

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 the possibility that patients 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. 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 kids and adolescents. After such events and medical warnings, physicians must update their beliefs on different drug treatments and may react differently to these warnings.

We first show some difference-in-difference estimation of the change in the prescription probability of SSRI drugs before and after the warning for kids and adolescents relative to other antidepressants and to older patients. The evidence shows a decline in the prescriptions of SSRIs and placebo regressions show that it coincides with the time of the warning. As such difference-in-difference estimation cannot disentangle the effect of the warning on the preferences for the different types of drugs, we use a discrete choice model to estimate physician preferences.

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 decision model allows us to conduct counterfactual analysis and investigate the impact of different policies on physicians' prescribing behavior which would not be possible with reduced form analysis.

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 kids and adolescents less often after the warning, but many still do not adhere 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 kids and adolescents decreases 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 changes very heterogeneously across physicians. It seems that some physicians interpret the warning as "good" or "bad" news for age groups other than kids and adolescents.

Finally, thanks to a counterfactual simulation of the decision model, we evaluate the substitution of SSRIs towards other drug categories that would result from a ban on prescriptions of SSRI drugs to kids and adolescents and compare the substitution patterns with those in the case of the warning. Banning SSRIs for kids and adolescents leads to a substitution to other alternatives just like the warning does, but of course all SSRI prescriptions disappear and are replaced by alternatives. However, the ban leads to a lower level of substitution to other antidepressants and a higher level of substitution towards drugs other than antidepressants, relative to the warning. In other words, a physician stopping to prescribe SSRIs to kids and adolescents after a warning is more likely to substitute with any other antidepressant than he or she would do in the case of a ban. This happens because the warning seems to less negatively affect the preferences for non-SSRI antidepressants compared to drugs other than antidepressants.

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 co-payments 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), Ching et al. (2013), Ching and Lim (2020)). Our work 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)). 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. 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. Berez et al. (2018) study the physicians' response to information on ineffectiveness of pulmonary artery catheters (PACs). They find that the use of PACs declined after the release of evidence on the lack of benefit from their use and that older physicians' use of PACs was influenced by the practice patterns of their junior colleagues. Howard et al. (2017) use a negative informational shock (namely the fact that a common knee operation does not improve outcomes for patients with osteoarthritis) to study the impact of physicians' agency relationships on treatment decisions. They show that providers at physician-owned surgery centers abandoned common knee surgeries at a lesser rate than physicians practicing in hospitals. Howard and Hockenberry (2019) show that episiotomy rate declined from 54% in 1994 to 13% in 2010 but that older physicians were more likely to perform it and were slower to adjust their practices in response to evidence showing that routine episiotomy is unnecessary. 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.

The paper proceeds as follows: 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 shows reduced form evidence of the effect of the warning on prescriptions. Section 4 presents our model and identification strategy. Section 5 shows the results of the empirical estimation on antidepressants and depression treatment in France, and section 6 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-old¹). Finally, depression also increases health-care expenditures. Depressed people visit their generalists for somatic complaints three times more often than nondepressed people (Kessler et al. (2003)).

The most commonly used modern antidepressants are those from the second generation, which generally dominate those from the first generation. 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%

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

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 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 public health authority, 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 kids 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 kids 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 kids 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 kids 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 (called the "Cegedim Strategic Data Longitudinal Patient Database"), 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 their general practitioner.

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

Group	All Ages	Kids 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 kids and adolescents. These other drug treatments prescribed by physicians are antipsychotics, anxiolytics, hypnotics, or antiepileptics. For any visit to these physicians, as soon as the physician diagnoses a depression (even mild), he or she almost always prescribes some medicine, which can be an antidepressant or another drug from these other classes (only 0.4% of depression diagnostic end up with no drug prescription).

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 kids 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 kids 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		Kids 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 25th percentile, the median and the 75th percentile across physicians of the prescription probability of each drug class for the periods before and after the SSRI warning in 2004. We observe a substantial level of heterogeneity across physicians. For instance, before the warning for kids and adolescents, 25% of the physicians prescribe an SSRI less than 20% of the time when they diagnose depression, whereas 25% prescribe an SSRI more than 73% of the time when they diagnose depression. We observed heterogeneity in physicians’ prescribing behavior for other age groups as well.

The comparison before and after the warning shows 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 kids 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 kids 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. They 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. Off-label use of a drug, that is prescription of a drug for an indication other than the indications it is approved for, was allowed in France during our sample period (for details see Tunçel (2020)). 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. Moreover changes in quantiles in the population can come from a few physicians dramatically changing their prescription behavior or many physicians changing their behavior but by very little. Our modeling of treatment decisions by physicians will thus try to disentangle the effect of physician preferences from that of patient heterogeneity, and identify individual changes themselves.

