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"Identifying the Effects of Scientific Information and Recommendations on Physicians' Prescribing Behavior"

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Abstract

We investigate how the prescribing behavior of physicians reacts to scientific information and recommendations released by public authorities. Taking the example of antidepressant drugs, we use French panel data on exhaustive prescriptions made by a representative sample of general practitioners to more than 110,000 depressed patients between 2000 and 2008. New results revealing an increase in suicidal thinking among children taking selective serotonin reuptake inhibitors (SSRIs) were reported in 2004 and prompted the release of new guidelines by public health authorities. We identify the effect of this unexpected warning on physicians' drug choices while addressing that possibility that patient heterogeneity may be correlated with unobserved physician characteristics. While the warning decreased the average probability of prescribing SSRIs, we find that physicians' responses to the warning were very heterogeneous and larger if the physician had a higher preference for prescribing SSRIs before the warning.

Keywords: Physician behavior, prescription, antidepressants, mixed logit

JEL Codes: I10, D12, C25

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1 Introduction

Understanding physicians' prescribing behavior is important for public health and public finance. Physician prescription activity depends on physicians' judgment and continuous updating of their medical knowledge through scientific information and the public recommendations of health authorities. Moreover, prescription of treatments to patients is a difficult and partially subjective choice that implies cost-benefit trade-offs depending on drug efficacy, patient condition and the evaluation of both by the physician.

Using an important medical information change disseminated through a public warning by health authorities, we study whether and how recommendations affect physicians' decision-making, using the example of antidepressant drugs in France. We use panel data covering 2000 to 2008 and containing exhaustive prescriptions made by a representative sample of 386 general practitioners to more than 110,000 depressed patients. We identify changes in the prescribing behavior of physicians after the release of a warning in relation to new scientific evidence on the efficacy and side effects of antidepressants during that period. As medical journals publish new evidence and public health authorities adjust their recommendations, doctors may update their prescribing behavior. During the study period, important new evidence on antidepressants' efficacy and side effects were published and transmitted through new official recommendations to physicians. There were new results in 2004 showing that using selective serotonin reuptake inhibitors (SSRIs) for depression treatment increases suicidal thinking in children. After such events and medical warnings, physicians must update their beliefs on different drug treatments and may react differently to these warnings.

We develop a model of prescribing behavior with physician and patient heterogeneity and show how we can identify the effect of a warning on individual physicians' specific preferences when unobserved heterogeneity in patients' health state may be correlated with physicians' heterogeneity. Such a correlation could be the result of endogenous matching on unobservable characteristics between physicians and patients. Assuming stable preferences of physicians during the periods before and after the warning, we can assess whether the heterogeneity in treatments is due to unobservable differences in patient or physician preferences (on drug efficacy or side effects, for example). We are able to test not only whether changing scientific information affects physicians' prescriptions but also whether it affects physicians differently.

Our empirical results show that physicians' behavior is very heterogeneous in terms of propensity to prescribe different kinds of antidepressants and that government warnings also have very heterogeneous effects on physicians' prescribing behavior. We find that physicians prescribe antidepressants to children and

adolescents less often after the warning, but many still do not adhere to to the recommendation. SSRIs are still prescribed to this age group by 62% of physicians, despite the warning advising against this. We observe that prescription of SSRIs to children and adolescents decrease in favor of either serotonin and norepinephrine reuptake inhibitors (SNRIs) or drugs other than antidepressants. We also find that after the warning, the probability of prescribing an SSRI to young adults, adults and elderly people responds very heterogeneously across physicians. It seems that some physicians interpret the warning as "good" or "bad" news for age groups other than children and adolescents as well. Finally, we also evaluate the substitution of SSRIs towards other drug categories that would result from a ban on rather than a warning against prescribing SSRI drugs to children and adolescents. The effect is much stronger in the case of a ban, and we also observe that the level of substitution towards drugs other than antidepressants would be much higher in the case of such a ban than the substitution resulting from the warning.

Our work adds some empirical evidence on the role of information in physicians' prescribing behavior. Previous literature on prescribing behavior has addressed issues related to physician-induced demand (Mcguire (2000), Dickstein (2016)) and its relationship to drug prices, patient copayments and the availability of generic drugs, as well as physician learning (Ching (2010),Coscielli and Shum (2004), Crawford and Shum (2005), Dickstein (2018), Janakiraman et al. (2009)). For example, Coscielli and Shum (2004) and Crawford and Shum (2005) model the learning process of physicians with a dynamic discrete choice model on antiulcer drugs. Dickstein (2018) develops a model where physicians sequentially search for the best match between a patient and a drug, allowing for correlations across drugs in the learning process. Ching et al. (2013) incorporates consumer learning and heterogeneity into a dynamic oligopoly model to examine the impact of shortening the expected generic approval time. Ching and Lim (2020) models correlated learning where Canadian patients/doctors can observe a statin's efficacy in reducing cholesterol levels but are uncertain about whether the drug can reduce heart-disease risks.

Our work also relates to the evidence on the role of physicians' heterogeneity of skills, beliefs and preferences, which has been documented recently (Berndt et al. (2015), Currie and Macleod (2017), Cutler et al. (2019), Currie and Macleod (2020)). Currie and Macleod (2017) examine the decision-making of physicians. They show that better decision-making improves birth outcomes by reducing C-section rates at the bottom of the risk distribution and increasing them at the top of the distribution. Cutler et al. (2019) shows how much regional variation in health-care expenditures in the US comes from patient demand-side factors as opposed to physician supply-side factors. The results show that the most important factor is physician

beliefs about treatment. They estimate that in Medicare, 35 percent of spending on end-of-life care and 12 percent of spending on care for heart-attack patients are associated with physician beliefs unsupported by clinical evidence. Berndt et al. (2015) shows that many psychiatrists have significantly heterogeneous prescription patterns and concentrate on distinct drugs. The authors find some evidence of a relationship between prescription volumes and prescribing behavior that is consistent with a learning-by-doing model among physicians. Stern and Trajtenberg (1998) show that the exercise of physician authority is likely to be related to skills. Finally, Currie and Macleod (2020) investigate how physician diagnostic skills, tastes, and beliefs impact physician decision-making. The authors use a model in which physician experimentation allows for learning about the match quality between a particular drug and an individual in the case of antidepressant medication.

While there is extensive literature on physicians' learning and experimentation, papers studying the role of new scientific evidence and public recommendations on physicians' prescriptions are sparse. Some have evaluated how prescriptions change after drug withdrawal. Collins et al. (2013) show that the Vioxx withdrawal had both positive and negative effects for specific substitute drugs and led to an overall increase in the usage of competing products. When a new drug is introduced, physicians need to learn about their existence and efficacy. Ferreyra and Kosenok (2011) show that physicians' initial pessimism and uncertainty can have large negative effects on their propensity to prescribe a new drug and on expected health outcomes. Physician beliefs are crucial to explaining their heterogeneous prescribing behavior (Berndt et al. (2015)) and are also directly affected by both scientific knowledge and personal experience with their patients. Our new approach and results shed light on how to evaluate the impact of medical warnings on physicians and on their wide heterogeneity of responses.

In Section 2, we first present some background descriptive information on antidepressants, public health warnings and recommendations, the data and some stylized descriptive statistics. Section 3 presents our model and identification strategy. Section 4 shows the results of the empirical estimation on antidepressants and depression treatment in France, and section 5 concludes.

2 Institutional Background, Data and Stylized Facts

2.1 Depression and Antidepressants

Depression affects 20% of French residents during their lifetimes. According to the World Health Organization, it is the leading cause of ill health and disability worldwide (James et al. (2018)). It is also costly because patients suffer from a decrease in their productivity. More than 60% of depressed people have symptoms severe enough to keep them from performing daily tasks (Kessler et al. (2003)). Depression also increases suicide attempts and hence mortality: the risk of suicide is 13-30 times higher among depressed people than among nondepressed people, and suicide is among the top leading causes of death in high-income countries (and is the second leading cause of death among 15-to-29-year-olds[1]). Finally, depression also increases health-care expenditures. Depressed people visit their generalist care providers for somatic complaints three times more often than nondepressed people (Kessler et al. (2003)).

The most commonly used modern antidepressant are those from the second generation, which generally dominate those from the first generation of medicines. The only first-generation antidepressants still used are those in the category of tricyclic antidepressants (TCAs), with the active ingredients amitriptyline, clomipramine, dosulepin, imipramine, maprotiline, and trimipramine. Molecules of the second generation are classified into three distinct subclasses according to their effect on the concentration of serotonin and norepinephrine in the brain. These subclasses are selective serotonin reuptake inhibitors (SSRIs), with the active ingredients citalopram, escitalopram, fluoxetine, paroxetine, and sertraline; serotonin-norepinephrine reuptake inhibitors (SNRIs), with the molecules milnacipran and venlafaxine; and "other antidepressants", which include medicines with the molecules mianserine, mirtazapine and tianeptine.

