradel V, Lapeyre-Mestre M, Micallef J. Evolution of doctor shopping for oxycodone in the 67 million inhabitants in France as a proxy for potential misuse or abuse. Pain. 2021; 162(3):770-777. doi: 10.1097/j.pain.0000000000002093.

15. Adewumi AD, Maravilla JC, Alati R, Hollingworth SA, Hu X, Loveday B, Connor JP. Multiple opioid prescribers: A genuine quest for treatment rather than aberrant behaviour. A two-decade population-based study. Addict Behav. 2020; 108:106458. doi: 10.1016/j.addbeh.2020.106458.

16. Winther RB, Bramness JG. Legemiddelshopping av vanedannende medikamenter i Norge [Prescription shopping of addictive drugs in Norway]. Tidsskr Nor Laegeforen. 2009; 129(6):517-20. Norwegian. doi: 10.4045/tidsskr.09.34414.

17. Cepeda MS, Fife D, Vo L, Mastrogiovanni G, Yuan Y. Comparison of opioid doctor shopping for tapentadol and oxycodone: a cohort study. J Pain. 2013; 14(2):158-64. doi: 10.1016/j.jpain.2012.10.012.

18. Cepeda MS, Fife D, Yuan Y, Mastrogiovanni G. Distance traveled and frequency of interstate opioid dispensing in opioid shoppers and nonshoppers. J Pain. 2013; 14(10):1158-61. doi: 10.1016/j.jpain.2013.04.014.

19. Cepeda, M. S., Fife, D., Berwaerts, J., Friedman, A., Yuan, Y., & Mastrogiovanni, G. Doctor shopping for medications used in the treatment of attention deficit hyperactivity disorder: shoppers often pay in cash and cross state lines. The American journal of drug and alcohol abuse. 2015; 41(3), 226–229. https://doi.org/10.3109/00952990.2014.945591.

20. Schneberk, T., Raffetto, B., Friedman, J., Wilson, A., Kim, D., & Schriger, D. L. Opioid prescription patterns among patients who doctor shop; Implications for providers. PloS one. 2020; 15(5), e0232533. https://doi.org/10.1371/journal.pone.0232533.

21. Lu TH, Lee YY, Lee HC, Lin YM. Doctor Shopping Behavior for Zolpidem Among Insomnia Patients in Taiwan: A Nationwide Population-Based Study. Sleep. 2015; 38(7):1039-44. doi: 10.5665/sleep.4806.

22. Pottegård A, Schmidt SAJ, Wallach-Kildemoes H, Sørensen HT, Hallas J, Schmidt M. Data Resource Profile: The Danish National Prescription Registry. Int J Epidemiol. 2017; 46(3):798-798f. doi: 10.1093/ije/dyw213.

23. Sinnott, S. J., Polinski, J. M., Byrne, S., & Gagne, J. J. Measuring drug exposure: concordance between defined daily dose and days' supply depended on drug class. Journal of clinical epidemiology. 2016; 69, 107–113. https://doi.org/10.1016/j.jclinepi.2015.05.026

24. Merlo, J., Wessling, A. & Melander, A. Comparison of dose standard units for drug utilisation studies. E J Clin Pharmacol. 1996; 50, 27–30. https://doi.org/10.1007/s002280050064.

25. WHO Collaborating Centre for Drug Statistics Methodology. https://www.whocc.no/ddd/definition_and_general_considera/. Accessed 19 April 2021.

26. Nielsen S, Gisev N, Bruno R, Hall W, Cohen M, Larance B, Campbell G, Shanahan M, Blyth F, Lintzeris N, Pearson S, Mattick R, Degenhardt L. Defined daily doses (DDD) do not accurately reflect opioid doses used in contemporary chronic pain treatment. Pharmacoepidemiol Drug Saf. 2017; 26(5):587-591. doi: 10.1002/pds.4168.

27. Oslo: Helsedirektoratet. Det bør ikke brukes flere forskjellige opioider og/eller ikke kort- og lengevirkende legemidler. Norwegian. https://www.helsedirektoratet.no/veiledere/opioider/ved-oppstart-av-opioidbehandling/flere-

opioider-samtidig/det-bor-ikke-brukes-flere-forskjellige-opioider-ogeller-ikke-kort-og-lengevirkende-legemidler. Accessed 19 April 2021.

28. Handal M, Skurtveit S, Mørland JG. Samtidig bruk av ulike benzodiazepiner [Co-medication with benzodiazepines]. Tidsskr Nor Laegeforen. 2012;132(5):526-30. Norwegian. doi: 10.4045/tidsskr.11.0321.

29. Alogaili F, Abdul Ghani N, Ahmad Kharman Shah N. Prescription drug monitoring programs in the US: A systematic literature review on its strength and weakness. Journal of Infection and Public Health. 2020; 13(10):1456-1461. doi: 10.1016/j.jiph.2020.06.035.

30. Mossialos E, Djordjevic A, and Wharton G, International Profiles of Health Care Systems, The Commonwealth Fund. 2020; https://www.commonwealthfund.org/sites/default/files/2020-12/International_Profiles_of_Health_Care_Systems_Dec2020.pdf. Accessed 19 April 2021.