Table 2.3: *Quantiles of Average Prescription Probabilities Across Physicians Before and After the Warning*

Group		All Ages			Kids 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. Antidep.	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
	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. Drugs	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
	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

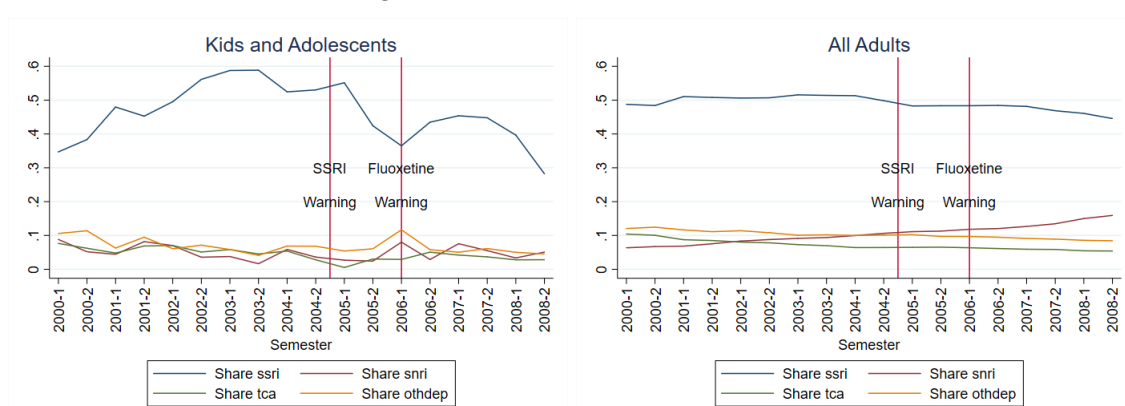
3 Reduced Form Evidence

Before developing our discrete choice model to identify the effect of the warning on physicians preferences, we document some reduced form evidence on the effect of the warning.

3.1 Changes in Aggregate Prescriptions

Figure 3.1 shows the shares of each drug category among all prescriptions for the kids and adolescents which is the target age group of the warning and for all the other ages. The SSRI warning seems to decrease the propensity to prescribe SSRI while not substantially increasing the other categories of antidepressants, meaning that the outside option of not prescribing any antidepressant becomes more important for kids and adolescents after the warning. For other age categories, we can see a decrease in the market share of SSRI prescriptions while that of SNRI goes up and compensate the decrease such that the share of not prescribing any antidepressant is stable.

Figure 3.1: *Market Shares Over Time*



Notes: Horizontal axis denotes time in semester of each year. Market shares do not sum to one because the alternative of not prescribing any antidepressant is not reported.

Appendix A.1 compares characteristics of patients before and after the warning and performs a balancing test of these observable characteristics. Results show statistically significant difference only in mean age for adults between periods before and after the warning and no difference in the mean age of kids and adolescents. The gender composition of patients by physician does not change with the warning, either. Even though the one year increase in mean age of adults is unlikely to be an important confounding factor of the before-after estimation of prescription choice preferences by physicians, our difference-in-difference estimation controls for observable characteristics such as the age category and gender of the patient.

3.2 Difference-in-Difference Estimation

We estimate a difference-in-difference model of the relative impact of the warning on prescriptions of SSRI to kids and adolescents, controlling for observable characteristics of patients and physicians. We regress the binary decision of prescribing SSRI or not on patient and physician characteristics such as age and gender, a linear annual trend and a dummy variable for the period after the warning (December 2004) as well as the interaction of this dummy variable with the indicator that the patient is in the kids and adolescents age category. The coefficient of this interaction should identify the relative impact of the warning on the choice of prescription of SSRI to kids and adolescents that the warning is supposed to deter. Table 3.1 reports the results of a difference-in-difference estimation of the effect of the warning on the probability to prescribe an SSRI drug using a linear regression model. The difference-in-difference is across kids-adolescents and other age groups and the before and after warning periods. Then, under the assumption that there is no spillover effect of the recommendation on adults, the coefficient of the interaction of the warning with the kids and adolescents age category dummy can be interpreted as the impact of the warning on prescriptions for this age group. However, if the warning also has some effect on adults, then this coefficient can be interpreted as the differential effect on kids vs. adults. We can then assume that these coefficients allow identifying the full policy effect under the additional assumption that there is no time effect concomitant with the warning. Column (1) shows the estimation without physician fixed effects while column (2) adds physician fixed effects. Under the assumptions above, the difference in difference identification conditions are valid, the results show that SSRI prescriptions decrease with the warning and decrease even more for kids and adolescents. Results of column (1) show that the warning decreases the probability to prescribe SSRI across all patients by 3.2% and the decrease is of an additional 9.8% for kids and adolescents. Column (2) reports the results when we control for physician fixed effects in which case the effect is a 2.8% decrease for all patients and an additional 9.9% decrease for kids and adolescents.

We then perform an additional set of robustness regressions because one may wonder if this warning effect could be confounded by some time effect that would present a structural break at the time of the warning. We thus regress the binary decision of prescribing SSRI or not on patient and physician characteristics, an indicator on kids and adolescents age category, dummy variables for each year as well as the interaction of these dummy variables with the indicator that the patient is in the kids and adolescents age category. The estimation leaves out year 2003, the year before the warning, as the reference group. Figure 3.2 plots these estimated interaction coefficients, for the years in the horizontal axis. The figure shows that SSRI prescription

probability for kids and adolescents decreases with the SSRI warning of December 2004 until the Fluoxetine recommendation happening in June 2006.

To provide further evidence that the warning effect in December 2004 is unique, we also implement the same estimation by difference-in-difference using only the data before the warning and test if some placebo warning would be identified at some point during the middle of the 2000-2004 period. Columns (3) and (4) of Table 3.1 present the results of this estimation, and show no significant effect of such placebo warning during that time period.