2.2 Health Care System

Health insurance is mandatory in France, and all residents are automatically enrolled in the insurance system depending on their occupational status under the French national health insurance system. A total of 90% of the population has supplementary health insurance to cover benefits not covered under mandatory health insurance. Even though health insurance plans differ across occupational groups, they are all regulated under the same statutory framework (Rodwin (2003)). As in the case of the Italian market, discussed by Crawford and Shum (2005), plans cannot compete by lowering insurance premiums, and physicians have uniform

[1] https://www.who.int/en/news-room/fact-sheets/detail/depression

per-visit payments that attenuate the agency problem, which may come into play in the case of a market with heterogeneous third-party payers. The heterogeneous constraints on physicians' choices induced by drug formularies in the US market do not come into play in the French market.

2.3 Scientific Information Release

Authorities such as the Food and Drug Administration (FDA) in the US or other health authorities in European countries monitor the use of drugs and outcomes in terms of public health to check and evaluate the efficacy and scrutinize the side effects or unintended effects of drugs, even after drugs are authorized and marketed. When new scientific evidence appears after drug introductions, it is usually diffused through scientific publications and then taken into account by health authorities in their recommendations to prescribers. In France, the pubic health authority, currently named ANSM (Agence Nationale de Sécurité du Médicament), is in charge of authorizing drugs and of regulating the use of prescription drugs by giving usage conditions and recommendations to physicians.

We collected all the information on the recommendations of the French authority on antidepressant usage. We also examined the US FDA recommendations and warnings as well as the medical literature to verify whether the French health authority was giving all relevant information that could influence physicians. These data show that recommendations and warnings between 2000 and 2008 usually occur in France around the same time as they do in the US and closely follow the medical literature. All important scientific news is monitored by these agencies and processed into official warnings and recommendations. During the period examined in this study, three important warnings were released. The first recommended not prescribing SSRI-type antidepressants to children and adolescents and was issued in December 2004 in France (a few weeks after the US FDA warning). The second one, released in June 2006, partially contradicted the 2004 warning by recommending Prozac (the fluoxetine molecule of the SSRI group) for use by adolescents and children above 8 years of age with moderate to severe depression. Finally, another warning was released in February 2008 for three different molecules that were deemed not effective enough to be prescribed except in the case of severe depression. These varying warnings also reflect the scientific debate about the role of SSRI drugs in depression treatment and their relationship with suicide, as shown in Gibbons et al. (2006), Gibbons et al. (2007) and Ludwig et al. (2009). Thus, although the health authorities' warnings and recommendations may clearly recommend not prescribing SSRIs to children and adolescents, this debate and the posterior

evidence show that it is conceivable that physicians had knowledge that may not align with recommendations, leading them not to follow recommendations.

In the context of these warnings released by the French health authority from the beginning of 2000 to the end of 2008, we are particularly interested in the impact of the warning on December 2004, which informed physicians that they should not prescribe SSRIs to children and adolescents under 18 due to the association of such drugs with an increase in suicidal thinking at this age. We focus on the period from January 2000 to June 2006 to avoid contamination from the June 2006 warning.

2.4 Data and Descriptive Statistics

We use a large panel data set on the exhaustive prescriptions made by 386 general practitioners to all of their patients in France between 2000 and 2008. This proprietary data set was provided by CEGEDIM, a global technology and services company specializing in health care. The data contain information on physicians, patients and patient visits. At the physician level, the data set includes age, gender and region of operation. At the patient level, it includes sociodemographic information (age, gender, employment) and information on health (chronic diseases, height, weight). The data include all information recorded at physician visits, including diagnoses, prescriptions, and exam results transmitted to the physician. Thus, we observe the diagnosis and all drugs and treatments (drug, dosage, renewal) that were prescribed by the physician on each visit. The unique patient- and physician-anonymized identification numbers allow us to follow physicians and patients during the nine years that the data cover, unless patients changed to general practitioners.

Table 2.1: *Share of Drugs Prescribed for Depression Diagnoses*

Group	All Ages	Children and Ado. (2-18)	Young Adults (18-25)	Adults (26-65)	Elderly People (65+)
SSRIs	0.50	0.50	0.58	0.52	0.43
SNRIs	0.09	0.05	0.10	0.10	0.06
TCAs	0.07	0.05	0.02	0.01	0.11
Other Antidepressants	0.11	0.07	0.08	0.09	0.15
Other Drugs	0.23	0.33	0.23	0.22	0.25
No. of Visits	517,241	2,564	16,795	372,406	125,441

Table 2.1 shows the shares of each drug prescription for depression diagnoses. SSRIs are the most commonly prescribed antidepressants. Across all age groups, more than 50% of the patients receive an SSRI-type antidepressant prescription upon depression diagnosis. The prescription rate of "other drugs" that are not antidepressants ranges from 22% for adults to 33% for children and adolescents.

Next, Table 2.2 shows the shares of drug prescriptions for depression diagnoses for the periods before and after the warning about SSRIs in 2004. For all age groups, the share of SSRI-type antidepressant prescriptions decreases after the warning, with the largest decrease being in prescriptions for children and adolescents, from 51% to 46%. It is striking to see that this decrease is far from an exact compliance with the warning and that the warning also leads to decreases in other age categories. While prescribing fewer SSRI drugs, physicians switch to other antidepressants and to drugs other than antidepressants. For children and adolescents, the share of "other drugs" increases by 10 percentage points after the warning, whereas for other age groups, the share of SNRI-type antidepressants and "other drugs" both increase by 2 to 4 percentage points. However, these averages mask large heterogeneity across physicians.

Table 2.2: *Drug Prescription Average Probabilities – Before and After the Warning*

Group	All Ages		Children and Ado. (2-18)		Young Adults (19-25)		Adults (26-65)		Elderly People (65+)	
	Before	After	Before	After	Before	After	Before	After	Before	After
SSRIs	0.51	0.48	0.51	0.46	0.59	0.54	0.53	0.50	0.44	0.42
SNRIs	0.09	0.11	0.05	0.03	0.09	0.12	0.10	0.13	0.05	0.08
TCAs	0.08	0.06	0.05	0.02	0.02	0.02	0.07	0.05	0.12	0.10
Oth. Antidep.	0.11	0.10	0.07	0.07	0.08	0.07	0.10	0.09	0.15	0.14
Oth. Drugs	0.22	0.24	0.31	0.41	0.22	0.26	0.21	0.23	0.24	0.26

Table 2.3 shows the 25%, the median and the 75% quantiles across physicians of the prescription probability of each drug class. We observe a substantial level of heterogeneity across physicians. For instance, for children and adolescents, 25% of the physicians prescribe an SSRI less than 25% of the time when they diagnose depression, whereas 25% prescribe an SSRI more than 67% of the time when they diagnose depression. We observed heterogeneity in physicians' prescribing behavior for other age groups as well.

Table 2.3: *Quantiles of Average Prescription Probabilities Across Physicians*

Group	All Ages			Children and Adolescents			Young Adults (18-25)			Adults (26-65)			Elderly People (65+)		
	Quantiles			Quantiles			Quantiles			Quantiles			Quantiles		
	25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%
SSRIs	0.42	0.49	0.55	0.25	0.47	0.67	0.44	0.55	0.66	0.44	0.50	0.58	0.34	0.43	0.53
SNRIs	0.06	0.10	0.14	0.00	0.00	0.00	0.03	0.08	0.15	0.07	0.11	0.16	0.02	0.06	0.11
TCAs	0.04	0.06	0.09	0.00	0.00	0.00	0.00	0.00	0.02	0.03	0.05	0.09	0.04	0.08	0.15
Oth. Antidep.	0.06	0.09	0.13	0.00	0.00	0.08	0.01	0.05	0.11	0.05	0.08	0.12	0.07	0.12	0.19
Oth. Drugs	0.17	0.22	0.30	0.14	0.31	0.53	0.15	0.22	0.32	0.16	0.22	0.28	0.15	0.23	0.33

Table 2.4 reports the quantiles of prescription probabilities separately for the periods before and after the SSRI warning in 2004. We see that the probability of prescribing SSRIs decreases at each quantile for every age group. However, there is still a substantial level of heterogeneity across physicians even after the warning.

For instance, for children and adolescents, the value for the first quartile for SSRI prescription probability is 20% before the warning and 0% after the warning. This shows that at least 25% of physicians never prescribe SSRIs to children and adolescents after the warning, thus following the recommendation perfectly. Similarly, the value for the third quartile is 73% before the warning and decreases to 67% after the warning. Moreover, the average prescription probabilities for SNRIs and TCAs also decrease for a large part of the distribution, as many physicians stop prescribing SNRIs and TCAs and increase their prescriptions of drugs other than antidepressants, which are mainly drugs approved for other mental disorders and that are used off-label for depression treatment. It thus seems that the warning on SSRIs does not simply reduce prescriptions of SSRIs that would be substituted by other drugs in equal proportion to the prescription probability before the warning. In contrast, the reduction of SSRI prescriptions is accompanied by a reduction of SNRI and TCA prescriptions for many physicians, with an increase in other drug prescriptions. Such a pattern may come from the fact that patients are heterogeneous and physicians have different preferences on how different depressed patients should be treated in the absence of treatment with SSRI drugs. Our modeling of treatment decisions by physicians will thus try to disentangle the effect of physician preferences from that of patient heterogeneity.