31. Anell A, Glenngård AH, Merkur S. Sweden health system review. Health Syst Transit. 2012; 14:1–159. http://www.euro.who.int/__data/assets/pdf_file/0008/164096/e96455.pdf. Accessed 19 April 2021.

32. Sánchez-Sagrado T. La atención primaria en Suecia [Primary care in Sweden]. Semergen. 2016; 42(6):408-11. Spanish. doi: 10.1016/j.semerg.2015.09.019.

33. 1177 Vårdguiden. Välja hälsocentral i Västerbotten [Choose a health center in Västerbotten].; https://www.1177.se/Vasterbotten/sa-fungerar-varden/att-valja-vardmottagning/valja-halsocentral-i-vasterbotten/. Swedish. Accessed 19 April 2021.

34. 1177 Vårdguiden. Patientavgifter och högkostnadsskydd [Patient fees and high-cost protection]; https://www.1177.se/Vasterbotten/sa-fungerar-varden/kostnader-och-ersattningar/patientavgifter/. Swedish. Accessed 19 April 2021

35. 1177 Vårdguiden. Högkostnadsskydd för öppenvård [High-cost protection for outpatient care]; https://www.1177.se/Vasterbotten/sa-fungerar-varden/kostnader-och-ersattningar/hogkostnadsskydd-for-oppenvard/. Swedish. Accessed 19 April 2021.

36. 1177 Vårdguiden. Vad kostar läkemedel på recept? [What do prescription drugs cost?]; https://www.1177.se/Vasterbotten/behandling--hjalpmedel/behandling-med-lakemedel/att-fa-

recept-och-att-kopa-lakemedel/vad-kostar-lakemedel-pa-recept/. Swedish. Accessed 19 April 2021.

37. Law about the pharmaceutical benefit scheme in Sweden. Ministry of Health and Social Affairs 2002; http://www.notisum.se/rnp/sls/sfs/20020160.pdf. Swedish. Accessed 19 April 2021.

38. National Board of Health and Welfare. The Swedish Prescribed Drug Register https://www.socialstyrelsen.se/en/statistics-and-data/registers/register-information/the-swedish-prescribed-drug-register/#:~:text=The%20Swedish%20Prescribed%20Drug%20Register%20provides%20the%20basis%20for%20the,prescribed%20drugs%20dispensed%20at%20pharmacies. Accessed 19 April 2021.

39. Schmitz A. Benzodiazepine use, misuse, and abuse: A review. The mental health clinician. 2016; 6(3), 120–126. https://doi.org/10.9740/mhc.2016.05.120.

40. Helsenorge. Changing your regular doctor. 2021; Available from: https://www.helsenorge.no/en/change-doctor-gp/about/. Accessed 19 April 2021.

41. Haffajee, R. L., Mello, M. M., Zhang, F., Zaslavsky, A. M., Larochelle, M. R., & Wharam, J. F. Four States With Robust Prescription Drug Monitoring Programs Reduced Opioid Dosages. Health affairs (Project Hope). 2018; 37(6), 964–974. https://doi.org/10.1377/hlthaff.2017.1321.

Appendix

Table A1. Estimation results of the fixed-effects model.

	Dependent variable: DDDs		
	Painkillers (1)	Anxiolytics (2)	Sleeping drugs (3)
Number of unique prescribers involved			
2	0.252*** (0.008)	0.443*** (0.027)	0.153*** (0.004)
3	1.612*** (0.049)	1.140*** (0.097)	1.312*** (0.016)
4	2.129*** (0.162)		2.855*** (0.090)
Number of unique drugs by ATC5			
2	0.419*** (0.008)	0.294*** (0.031)	0.209*** (0.006)
3	1.332*** (0.065)	0.926*** (0.158)	
Age	-0.048*** (0.013)	-0.742*** (0.026)	-0.0003*** (0.00005)
Age^2	-0.00003 (0.0001)	0.004*** (0.0002)	-0.0003*** (0.00005)
Municipality			
Bjurholm			0.053 (0.144)
Vindeln			0.249 (0.164)
Robertsfors			0.418*** (0.146)
Norsjö	-0.503*** (0.073)		0.356** (0.155)
Storuman	0.250 (0.289)	0.890 (0.583)	0.177 (0.213)
Sorsele	0.220 (0.308)		0.196 (0.195)
Vilhelmina	0.269 (0.283)		
Vännäs	-0.089 (0.277)		0.186 (0.153)
Åsele	0.083 (0.311)		
Umeå	-0.127 (0.262)	0.736** (0.293)	0.210 (0.133)
Lycksele	0.240 (0.278)	-4.154*** (0.612)	0.239 (0.145)
Skellefteå	0.076 (0.271)		0.174 (0.147)
Year			
2015	0.064*** (0.006)	0.351*** (0.012)	0.053*** (0.003)
2016	0.074*** (0.009)	0.921*** (0.019)	0.115*** (0.004)
2017		-1.099*** (0.040)	-0.926*** (0.027)
Observations	146,091	72,205	296,211
R^2	0.042	0.088	0.041
Adjusted R^2	0.022	0.079	0.028
F Statistic	347.678***	576.953***	651.164***

Notes: $^{*}p<0.1$; $^{**}p<0.05$; $^{***}p<0.01$; Numbers in parentheses are standard errors.