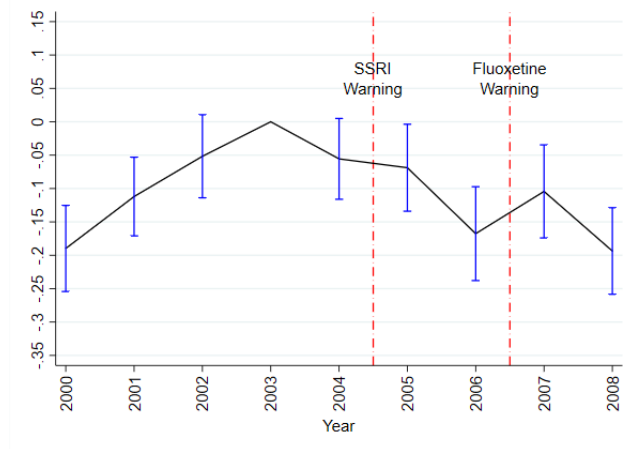
Table 3.1: *Difference-in-Difference Estimation of SSRI Prescription Probability*

Variables	(1) Warning	(2) Warning	(3) Placebo	(4) Placebo
Kids-Adolescents	-0.062 (0.053)	-0.089* (0.049)	-0.058 (0.057)	-0.084 (0.055)
Female Patient	0.040*** (0.006)	0.040*** (0.006)	0.040*** (0.006)	0.040*** (0.006)
Female Physician	-0.017** (0.007)		-0.019*** (0.007)	
Physician's Age	-0.001** (0.000)		-0.001*** (0.000)	
Warning	-0.032*** (0.004)	-0.028*** (0.004)	0.002 (0.004)	0.005 (0.004)
Kids-Adolescents*Warning	-0.098* (0.052)	-0.099* (0.051)	0.040 (0.056)	0.040 (0.053)
Annual Time Trend	Yes	Yes	Yes	Yes
Physician Fixed Effect	No	Yes	No	Yes
Observations	517,241	517,241	379,687	379,687

Notes: Columns (1) and (2) use data from July 2000 to July 2006 and the warning happening in December 2004. Columns (3) and (4) use data from July 2000 to December 2004 and a placebo warning in December 2002. Standard errors are clustered by patient as some patient may have several physician visits with depression treatment. Significance levels: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Given this reduced form evidence, we develop a prescription choice model that will allow us to understand which changes in preferences occurred and generated the estimated reduced form effects, and under which conditions we can interpret those changes as changes in the preferences of physicians or changes in patients unobserved states. Moreover, our model will also allow us to perform counterfactuals.

Figure 3.2: *Coefficient of Year Dummies Interacted with Kids and Adolescents Indicator on SSRI Prescription Probability*



Notes: Graph shows the coefficients and their 95% confidence interval of the kids*year interaction when the year dummy is defined as the date on horizontal axis. The omitted year is 2003 which is the year before the warning happening at the end of 2004.

4 Discrete Choice Model and Identification of Preference Change

4.1 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 can abstract from within-patient learning by focusing on the prescription at the first time the patient is diagnosed with depression, as at the first visit physicians still have not yet 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. However, 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 (he) depending on his characteristics θ_j and 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 ones, such as his depression state. As all patients are almost fully reimbursed, we 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 $d = 0, 1, \dots, D$, and we assume that the decision by physician i to prescribe treatment d for patient j visiting at $t(j)$ is based on maximizing

$$v(\beta_{id}^{t(j)}, \theta_j) - \varepsilon_{ijd} \quad (4.1)$$

where $v(\cdot, \cdot)$ is non decreasing 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 non deterministic functions of the patient depression state θ_j assessed by the physician. We normalize $v(\beta_{i0}^t, \theta_j) = 0$, where by convention treatment 0 corresponds to drugs other than antidepressants.

We denote the treatment chosen by physician i for patient j as $y_{ij} \in \{0, 1, \dots, D\}$. Using (4.1) 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

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

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 depend on the physician preferences $\beta_i^t = (\beta_{i1}^t, \dots, \beta_{iD}^t)$ and on the period t .

Denoting as $F(\theta_j | \beta_i^t, t)$ the cumulative distribution function of θ_j conditional on the physician preferences β_i^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

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

which is a function of physician preferences β_i^t . Matching between patients and physicians generates some possible dependence in the cumulative distribution function $F(\theta_j | \beta_i^t, t)$. However, even if patients are random-

ized to physicians such that $F(\theta_j|\beta_i^t, t) = F(\theta_j)$, 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 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 change only at the warning at time t_1 , hence they may be different in the periods before and after the warning. While a time trend in preferences could be added, it would lead to prohibitively hard numerical estimation problems in our empirical specification. We thus assume that:

$$\begin{aligned}\beta_{id}^t &= \beta_{id}^0 \text{ if } t \leq t_1 && \text{(before warning)} \\ &= \beta_{id}^1 \text{ if } t > t_1 && \text{(after warning)}\end{aligned}\tag{4.2}$$

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 patient 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:

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

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. Moreover, we allow the full distribution of preferences of each physician across all patients' status to vary with the warning, and for example not only the mean preferences. With the normality assumption made later, we will allow the mean and variance of physician specific preferences to change with the warning.

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

$$F(\omega_{1ij}^0, \omega_{1ij}^1, \dots, \omega_{Dij}^0, \omega_{Dij}^1|i, \tau(j) = 0) = F(\omega_{1ij}^0, \omega_{1ij}^1, \dots, \omega_{Dij}^0, \omega_{Dij}^1|i, \tau(j) = 1) \quad (4.3)$$

This implies that 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 and 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

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

The stability assumption that physician preferences may only change at the time of the warning allows us to identify whether preferences change even if there is endogenous matching between patients and physicians. The assumption of stability of preferences is usual in many studies of discrete choice prescribing behavior when continuous learning is not the focus (for example, Dickstein (2016)). Allowing physicians preferences to vary over time more freely than just allowing a difference between before and after the warning is conceptually possible with our approach but numerically too difficult. Moreover, our reduced form evidence of Section 3 shows that the time of the warning seems to be the time where we can observe a structural break in prescription decisions of SSRIs.