Table 2.4: *Quantiles of Average Prescription Probabilities Across Physicians Before and After the Warning*

Group		All Ages			Children and Adolescents			Young Adults (18-25)			Adults (26-65)			Elderly People (65+)		
		Quantiles			Quantiles			Quantiles			Quantiles			Quantiles		
		25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%
SSRIs	Before	0.43	0.50	0.57	0.20	0.50	0.73	0.45	0.58	0.70	0.45	0.52	0.59	0.33	0.44	0.55
	After	0.40	0.47	0.54	0.00	0.44	0.67	0.36	0.52	0.66	0.42	0.49	0.57	0.32	0.42	0.54
SNRIs	Before	0.04	0.07	0.12	0.00	0.00	0.00	0.00	0.04	0.12	0.04	0.08	0.13	0.01	0.03	0.08
	After	0.08	0.11	0.17	0.00	0.00	0.00	0.00	0.07	0.17	0.08	0.13	0.18	0.02	0.07	0.14
TCAs	Before	0.04	0.07	0.11	0.00	0.00	0.00	0.00	0.00	0.03	0.03	0.06	0.10	0.03	0.09	0.17
	After	0.03	0.05	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.04	0.07	0.02	0.06	0.13
Oth.	Before	0.07	0.10	0.14	0.00	0.00	0.10	0.00	0.04	0.12	0.05	0.09	0.13	0.07	0.12	0.21
Antidep.	After	0.05	0.09	0.13	0.00	0.00	0.00	0.00	0.02	0.10	0.04	0.07	0.12	0.06	0.10	0.19
Oth.	Before	0.16	0.21	0.29	0.10	0.25	0.50	0.12	0.20	0.33	0.15	0.20	0.28	0.13	0.23	0.32
Drugs	After	0.18	0.23	0.32	0.15	0.45	0.71	0.14	0.25	0.38	0.17	0.22	0.30	0.15	0.24	0.35

3 Discrete Choice Model and Identification of Preference Change

3.1 Discrete Choice Model with Unobserved Heterogeneity

We develop a discrete choice model of antidepressant prescriptions of physicians for each patient diagnosed with depression. We assume that each physician i receives patient j with some depression state that the physician is able to observe. In a given sample period, a physician has J patients diagnosed with depression (J does not need to be the same across physicians). We examine the physician prescription choices at time $t(j)$ when depression is diagnosed for patient j. We use all prescriptions over the sample period if a patient has multiple depression spells. We abstract from questions over within-patient learning that relate to the fact that when depression is diagnosed for the first time, physicians still have not learned any patient-specific responses to treatments. For follow-up depression treatments, learning about the patient's response to each drug may play a role in a physician's choice of treatment, but when we select only the first depression-related visit for each patient, we obtain estimates of physician preferences that are highly correlated with those obtained using all patient visits. Learning may still occur, but our approach only allows for the modeling and identification of the effect of the warning with heterogeneity across physicians, not accounting for possible within-patient learning.

Each physician i (she) can choose to prescribe some antidepressant d to patient j depending on the characteristics of the patient (he) θ_j and on her own taste or preference parameter, denoted β_{id}^t, for drug d at period t. The patient characteristics θ_j may include observable characteristics and unobservable characteristics, such as his depression state. Note that in the context of France, the very large majority of patients are fully reimbursed. We thus do not consider the price of drugs as a determinant of this choice, although this is a testable assumption.

We assume that the utility of prescription decisions depends on physician preferences and patient characteristics, including his depression state. Each physician can choose among $D+1$ treatments, indexed by $d = 0, 1, .., D$, and we assume that the decision by physician i to prescribe treatment d for patient j is based on maximizing

$$v(\beta_{id}^{t(j)}, \theta_j) - \varepsilon_{ijd} \tag{3.1}$$

where $v(.,.)$ is nondecreasing in both arguments and ε_{ijd} is an individual idiosyncratic deviation for treatment d perceived by physician i and specific to patient j. The random term ε_{ijd} allows decisions to be nondeterministic functions of the patient depression state θ_j assessed by the physician. We normalize $v\left(\beta_{i0}^t, \theta_j\right) = 0$, where by convention treatment 0 corresponds to drugs other than antidepressants.

We denote as $y_{ij} \in \{0, 1, .., D\}$ the treatment chosen by physician i for patient j. Using (3.1) and the assumption that ε_{ijd} are i.i.d. type-I extreme value, the probability that physician i prescribes treatment d to patient j is

$$P(y_{ij} = d|\beta_{id}^{t(j)}, \theta_j) = \frac{\exp(v(\beta_{id}^{t(j)}, \theta_j))}{1 + \sum_{\tilde{d}=1}^{D} \exp(v(\beta_{i\tilde{d}}^{t(j)}, \theta_j))}$$

We observe many patients and physicians, which implies that we can identify averages of these probabilities in the population. Such identification needs to account for the fact that patients who visit a given physician may have heterogeneous distributions of health that is possibly correlated with physicians' preferences for treatments. This could come from common unobserved correlated effects or from patients having some information on physicians' abilities and preferences. Thus, the cumulative distribution of patients' θ_j may not be identical across physicians, and we allow it to depend on the physician preferences β_{id}^t and on the period t.

Denoting as $F\left(\theta_j|\beta_{id}^t, t\right)$ the cumulative distribution function of θ_j conditional on the physician preferences β_{id}^t during t, the probability that a physician i prescribes drug d to a patient is an average of the conditional probability to each patient type, with

$$P(y_{ij} = d|\beta_{id}^{t(j)} = \beta_{id}^t, t) = \int \frac{\exp(v(\beta_{id}^t, \theta_j))}{1 + \sum_{\tilde{d}=1}^{D} \exp(v(\beta_{i\tilde{d}}^t, \theta_j))} dF(\theta_j|\beta_i^{t(j)} = \beta_{id}^t, t)$$

which is a function of physician preferences β_{id}^t. Matching between patients and physicians generates some possible dependence in the cumulative distribution function $F(\theta_j|\beta_i^{t(j)} = \beta_{id}^t, t)$. However, even if patients are randomized to physicians such that $F(\theta_j|\beta_i^{t(j)} = \beta_{id}^t, t) = F(\theta_j)$, it remains the case that the prescription probability depends on the distribution function $F(\theta_j)$ and on the preferences of physician i. Disentangling the distribution of unobserved heterogeneity θ_j from this mixture model is a difficult problem of deconvolution.

However, we show below how we can separately identify the change in preferences and patient heterogeneity by assuming that the distribution of patient characteristics is stable over time and that physician preferences β_{id}^t may only change between the period before the warning occurs at time t_1 and after. We thus assume

that:

$$\begin{aligned} \beta_{id}^{t} &= \beta_{id}^{0} \text{ if } t \leq t_1 \qquad \textit{(before warning)} \\ &= \beta_{id}^{1} \text{ if } t > t_1 \qquad \textit{(after warning)} \end{aligned} \tag{3.2}$$

Denoting as $\tau(j) = 1_{\{t(j)>t_1\}}$ the dummy variable for whether patient j visits physician i before or after the warning, we define the physician preference for drug d before the warning $\omega_{dij}^{0} \equiv v(\beta_{id}^{0}, \theta_j)$ and the change in preferences for drug d due to the warning $\omega_{dij}^{1} \equiv v(\beta_{id}^{1}, \theta_j) - v(\beta_{id}^{0}, \theta_j)$ such that:

$$\begin{aligned} v(\beta_{id}^{t(j)}, \theta_j) &= v(\beta_{id}^{0}, \theta_j)(1 - \tau(j)) + v(\beta_{id}^{1}, \theta_j)\tau(j) \\ &\equiv \omega_{dij}^{0} + \omega_{dij}^{1}\tau(j) \end{aligned}$$

This implies that the probability that physician i prescribes d to a patient θ_j at time period $\tau(j)$ is:

$$P(y_{ij} = d|i, j, \tau(j)) = \frac{\exp(\omega_{dij}^{0} + \omega_{dij}^{1}\tau(j))}{1 + \sum_{\tilde{d}=1}^{D} \exp(\omega_{\tilde{d}ij}^{0} + \omega_{\tilde{d}ij}^{1}\tau(j))}$$

and the average probability for physician i to prescribe d is then:

$$P(y_{ij} = d|i, \tau(j)) = \int \frac{\exp(\omega_{dij}^{0} + \omega_{dij}^{1}\tau(j))}{1 + \sum_{\tilde{d}=1}^{D} \exp(\omega_{\tilde{d}ij}^{0} + \omega_{\tilde{d}ij}^{1}\tau(j))} dF(\omega_{1ij}^{0}, \omega_{1ij}^{1}, .., \omega_{Dij}^{0}, \omega_{Dij}^{1}|i, \tau(j))$$

Although the warning concerns only one of the drugs d, we allow all utilities for each drug to be affected by the warning, as it is possible that the new information also affects the physician's beliefs about other drugs.