4.2 Econometric Specification

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

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

and $F(\cdot)$ is jointly normal with

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

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 .

We obtain a discrete choice model that corresponds to a random coefficient discrete choice logit for each physician i . While we add 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 ($y_{i1} = d_1, y_{i2} = d_2, \dots, y_{iJ} = d_J$) for her J patients is

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

where

$$P(y_{ij} = d | i, \tau(j)) = \int \frac{\exp(\omega_{dij}^0 + \omega_{dij}^1 \tau(j))}{1 + \sum_{\bar{d}=1}^D \exp(\omega_{\bar{d}ij}^0 + \omega_{\bar{d}ij}^1 \tau(j))} \prod_{\bar{d}=1}^D dF(\omega_{\bar{d}ij}^0, \omega_{\bar{d}ij}^1 | \alpha_{\bar{d}i}^0, \alpha_{\bar{d}i}^1, \sigma_{\bar{d}i0}^2, \sigma_{\bar{d}i1}^2, \rho_{\bar{d}i}) \quad (4.4)$$

With a large number of patients J per physician, we can identify the parameters $\alpha_{di}^0, \alpha_{di}^1, \sigma_{di0}^2, \sigma_{di1}^2, \rho_{di}$ for all physicians $i = 1, \dots, I$. Thus, if $\alpha_{di}^1 \neq 0$ or $\sigma_{di1}^2 \neq 0$, it will mean that physician preferences have changed with the warning, and we identify changes in the full distribution of preferences of each physician and not only a single preference parameter in case we would not allow heterogeneity across patients.

The marginal effect of the warning on physician i 's prescription probability to patient j is

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

and after identifying the parameters $\alpha_{di}^0, \alpha_{di}^1, \sigma_{di0}^2, \sigma_{di1}^2, \rho_{di}$ 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

$$\begin{aligned} & \Delta P(y_{ij} = d | (\alpha_{di}^0, \alpha_{di}^1, \sigma_{di0}^2, \sigma_{di1}^2, \rho_{di})_{d=1, \dots, D}) \\ \equiv & \int \left(\frac{\exp(\omega_{dij}^0 + \omega_{dij}^1)}{1 + \sum_{\bar{d}=1}^D \exp(\omega_{\bar{d}ij}^0 + \omega_{\bar{d}ij}^1)} - \frac{\exp \omega_{dij}^0}{1 + \sum_{\bar{d}=1}^D \exp \omega_{\bar{d}ij}^0} \right) dF \left((\omega_{\bar{d}ij}^0, \omega_{\bar{d}ij}^1)_{\bar{d}=1, \dots, D} | (\alpha_{\bar{d}i}^0, \alpha_{\bar{d}i}^1, \sigma_{\bar{d}i0}^2, \sigma_{\bar{d}i1}^2, \rho_{\bar{d}i})_{\bar{d}=1, \dots, D} \right) \end{aligned} \quad (4.5)$$

The heterogeneity across physicians of parameters α_{di}^0 , α_{di}^1 , σ_{di0}^2 , σ_{di1}^2 , ρ_{di} combines the potential heterogeneity of behavior of physicians and the potential heterogeneity of patients since endogenous matching is possible, and cannot be disentangled without additional assumptions. For example, before the warning, the distribution of ω_{dij}^0 for physician i can come from the fact that the physician has very varying preferences of what the value of a treatment d is across mildly varying health states of patients or from the fact that her patients have very heterogenous health states. However, assuming stability of the distribution of patients for a given physician before and after the warning allows us to interpret differences in the distributions of ω_{dij}^0 and ω_{dij}^1 as changes in preferences for a given physician. The maintained intuitive argument behind our assumptions is that the warning can change physician preferences but would not change the depression likelihood and intensity of patients.

5 Empirical Results

5.1 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 prescribe², and we ignore coprescriptions, which represent less than 3% in depression treatment.

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 such that $\alpha_{di}^0(g_j, a_j) \equiv \alpha_{di}^0 + \alpha_{di}^g g_j + \alpha_{di}^a a_j$. The estimation of the random

²Among 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.

coefficient logit model thus has 8 random effects $\omega_{dij}^0, \omega_{dij}^1$ for $d = 1, 2, 3, 4$ at the patient level j and 28 parameters $\alpha_{di}^0, \alpha_{di}^1, \alpha_{di}^a, \alpha_{di}^g, \sigma_{di0}, \sigma_{di1}, \rho_{di}$ for $d = 1, 2, 3, 4$ for each physician $i = 1, \dots, 386$. For 48 physicians, the model parameters cannot be estimated even with added restrictions because of the existence of too few patients with depression diagnoses. 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 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 5.1 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_{di}^1 is significantly negative for SSRIs, and that the warning increases his preference towards SNRIs, as α_{di}^1 is positive for SNRIs albeit significant only at the 10% level. The parameter σ_{di0} 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_{di1} 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. 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.2 in the appendix.

Table 5.1: *Random Coefficient Logit Estimation for a Single Physician i*

Drugs:	Patient’s		Baseline		Warning		Correlation
	Age	Gender	Mean	SD	Mean	SD	
	α_{di}^g	α_{di}^a	α_{di}^0	σ_{di0}	α_{di}^1	σ_{di1}	ρ_{di}
SSRIs	-0.07 (.01)	-0.47 (.39)	4.04 (.66)	3.21 (.36)	-1.86 (.52)	8.26 (1.35)	0.93 (.99)
SNRIs	-0.06 (.01)	0.19 (.45)	1.85 (.74)	3.24 (.33)	0.78 (.47)	5.30 (1.08)	-1.58 (.96)
TCAs	-0.01 (.02)	-0.29 (.61)	-2.64 (1.18)	2.77 (.41)	0.83 (.99)	4.49 (1.58)	0.56 (.71)
Other Antidep.	-0.18 (.04)	-0.36 (.60)	6.02 (1.59)	3.45 (.42)	-2.69 (1.38)	7.55 (2.46)	6.49 (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.

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

5.2 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 5.2 reports the quantiles of prescription probability for each choice alternative with before and after warning preferences. These predicted probabilities should be equal to those in Table 2.3 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 kids 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 kids, 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.

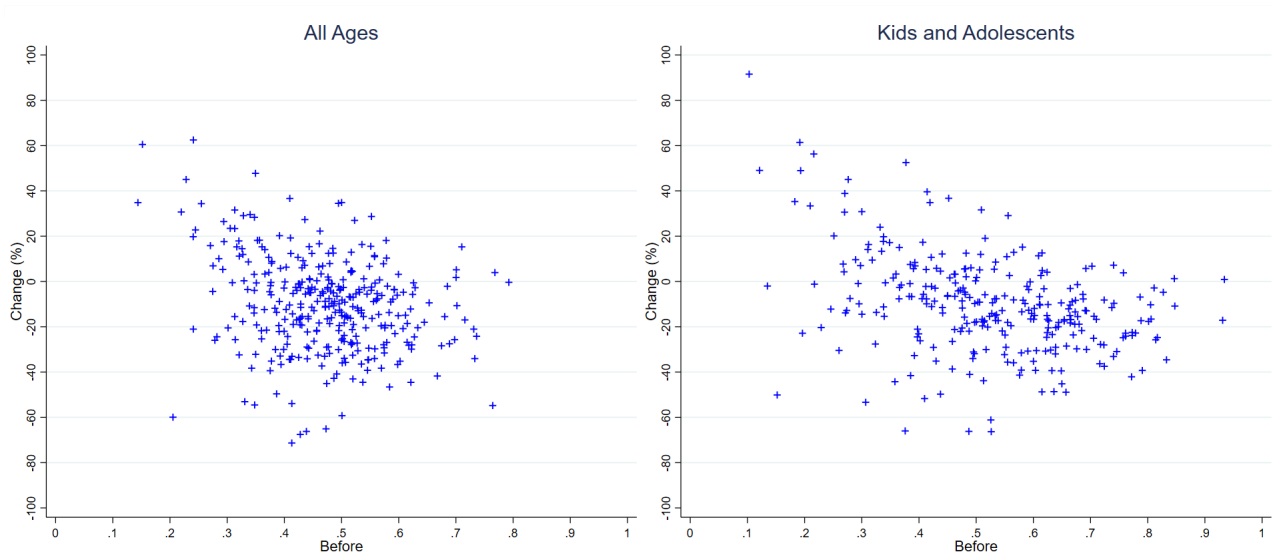
Figure 5.1 shows the decrease in percentage of the baseline prescription probability for each physician. The decrease is on average slightly higher and less variable across the physicians who have a large prescription probability of SSRI before the warning.

We also compute the change after the warning in the prescription probabilities for each drug category and for each physician. Table 5.3 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

Table 5.2: *Heterogeneity across Physicians of Average Prescription Probabilities Before/After Warning*

Group		All Ages			Kids 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
	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
Antidep.	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
	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

Figure 5.1: *Effect of Warning on Average Prescription Probability by Physician and Drug as Percentage of Baseline Prescription Probability*



Notes: Scatter plot of the change in predicted physician-level prescription probability after the warning as a percentage of the before-warning probability. Each point represents a physician-level probability. The left graph shows the mean choice probabilities and the changes for any patient, and the right graph shows the mean choice probabilities and the changes for kids and adolescents.

(the 75% quantile is +0.01). According to Tables 5.3 and 5.4, physicians who decrease their prescriptions of SSRIs substitute towards SNRIs and “other drugs”.

Table 5.4 shows, for each drug class, the mean and standard deviation of the averages across patients of the physician-level prescription probability for the periods before and after the warning. It also reports 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

Table 5.3: *Heterogeneity across Physicians in Change in Prescription Probabilities due to the Warning*

Group	All Ages			Kids 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

and increases more for other drug classes than SSRIs. It is as if the warning is interpreted differently by heterogeneous physicians.