Now, we also assume that the distribution of patients' unobservable characteristics, such as their health state, are identical before and after the warning, that is,

$$F(\theta_j|i, t \leq t_1) = F(\theta_j|i, t > t_1)$$

or equivalently

$$F(\omega_{1ij}^{0}, \omega_{1ij}^{1}, .., \omega_{Dij}^{0}, \omega_{Dij}^{1}|i, \tau(j) = 0) = F(\omega_{1ij}^{0}, \omega_{1ij}^{1}, .., \omega_{Dij}^{0}, \omega_{Dij}^{1}|i, \tau(j) = 1) \tag{3.3}$$

This means the differences in treatment before and after the warning for a patient with characteristics θ_j comes only from the change in preferences of the physician. The fact that the distribution of θ_j is identical before

and after the warning for a given physician implies that there will be no change in prescription probability at the physician level before and after the warning if preferences do not change. Indeed, if $\beta_{id}^0 = \beta_{id}^1$ for $\forall d$, then $\omega_{dij}^1 = v(\beta_{id}^1, \theta_j) - v(\beta_{id}^0, \theta_j) = 0$ and

$$P(y_{ij} = d|i, \tau(j) = 0) = \int \frac{\exp(\omega_{dij}^0)}{1 + \sum_{\tilde{d}=1}^{D} \exp(\omega_{\tilde{d}ij}^0 +)} dF(\omega_{1ij}^0, \omega_{1ij}^1, .., \omega_{Dij}^0, \omega_{Dij}^1|i) = P(y_{ij} = d|i, \tau(j) = 1)$$

This shows that we can identify the change in physician preferences due to the drug warning using the stability condition of preferences before and after the warning (3.2) and the stability condition of the distribution of patient states for each physician before and after the warning (3.3). The model thus allows, for example, an endogenous patient and physician matching process such that physicians receive heterogeneous distributions of patients.

3.2 Econometric specification

To estimate the model, we need to specify a parametric distribution for unobservables. We assume that the $\omega_{1ij}^0, \omega_{1ij}^1, .., \omega_{Dij}^0, \omega_{Dij}^1$ are independent across alternatives d, that is

$$F\left(\omega_{1ij}^0, \omega_{1ij}^1, .., \omega_{Dij}^0, \omega_{Dij}^1|i\right) = \prod_{d=1}^{D} F\left(\omega_{dij}^0, \omega_{dij}^1|i\right)$$

and $F(.)$ is jointly normal with

$$\left(\omega_{dij}^0, \omega_{dij}^1\right) \overset{iid}{\sim} N\left(\begin{pmatrix} \overline{\alpha}_{di}^0 \\ \overline{\alpha}_{di}^1 \end{pmatrix}, \begin{bmatrix} \sigma_{di0}^2 & \rho_{di} \\ \rho_{di} & \sigma_{di1}^2 \end{bmatrix}\right)$$

where we allow some nonzero correlation between ω_{dij}^0 and ω_{dij}^1, implying that we allow the change in physician i's preference for drug d due to the warning ω_{dij}^1 to be correlated with the physician's preference before the warning ω_{dij}^0.

This implies that we obtain a discrete choice model that corresponds to a random coefficient discrete choice logit for each physician i. While we add these functional form restrictions for practical estimation, McFadden and Train (2000) show that mixed logit (random coefficient logit) models are flexible enough to approximate any discrete choice model. The conditional choice probability that physician i chooses

$(y_{i1} = d_1, y_{i2} = d_2, .., y_{iJ} = d_J)$ for her J patients is

$$\prod_{j=1}^{J} P\left(y_{ij} = d|i, \tau\left(j\right)\right)$$

where

$$P\left(y_{ij} = d|i, \tau\left(j\right)\right) = \int \frac{\exp\left(\omega_{dij}^{0} + \omega_{dij}^{1}\tau\left(j\right)\right)}{1 + \sum_{\tilde{d}=1}^{D} \exp\left(\omega_{\tilde{d}ij}^{0} + \omega_{\tilde{d}ij}^{1}\tau\left(j\right)\right)} \prod_{\tilde{d}=1}^{D} dF\left(\omega_{\tilde{d}ij}^{0}, \omega_{\tilde{d}ij}^{1} | \overline{\alpha}_{\tilde{d}i}^{0}, \overline{\alpha}_{\tilde{d}i}^{1}, \sigma_{\tilde{d}i0}^{2}, \sigma_{\tilde{d}i1}^{2}, \rho_{\tilde{d}i}\right) \quad (3.4)$$

With a large number of patients J per physician, we can identify the parameters $\overline{\alpha}_{di}^{0}, \overline{\alpha}_{di}^{1}, \sigma_{di0}^{2}, \sigma_{di1}^{2}, \rho_{di}$ for all physicians $i = 1, .., I$. Thus, if $\overline{\alpha}_{di}^{0} \neq \overline{\alpha}_{di}^{1}$ or $\sigma_{di0} \neq \sigma_{di1}$, it will mean that physician preferences have changed with the warning.

We can then define the marginal effect of the changes in preferences of physician i on each prescription probability to patient j as

$$\Delta P\left(y_{ij} = d|i, j\right) \equiv \frac{\exp(\omega_{dij}^{0} + \omega_{dij}^{1})}{1 + \sum_{\tilde{d}=1}^{D} \exp(\omega_{\tilde{d}ij}^{0} + \omega_{\tilde{d}ij}^{1})} - \frac{\exp \omega_{dij}^{0}}{1 + \sum_{\tilde{d}=1}^{D} \exp \omega_{\tilde{d}ij}^{0}}$$

and after identifying the parameters $\overline{\alpha}_{di}^{0}, \overline{\alpha}_{di}^{1}, \sigma_{di0}^{2}, \sigma_{di1}^{2}, \rho_{di}$ for all physicians, we can obtain any moment or quantile of the distribution of the marginal effect on the prescription of drug d both within and across physicians. For example, the average marginal effect on the prescription of drug d for physician i is

$$\begin{aligned} & \Delta P\left(y_{ij} = d|(\overline{\alpha}_{di}^{0}, \overline{\alpha}_{di}^{1}, \sigma_{di0}^{2}, \sigma_{di1}^{2}\rho_{di})_{d=1,..,D}\right) \quad (3.5) \\ \equiv & \int \left(\frac{\exp(\omega_{dij}^{0} + \omega_{dij}^{1})}{1 + \sum_{\tilde{d}=1}^{D} \exp(\omega_{\tilde{d}ij}^{0} + \omega_{\tilde{d}ij}^{1})} - \frac{\exp \omega_{dij}^{0}}{1 + \sum_{\tilde{d}=1}^{D} \exp \omega_{\tilde{d}ij}^{0}} \right) dF\left((\omega_{\tilde{d}ij}^{0}, \omega_{\tilde{d}ij}^{1})_{\tilde{d}=1,..,D} | (\overline{\alpha}_{\tilde{d}i}^{0}, \overline{\alpha}_{\tilde{d}i}^{1}, \sigma_{\tilde{d}i0}^{2}, \sigma_{\tilde{d}i1}^{2}, \rho_{\tilde{d}i})_{\tilde{d}=1,..,D}\right) \end{aligned}$$

The heterogeneity across physicians of parameters $\overline{\alpha}_{di}^{0}$, $\overline{\alpha}_{di}^{1}$, $\sigma_{di0}^{2}, \sigma_{di1}^{2}$, ρ_{di} combines the potential heterogeneity of behavior of physicians and the potential heterogeneity of patients across physicians, which cannot be disentangled without additional assumptions. For example, before the warning, the heterogeneity of the distribution of $\omega_{\tilde{d}ij}^{0}$ across physicians i cannot be interpreted as heterogeneity of physician preferences because it combines the heterogeneity of physicians with the unobserved heterogeneity of patients, unless we add some specific untestable assumptions on the matching between patients and physicians. However, assuming stability of the distribution of patients for a given physician before and after the warning is a

weaker assumption, allowing us to interpret differences in the distributions of ω^0_{dij} and ω^1_{dij} as changes in preferences for a given physician.

4 Empirical Results

4.1 Model Estimates

We thus implement the estimation of this random coefficient logit model for each physician. We consider the alternative choices of antidepressant classes as SNRIs, SSRIs, TCAs, and "other antidepressants" (mianserine, mirtazapine, tianeptine) while the category "other drugs" is the normalized outside option and gathers drugs that are not antidepressants. The latter are mostly drugs not approved for depression treatment but used off-label in depression treatment by physicians. These drugs are mostly antipsychotics (i.e. olanzapine) or anxiolytics (i.e., alprazolam, bromazepam, prazepam). The discrete choice model thus has 5 alternatives that almost all physicians prescribe[2], and we ignore coprescriptions, which represent less than 3% of depression treatments.