19 months after the 2004 warning, in 2006, the health authorities released some new information, partially contradicting the 2004 warning by recommending one SSRI molecule (Fluoxetine, sold under trade name Prozac) for kids and adolescents. One may wonder if some physicians' response to the 2004 warning is limited because of private information that Fluoxetine should indeed be used. To address this concern, for each physician, we compute the share of Fluoxetine prescriptions in the period before the SSRI warning and in the period after the SSRI warning but before the Fluoxetine warning. Among the physicians who prescribe SSRIs after the warning, only 19% of them prescribe Fluoxetine more than half of the time in the after-warning period, whereas 27% of them prescribe Fluoxetine more than half of the time before the warning. Moreover, only 16% of the physicians prescribing SSRI after the warning increase their share of Fluoxetine prescriptions with the warning. Among physicians who strictly follow the recommendation to stop SSRI prescriptions to kids and adolescents, the average share of Fluoxetine in SSRI prescriptions before the warning is 17% (and none after since they stop prescribing SSRIs). However, among those who do not follow the recommendation, the average share of Fluoxetine is 12% before the warning and 10% after the warning, showing no significant change. These results show that among those who deviate from the 2004 warning, only 19% do so in a way that is consistent with the 2006 recommendation. Therefore, it is not necessarily the case that the physicians that do not strictly follow the 2004 warning are "better" physicians who could anticipate the 2006 Fluoxetine recommendation.

Our model also allows us to identify the effect of the warning on the within physician variation of preferences. The results show an increase in the within-physician variance of the probability of prescribing SSRIs and 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.

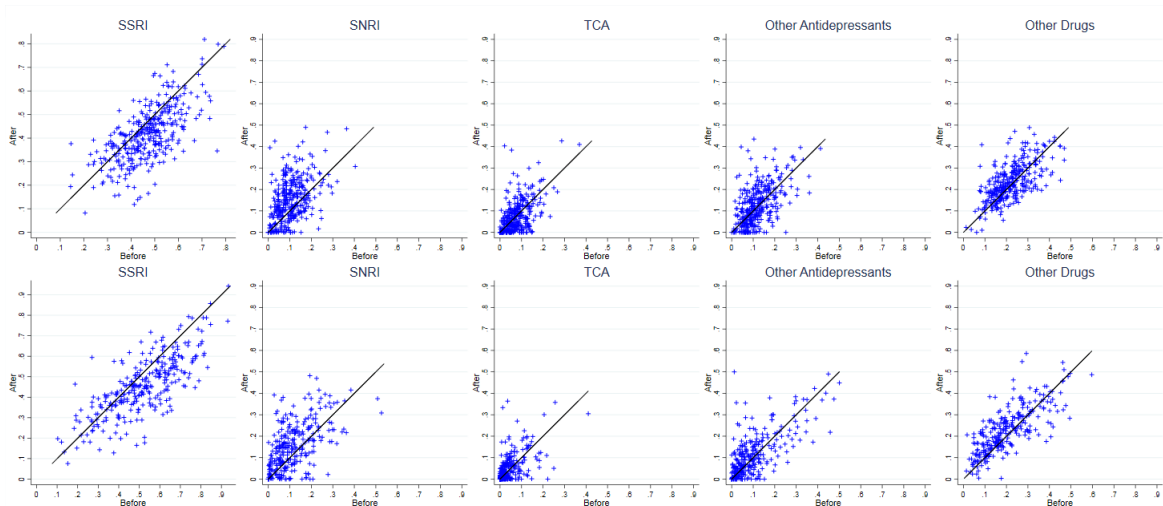
Table 5.4: *Distribution of Physician Prescription Probabilities Before/After Warning*

Drug	Across Physicians						Within-Physician		
	Before	Mean After	Change	Standard Deviation Before	Standard Deviation After	Change	Standard Deviation Before	Standard Deviation 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.

Figure 5.2 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 kids 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, whereas the other half decrease their prescriptions of these drugs. The figure shows substitution from SSRIs towards SNRIs. For kids and adolescents, we observe similar responses to the warning, except that many more physicians substitute SSRIs with “other drugs”, not only with SNRIs.

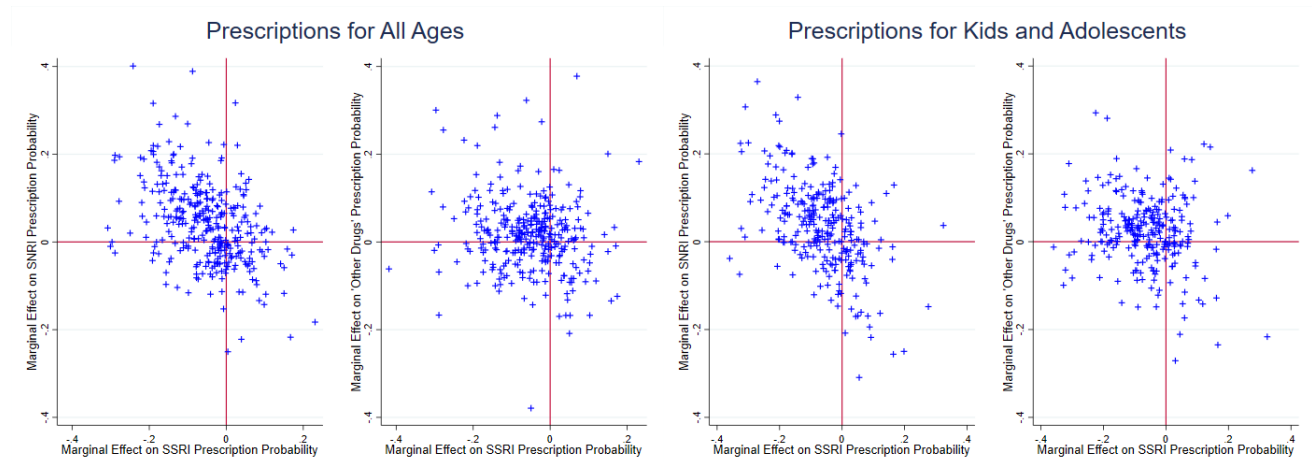
Figure 5.2: *Effect of Warning on Average Prescription Probability by Physician and Drug as Function of Baseline Prescription Probability*



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 kids and adolescents.

Figure 5.3 shows the substitution patterns between SSRIs and other drugs using estimates of the marginal effect of the warning on each probability as in equation (4.5). 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. 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 kids and adolescents, an even higher number of physicians are in the upper-left corner of the graph.

Figure 5.3: *Effect of Warning on Average Prescription Probability by Physician*

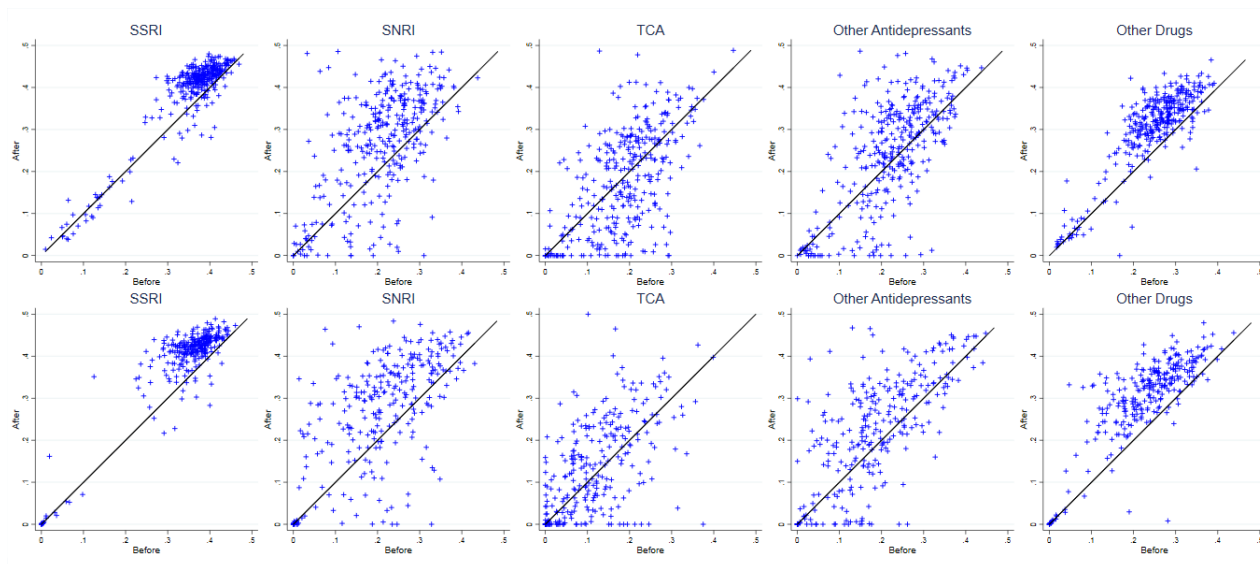


Notes: Plots of changes in the physician-level mean probability of prescribing SSRIs versus SNRIs and “other drugs”.

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 5.4 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 5.4 shows that this is also true within the age category of kids 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 kids and adolescents even though the warning concerns only 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 because the effect of the warning on their preferences proves to be very heterogeneous.

Figure 5.4: *Effect of Warning on Within-Physician Variance of Prescription Probability*



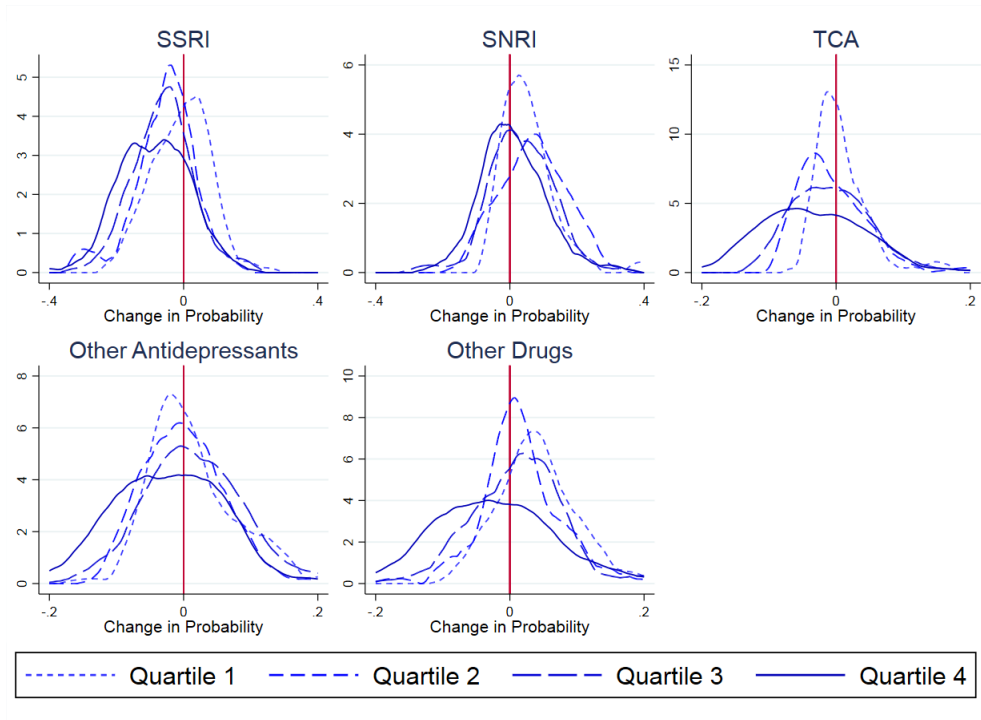
Notes: Scatter plot of physician-level variance of prescription probability after the warning as a function of the before-warning probability. Each point represents one physician-level variance observation. The first row shows the variance of choice probabilities for any patient, and the second row shows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