We allow the patient's observable characteristics, such as gender (g_j) and age (a_j) to affect the mean utility of the discrete choice model by specifying the joint distribution of random coefficients as follows:

$$\left(\omega^0_{dij}, \omega^1_{dij}\right) \overset{iid}{\sim} \mathcal{N}\left(\begin{pmatrix} \overline{\alpha}^0_{di}\left(g_j, a_j\right) \\ \overline{\alpha}^1_{di}\left(g_j, a_j\right) \end{pmatrix}, \begin{bmatrix} \sigma^2_{di0} & \rho_{di} \\ \rho_{di} & \sigma^2_{di1} \end{bmatrix}\right)$$

where

$$\begin{aligned} \overline{\alpha}^0_{di}\left(g_j, a_j\right) &= \alpha^0_{di} + \alpha^g_{di} g_j + \alpha^a_{di} a_j \\ \overline{\alpha}^1_{di}\left(g_j, a_j\right) &= \alpha^1_{di} + \alpha^g_{di} g_j + \alpha^a_{di} a_j \end{aligned}$$

The estimation of the random coefficient logit model thus has 8 random effects ω^0_{dij}, ω^1_{dij} for $d = 1, 2, 3, 4$ at the patient level j and 28 parameters $\alpha^a_{di}, \alpha^1_{di}, \alpha^0_{di}, \alpha^g_{di}, \sigma_{di0}, \sigma_{di1}, \rho_{di}$ for $d = 1, 2, 3, 4$ for each physician $i = 1, .., 386$. For 48 physicians, the model parameters cannot be estimated even with added restrictions because of the existence of too few patients with depression diagnoses. Thus, for 91 physicians, the correlation ρ_{di} is very imprecisely estimated, with a very large standard error, in which case we estimate the same model

[2]Among all the physicians, only 3 never prescribe an SNRI, 8 never prescribe a TCA and only one never uses other antidepressants. All of the physicians prescribe SSRIs.

with the additional restriction of no-correlation ($\rho_{di} = 0$). For an additional subset of 32 physicians, the variance coefficients σ_{di0} or σ_{di1} are too imprecisely estimated, in which case we also impose that $\sigma_{di0} = 0$ and $\sigma_{di1} = 0$. As a result, there are no restrictions on parameters for the remaining 215 physicians. We thus obtain all parameter estimates for 338 physicians (we have imposed $\rho_{di} = 0$ for 91 of them and $\rho_{di} = \sigma_{di0} = \sigma_{di1} = 0$ for 32).

Table 4.1 reports the results of this random coefficient model for one of the physicians. The results show that the warning makes this physician's preference towards SSRIs decrease, as α^1_{di} is significantly negative for SSRIs, and that the warning increases his preference towards SNRIs, as α^1_{di} is positive for SNRIs albeit significant only at the 10% level. The parameter σ^0_{di} is positive and significant, showing that there is large heterogeneity in treatments before the warning. This heterogeneity is not surprising and is due to the heterogeneity of patients for this physician. The parameter σ^1_{di} is also positive, showing, for example, that this physician's preferences are affected by the warning such that her decision utility for SSRIs has an even larger variance after the warning, and the parameter ρ_{di} being positive for SSRIs shows that the larger the variance before the warning, the larger it is after. As a result, this physician decreases SSRI prescriptions after the warning and substitutes towards SNRIs and the reference alternative, "other drugs". The distribution of estimated parameters across all physicians is provided in Table A.1 in the appendix.

Table 4.1: *Random Coefficient Logit Estimation for a Single Physician i*

	Patient's		Baseline		Warning		
	Age	Gender	Mean	SD	Mean	SD	Correlation
Drugs:	α^g_{di}	α^a_{di}	α^0_{di}	σ_{di0}	α^1_{di}	σ_{di1}	ρ_{di}
SSRIs	-0.07	-0.47	4.04	3.21	-1.86	8.26	0.93
	(.01)	(.39)	(.66)	(.36)	(.52)	(1.35)	(.99)
SNRIs	-0.06	0.19	1.85	3.24	0.78	5.30	-1.58
	(.01)	(.45)	(.74)	(.33)	(.47)	(1.08)	(.96)
TCAs	-0.01	-0.29	-2.64	2.77	0.83	4.49	0.56
	(.02)	(.61)	(1.18)	(.41)	(.99)	(1.58)	(.71)
Other Antidep.	-0.18	-0.36	6.02	3.45	-2.69	7.55	6.49
	(.04)	(.60)	(1.59)	(.42)	(1.38)	(2.46)	(1.98)
No. of visits	1397						

Notes: A negative gender coefficient means that the physician has a lower preference for this drug for female patients (dummy is 1 for female and 0 for male). Standard errors in parentheses.

The parameter estimates of the warning effect by physician are then informative about how each physician's preferences change with the warning, while those on demographics possibly mix the heterogeneity of physician preferences with the sorting of patients into physician practices based on the heterogeneity of patient states.

As all parameters change with the warning, it is easier to look at changes in prescription probabilities, as we do in the following.

4.2 Effects of the warning on choice probabilities

Using the model estimates, we can now predict the choice probabilities before and after the warning for each physician for any patient of any age and gender group. Table 4.2 reports the quantiles of prescription probability for each choice alternative before and after warning preferences. These predicted probabilities should be equal to those in Table 2.4 if there is no estimation error and if the model specification is correct. We can see that the results are similar, although our model imposes the restrictions that age and gender can affect only the mean utilities and not the variance. This shows that the choice modeling allows us to replicate moments of the physician-level choice probability distribution. As we can see below, the model also allows us to identify the physician-level heterogeneity of prescriptions within her set of patients. We observe a substantial level of heterogeneity across physicians, not only in terms of initial prescription probabilities but also in their responses to the warning. For instance, for children and adolescents, for 25% of the physicians, the before-warning probability of prescribing SSRIs is less than 0.41, whereas for 25%, it is more than 0.64. We also observe heterogeneity in terms of their response to the warning. At every quantile, the probability of prescribing SSRIs decreases for every age group. However, for children, adolescents and young adults, the decrease grows larger as the quantile grows larger, in terms of both percentage and percentage points, suggesting that the physicians prescribing SSRIs more often before the warning decrease their prescriptions more after the warning. We can also see that most of the substitution is towards SNRI drugs.

Table 4.2: *Heterogeneity across Physicians of Average Prescription Probabilities Before/After Warning*

Group		All Ages			Children and Adolescents			Young Adults (18-25)			Adults (26-65)			Elderly People (65+)		
		Quantiles (%)			Quantiles (%)			Quantiles (%)			Quantiles (%)			Quantiles (%)		
		25	50	75	25	50	75	25	50	75	25	50	75	25	50	75
SSRIs	Bef.	0.40	0.48	0.54	0.41	0.52	0.64	0.41	0.52	0.62	0.40	0.48	0.56	0.33	0.41	0.50
	Aft.	0.34	0.42	0.48	0.36	0.45	0.55	0.36	0.45	0.53	0.34	0.42	0.49	0.3	0.38	0.46
SNRIs	Bef.	0.06	0.10	0.14	0.05	0.10	0.18	0.06	0.10	0.16	0.06	0.10	0.15	0.05	0.08	0.14
	Aft.	0.08	0.14	0.22	0.07	0.15	0.23	0.07	0.15	0.23	0.08	0.14	0.22	0.07	0.13	0.20
TCAs	Bef.	0.04	0.07	0.10	0.01	0.03	0.06	0.01	0.03	0.06	0.03	0.06	0.09	0.05	0.10	0.17
	Aft.	0.01	0.06	0.11	0.00	0.03	0.07	0.01	0.03	0.08	0.01	0.05	0.10	0.02	0.07	0.15
Oth.	Bef.	0.07	0.11	0.16	0.03	0.07	0.13	0.03	0.08	0.14	0.06	0.10	0.15	0.07	0.13	0.20
Antidep.	Aft.	0.06	0.11	0.18	0.03	0.09	0.16	0.03	0.09	0.17	0.05	0.11	0.18	0.06	0.13	0.21
Oth.	Bef.	0.16	0.22	0.28	0.12	0.19	0.28	0.13	0.19	0.28	0.16	0.21	0.27	0.15	0.22	0.30
Drugs	Aft.	0.18	0.22	0.29	0.16	0.22	0.29	0.16	0.22	0.29	0.18	0.22	0.29	0.17	0.22	0.29

We then also compute the change after the warning in the prescription probabilities for each drug category and for each physician. Table 4.3 reports the quantiles across physicians for the change in prescription probabilities. For all the age groups but the elderly, 25% of physicians decrease their probability of prescribing SSRIs by at least 12 percentage points. For elderly patients, the 25% of physicians who decrease SSRI prescriptions the most show a decrease of a maximum of 9 percentage points. In contrast, across all age groups, 25% of the physicians either do not respond to the warning at all or increase their average probability of prescribing SSRIs (the 75% quantile if +0.01). According to Tables 4.3 and 4.4, physicians who decrease their prescriptions of SSRIs substitute towards SNRIs and "other drugs".

Table 4.3: *Heterogeneity across Physicians in Change in Prescription Probabilities due to the Warning*

Group	All Ages			Children and Adolescents			Young Adults (18-25)			Adults (26-65)			Elderly People (65+)		
	Quantiles (%)			Quantiles (%)			Quantiles (%)			Quantiles (%)			Quantiles (%)		
	25	50	75	25	50	75	25	50	75	25	50	75	25	50	75
SSRIs	-0.12	-0.05	0.01	-0.13	-0.06	0.01	-0.13	-0.06	0.00	-0.13	-0.05	0.00	-0.09	-0.03	0.04
SNRIs	-0.02	0.04	0.10	-0.02	0.04	0.09	-0.02	0.04	0.10	-0.02	0.04	0.10	-0.02	0.04	0.10
TCAs	-0.05	-0.01	0.03	-0.02	0.00	0.03	-0.02	0.00	0.03	-0.04	-0.01	0.03	-0.07	-0.02	0.02
Oth. Antidep.	-0.05	0.00	0.05	-0.03	0.00	0.05	-0.03	0.00	0.05	-0.04	0.00	0.05	-0.06	-0.01	0.05
Oth. Drugs	-0.02	0.02	0.05	-0.01	0.03	0.06	-0.02	0.02	0.06	-0.03	0.02	0.06	-0.03	0.01	0.06

Table 4.4 shows, for each drug class, the mean, median and standard deviation of the average across patients of the physician-level prescription probability for the periods before and after the warning as well as the within-physician changes in variance of prescription probabilities. It shows that the average probability of prescribing SSRIs decreases with the warning by 5.3 percentage points. Physicians substitute away from SSRIs towards SNRIs. It also shows that the heterogeneity across physicians increases after the warning and increases more for other drug classes than SSRIs. It is as if the warning is interpreted differently by heterogeneous physicians. We also observe an increase in the within-physician variance of the probability of prescribing SSRIs or SNRIs, meaning that after the warning, physicians make less homogeneous decisions across patients than before. The figures below help clarify the changes across the different drug categories.

Figure 4.1 plots the average physician prescription probability for all drugs with before-warning preferences on the horizontal axis and after-warning preferences on the vertical axis. The first row reports the average prescription probability by physician for all patients and the second row for only children and adolescents. We see that with the warning, a majority of physicians decrease their SSRI prescriptions and increase their SNRI prescriptions. We do not observe a clear trend for other choice alternatives. For instance, for TCAs and "other antidepressants", half of the physicians increase their prescriptions of these drugs after the warning,

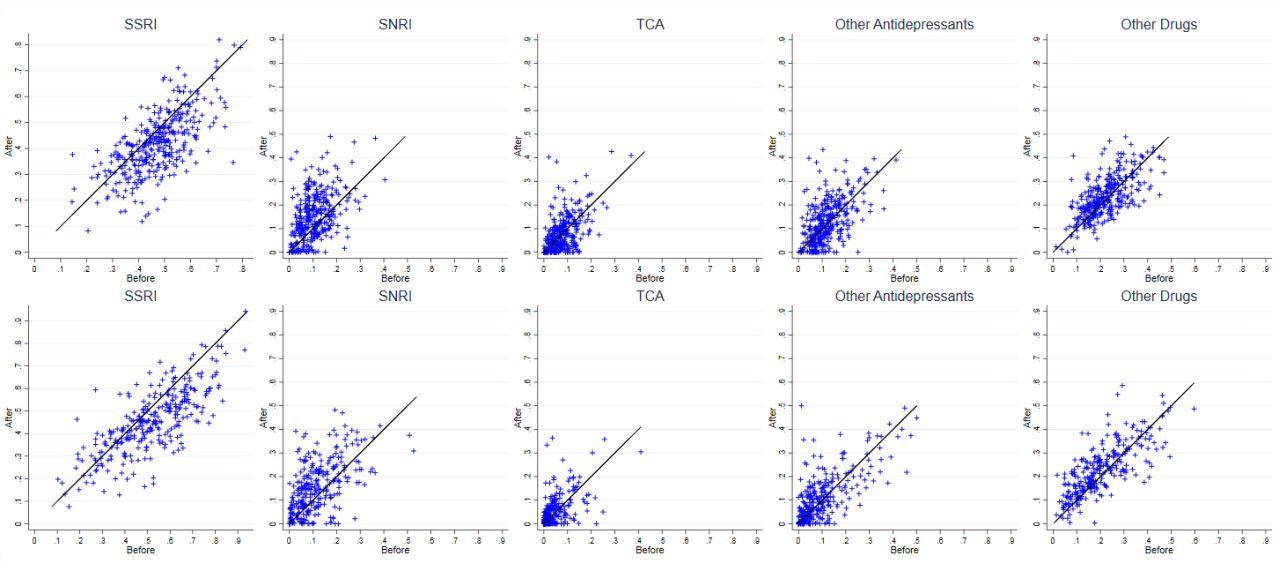
Table 4.4: *Distribution of Physician Prescription Probabilities Before/After Warning*

	Across Physicians						Within-Physician		
	Mean			Standard Deviation			Standard Deviation		
Drug	Before	After	Change	Before	After	Change	Before	After	Change
SSRIs	0.470	0.417	-0.053	0.111	0.117	0.006	0.354	0.388	0.034
SNRIs	0.106	0.152	0.046	0.065	0.101	0.036	0.209	0.268	0.059
TCAs	0.077	0.073	-0.004	0.052	0.074	0.022	0.185	0.179	-0.006
Oth. Antidep.	0.119	0.125	0.006	0.068	0.091	0.023	0.221	0.242	0.021
Oth. Drugs	0.227	0.241	0.014	0.093	0.103	0.010	0.248	0.305	0.057

Note: Mean and standard deviation across physicians in the first six columns and within-physician standard deviation of prescription probabilities in the next three columns.

whereas the the other half decrease their prescriptions of these drugs. The figure shows substitution from SSRIs towards SNRIs. For children and adolescents, we observe similar responses to the warning, except that many more physicians substitute SSRIs with "other drugs", not only with SNRIs.

Figure 4.1: *Effect of Warning on Average Prescription Probability by Physician and Drug as Function of Baseline Prescription Probability*

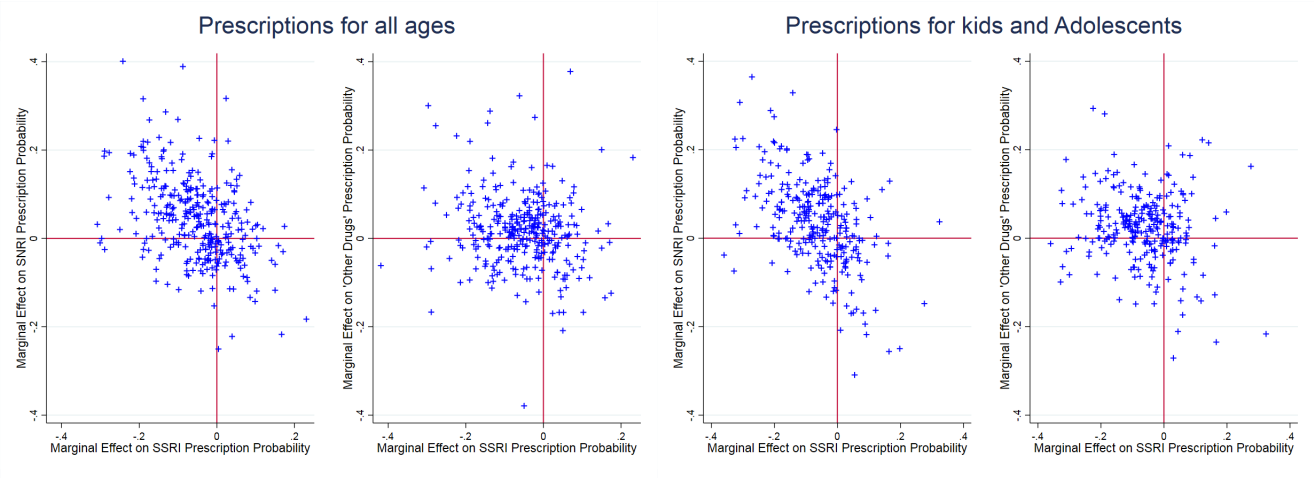


Notes: Scatter plot of predicted physician-level prescription probability after the warning as a function of the before-warning probability. Each point represents a physician-level probability. The first row shows the mean choice probabilities for any patient, and the second row shows the mean choice probabilities for children and adolescents.

Figure 4.2 shows the substitution patterns between SSRIs and other drugs using estimates of the marginal effect of the warning on each probability as in equation (3.5). The left (right) panel plots, for each physician, the change in the probability of prescribing SSRIs on the horizontal axis and the change in the probability of prescribing SNRIs ("other-drugs") on the vertical axis. Figure 4.2 plots the substitution patterns across all patients and only for children and adolescents. The majority of the physicians are located in the upper-left corner of the graph, meaning that they are the ones substituting away from SSRIs towards SNRIs and/or

"other drugs". For children and adolescents, an even higher number of physicians are in the upper-left corner of the graph.

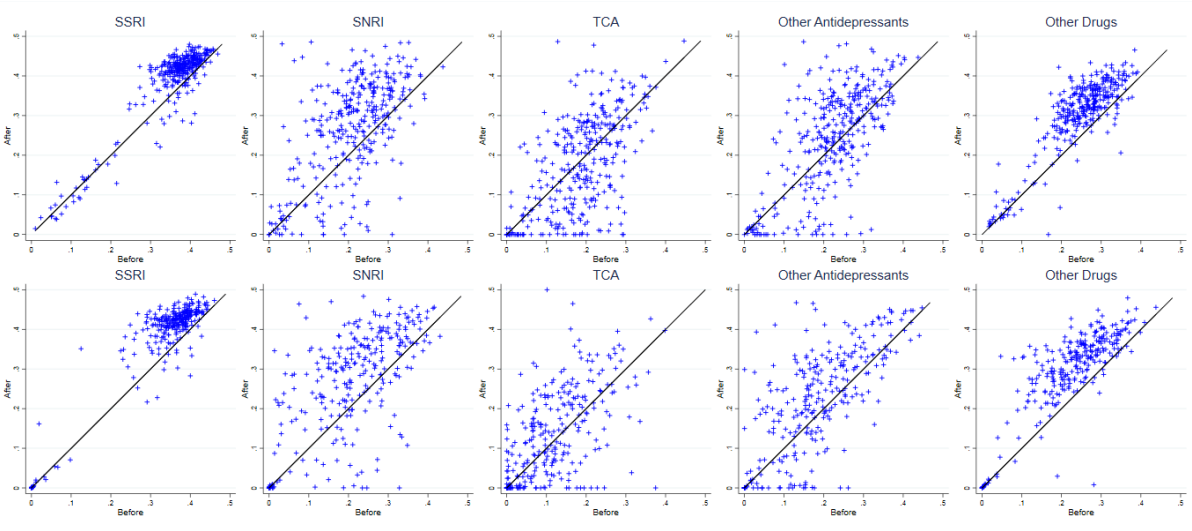
Figure 4.2: *Effect of Warning on Average Prescription Probability by Physician*



Notes: Plots of changes in the physician-level mean probability of prescribing SSRIs versus SNRIs and "other drugs".

As we have seen earlier, the warning affects not only the mean physician preference towards each drug but also its variance, meaning that it affects the way physicians prescribe heterogeneously across patients. Figure 4.3 plots the within-physician variance of the prescription probability with before-warning preferences on the horizontal axis and after-warning preferences on the vertical axis for all patients. The figure shows that the physician-level variance in the probability of prescribing SSRIs increases for almost all physicians except for those with a lower variance before the warning, who do not seem to be affected. This shows that the warning does not lead physicians to prescribe uniformly across patients after the warning, and the second row of graphs in Figure 4.3 shows that this is also true within the age category of children and adolescents. For a majority of the physicians, the within-physician variance in the probability of prescribing SNRIs and "other drugs" also increases after the warning. We do not see such a clear effect for other alternatives. For TCAs and "other antidepressants", the within-physician variance of the prescription probability slightly increases for approximately half of the physicians and slightly decreases for the other half. We observe very similar patterns for children and adolescents even though the warning concerns only and all the patients in this age group. Contrary to what may have been expected, the warning does not lead to more uniform treatment choices across physicians, probably because physicians are very heterogeneous ex ante and the effect of the warning on their preferences also proves to be very heterogeneous.

Figure 4.3: *Effect of Warning on Within-Physician Variance of Prescription Probability*



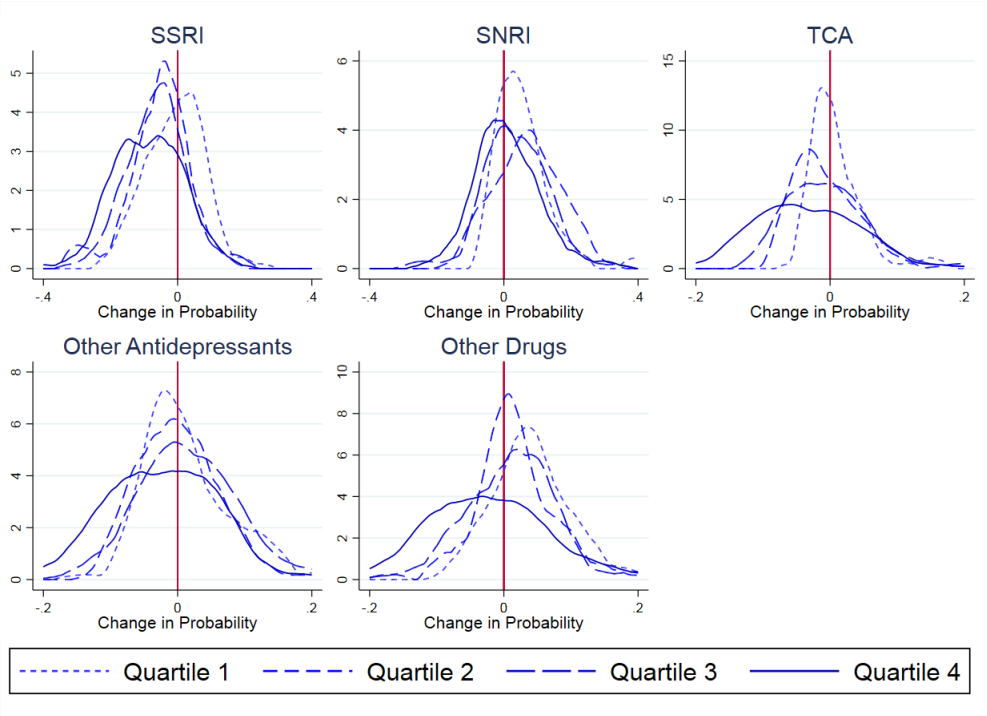
Notes: Scatter plot of physician-level variance of prescription probability after the warning as a function of the before-warning probability. Each point represents one physician-level variance observation. The first row shows the variance of choice probabilities for any patient, and the second row shows the variance of choice probabilities for children and adolescents.

Another way to examine the heterogeneity of the effects of the warning consists of looking at the changes in the distribution of prescription probabilities across physicians depending on their before-warning choice probability. Figures 4.4 and 4.5 plot these densities of the average change in physician prescription probability by quartile of the ex ante prescription probability for all patients and for children and adolescents, respectively. For SSRIs, the largest decrease in prescription probability after the warning is among physicians in the highest quartile (quartile 4) in terms of ex ante probability of prescribing SSRIs. The smallest decrease is among physicians in the lowest quartile (quartile 1). Similarly, the largest increase in the probability of prescribing SNRIs and "other drugs" is among those who were prescribing those categories least often before the warning (quartiles 1 and 2 in the figures for SNRIs and "other drugs"). The patterns are similar across all patients and for children and adolescents only.

When looking at the correlation of the physician-level probabilities of prescribing any of these drug categories with observable physician characteristics, we find no significant correlation with physician age or gender but find some with the number of depressed patients per year seen by the physician. The only significant correlations between prescription probabilities before and after the warning are for SSRIs and other drugs. The more patients seen by a physician, the higher is her probability of prescribing SSRIs both before and after the warning (without correlation with the change) and the lower her probability of prescribing other drugs. We observe this correlation without any possibility of assessing causality that could go both

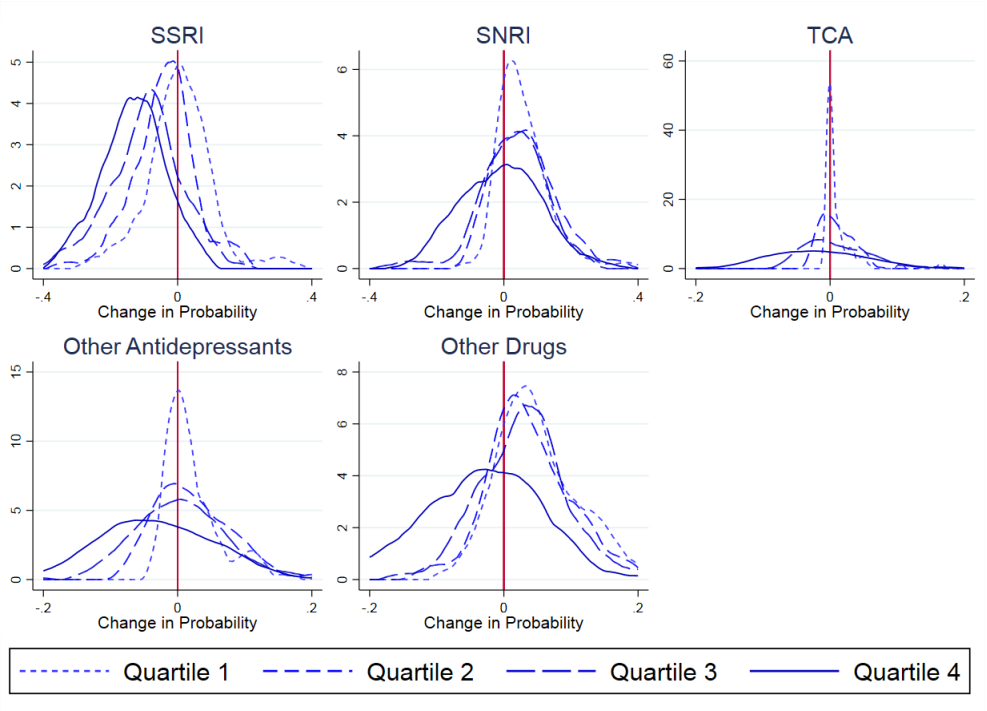
ways; thus, the finding calls for more research on the long-term determinants of physician preferences and abilities.

Figure 4.4: *Effect on Prescription Probability by Quartile – All Ages*



Notes: Kernel density estimates of physician-level changes in prescription probability by quartile of ex ante choice probability.

Figure 4.5: *Effect on Prescription Probability by Quartile – Children and Adolescents*



Notes: Kernel density estimates of physician-level changes in prescription probability by quartile of ex ante choice probability.

4.3 Comparing the Effects of the Warning with Those of a Ban

In the previous section, we show that the warning on SSRIs on average reduces physician prescriptions of SSRIs but also has very heterogeneous effects. Given that the warning was clear on the fact that SSRIs should not be prescribed (or should only be prescribed as a last resort) to children and adolescents, we may consider the possible effect of a complete ban like those sometimes imposed on drugs that are uniformly considered too unsafe. This is what happened, for example, when the antiinflammatory Vioxx was pulled from the market. We thus look at the counterfactual effects of a ban of SSRI drugs for children and adolescents to compare physicians' substitution of drug prescriptions. Of course, in the case of a ban, SSRI prescriptions to children and adolescents would disappear, while the warning is far from yielding such an effect. A ban would also annihilate the heterogeneity across physicians in the probabilities of prescribing SSRIs. That said, the model still allows us to compare the changes in prescriptions of other drugs.

Banning SSRI drugs for use by children and adolescents could, however, not only change the ability to prescribe SSRIs but also affect the preferences of physicians towards other drugs, just as the warning has done. As we do not observe such a ban, we compare the effects of both the ban and the warning using the ex ante and ex post physician preferences (before and after the warning).

Our model allows us to simulate the prescription probabilities in the absence of SSRIs as follows. With the same notation as in equation (3.4), the choice probability of any drug d that is not an SSRI based on prewarning preferences is:

$$P\left(y_{ij}=d|i,\tau\left(j\right)=0,\text{no SSRI}\right)=\int\frac{\exp(\omega_{dij}^{0})}{1+\sum_{\{\tilde{d}\neq SSRI\}}\exp(\omega_{\tilde{d}ij}^{0})}\prod\nolimits_{\{\tilde{d}\neq SSRI\}}dF\left(\omega_{\tilde{d}ij}^{0}|\overline{\alpha}_{\tilde{d}i}^{0},\sigma_{\tilde{d}i0}^{2}\right) \tag{4.1}$$

while with postwarning preferences, it is:

$$P\left(y_{ij}=d|i,\tau\left(j\right)=1,\text{no SSRI}\right)=\int\frac{\exp(\omega_{dij}^{1})}{1+\sum_{\{\tilde{d}\neq SSRI\}}\exp(\omega_{\tilde{d}ij}^{1})}\prod\nolimits_{\{\tilde{d}\neq SSRI\}}dF\left(\omega_{\tilde{d}ij}^{1}|\overline{\alpha}_{\tilde{d}i}^{1},\sigma_{\tilde{d}i1}^{2}\right) \tag{4.2}$$

Table 4.5 shows the mean choice probability of each drug category with or without the ban using pre- or postwarning preferences. Given that the decrease in SSRIs is obviously much larger under a ban, the ban mostly leads to substitution to other non-antidepressant drugs rather than to SNRIs or other antidepressants. The SSRI warning leads to a modest decrease in SSRI prescriptions, half of which is directed towards SNRI drugs (see the last column of Table 4.5); however, while the ban on SSRIs leads to a much larger effect, more than half of the decrease in SSRI prescriptions goes to drugs other than antidepressants. This means that the ban on SSRI drugs has a very different effect from that of the SSRI warning. We can see that the effect of the ban on SSRIs using postwarning preferences proportionately benefits other drugs more (0.298/0.452=0.66 is larger than 0.322/0.517=0.62). Of course, the ban on SSRIs also has quite a different effect on the within-physician variance of the prescription probability, as it lowers the variance in prescribing SSRIs (since the probability of prescribing SSRIs becomes zero for any patient of any physician), while the warning has the effect of increasing the variance.

Table 4.5: *Effects of an SSRI Ban versus the Warning on Physician Prescription Probabilities (Children and Adolescents (2-18))*

	With Prewarning Preferences			With Postwarning Preferences			Warning Only
	No Ban	With Ban	Change	No Ban	With Ban	Change	Change
Drug	P_d^0	$P_{d,ban}^0$	$P_{d,ban}^0 - P_d^0$	P_d^1	$P_{d,ban}^1$	$P_{d,ban}^1 - P_d^1$	$P_d^1 - P_d^0$
SSRIs	0.517	0.000	−0.517	0.452	0.000	−0.452	−0.065
SNRIs	0.122	0.207	+0.085	0.158	0.231	+0.073	+0.036
TCAs	0.043	0.078	+0.035	0.048	0.075	+0.027	+0.005
Oth. Antidep.	0.101	0.176	+0.075	0.112	0.169	+0.057	+0.011
Oth. Drugs	0.215	0.537	+0.322	0.234	0.532	+0.298	+0.019

Notes: Column titles denote the mean prescription probability for any child or adolescent patient across all physicians. P_d^0 is the mean prescription probability of drug d under prewarning preferences, and $P_{d,ban}^0$ is the mean prescription probability of drug d under prewarning preferences when SSRIs are banned. P_d^1 and $P_{d,ban}^1$ denote the same mean probabilities using postwarning preferences.

5 Conclusion

In this paper, we study how scientific information released by public authorities, such as a drug warning, affects the prescribing behavior of physicians. As physician prescribing behavior may depend on both physician preferences and on unobserved, possibly correlated characteristics of patients, we show that we cannot generally disentangle the heterogeneity in physician preferences from the heterogeneity in patient characteristics. However, using the long time dimension of panel data on physician prescriptions to a large set of patients before and after a warning that may have affected physicians' preferences, and assuming that the distribution of patient heterogeneity is stable over time before and after the warning, we can identify the change in preferences by allowing for physician-specific random effects in prescribing behavior.

Taking the example of antidepressant drugs, we use French panel data on exhaustive prescriptions of a representative sample of general practitioners to more than 110,000 depressed patients between 2000 and 2008. Changing scientific evidence on the efficacy and side effects of drugs can result in official warnings and recommendations. New results on the increase in suicidal thinking in children were reported in 2004 for selective serotonin reuptake inhibitors (SSRIs). We find that SSRI-type antidepressant prescriptions decreased after 2004 for children and adolescents, but the physicians responded to the new information very heterogeneously. We find that the drug warning increased the variance of physician prescribing behavior both across physicians and within individual physicians. One important result is that the warning reduced the probability of prescribing SSRIs to all patients in addition to children and adolescents and that this reduction was larger but also more heterogeneous for physicians with a higher mean probability of prescribing SSRIs before the warning. The method presented can be used to understand how physician behavior is affected by scientific information, warnings, and the entry and exit of new drugs by using panel data and assuming that the correlation between patients' unobserved characteristics and physicians' preferences is stable and not affected by the event. Finally, we compare the effect of the SSRI warning with a possible removal of market authorization for use of SSRIs by children and adolescents and show that not only is the magnitude of the effect of the warning much lower than that of a removal but also the substitution towards alternative drugs is very different. These results call into question the interpretation of drug warnings and recommendations by physicians and show how heterogeneous reactions can occur in relationship to physicians' ex ante preference for the different possible treatments.

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A Appendix

A.1 Full Model Estimates Table

Table A.1 reports the distribution of all coefficient estimates of the model across the 386 physicians.

Table A.1: *Distribution of Coefficient Estimates Across Physicians*

			Quantiles		
Drugs	Baseline parameters		*25 %*	*50 %*	*75 %*
SSRIs	Age	α^g_{di}	-0.04	-0.01	0.01
	Gender	α^a_{di}	-0.62	0.07	0.81
	Constant	α^0_{di}	0.30	1.55	3.06
	Std Deviation	σ_{di0}	2.41	3.12	4.10
SNRIs	Age	α^g_{di}	-0.05	-0.01	0.02
	Gender	α^a_{di}	-1.31	0.01	1.19
	Constant	α^0_{di}	-5.60	-2.75	-0.66
	Std Deviation	σ_{di0}	2.64	3.43	5.04
TCAs	Age	α^g_{di}	0.01	0.04	0.09
	Gender	α^a_{di}	-1.54	0.03	1.77
	Constant	α^0_{di}	-12.8	-7.73	-4.13
	Std Deviation	σ_{di0}	2.92	4.15	6.12
Other Antidep.	Age	α^g_{di}	-0.02	0.02	0.06
	Gender	α^a_{di}	-1.48	-0.35	0.58
	Constant	α^0_{di}	-6.81	-3.32	-0.95
	Std Deviation	σ_{di0}	2.50	3.46	4.74
	Warning effects				
SSRIs	Mean	α^1_{di}	-0.91	-0.28	0.47
	Std Deviation	σ_{di1}	1.20	2.17	3.54
	Correlation	ρ_{di}	-0.46	0.00	0.56
SNRIs	Mean	α^1_{di}	-4.47	-1.07	0.48
	Std Deviation	σ_{di1}	1.21	2.94	6.05
	Correlation	ρ_{di}	-0.51	0.00	1.10
TCAs	Mean	α^1_{di}	-9.41	-3.04	-0.30
	Std Deviation	σ_{di1}	0.61	1.96	4.10
	Correlation	ρ_{di}	-0.37	0.00	1.46
Other Antidep.	Mean	α^1_{di}	-4.82	-1.78	-0.17
	Std Deviation	σ_{di1}	0.69	1.92	4.10
	Correlation	ρ_{di}	-0.46	0.00	0.83

Notes: Coefficients of random coefficient logits with 338 physician-specific coefficients. Correlation coefficients ρ_{di} are not identified and thus restricted to zero for 91 physicians, and all random coefficients are not identified and thus are restricted to zero for 32 physicians. From the original sample, 48 physicians do not have enough visits with depression to be included in the model.