Another way to examine the heterogeneity of the effects of the warning consists in looking at the changes in the distribution of prescription probabilities across physicians depending on their before-warning choice probability. Figures 5.5 and 5.6 plot these densities of the average change in physician prescription probability by quartile of the ex ante prescription probability for all patients and for kids 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 kids 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 and only some positive between SNRI preferences and gender before the warning showing that female physicians like SNRI drugs more than males before the warning. We do not find significant correlation with age unlike

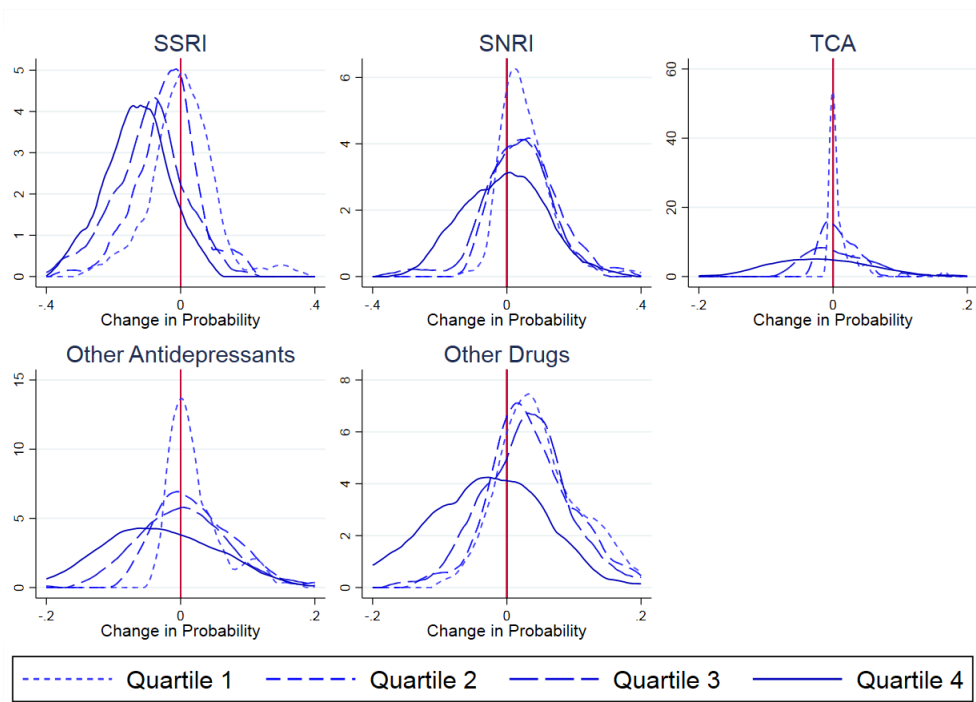
Howard and Hockenberry (2019) who show that older physicians react more slowly to new information. However, we find some correlation between the number of depressed patients per year seen by the physician and the physician-level prescription probabilities. The more patients seen by a physician, the higher is her probability of prescribing SSRIs both before and after the warning (without correlation with the change) and the lower her probability of prescribing SNRIs and ‘Other Drugs’ (for details see appendix A.3).

Figure 5.5: *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 5.6: *Effect on Prescription Probability by Quartile – Kids and Adolescents*



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

5.3 Comparing the Effects of the Warning with 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 kids and adolescents, we may consider the possible effect of a complete ban like those sometimes imposed on drugs that are uniformly considered too unsafe. A ban can be interpreted as strict guidelines adherence by physicians. This is what happened, for example, when the anti-inflammatory Vioxx was pulled from the market. We thus look at the counterfactual effects of a ban of SSRI drugs for kids and adolescents to compare physicians' substitution of drug prescriptions. Of course, in the case of a ban, SSRI prescriptions to kids and adolescents would disappear, while the warning is far from yielding such an effect. That said, the model allows us to compare the substitutions to other drugs in the case of a ban with the case of the warning, thanks to counterfactual prescription simulations. Substitution of SSRI by other drugs depends not only on the mean preferences of physicians that are heterogeneous but also on the variance term that depends on the distribution of patient types within a physician, which is what our model also allows us to obtain. For example, two physicians having the same preference but having different distributions of patient types (θ_j in our model) will substitute

differently SSRI by other drugs. As we allow this heterogeneity to be physician specific because of possibly endogenous matching of patients with physicians, this has consequences on the aggregate substitution rate of SSRI towards other drugs.

Banning SSRI drugs for use by kids 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 (4.4), the choice probability of any drug d that is not an SSRI based on prewarning ($\tau(j) = 0$) or postwarning ($\tau(j) = 1$) preferences is:

$$P(y_{ij} = d|i, \tau(j), \text{no SSRI}) = \int \frac{\exp(\omega_{dij}^0 + \omega_{dij}^1 \tau(j))}{1 + \sum_{\{\tilde{d} \neq \text{SSRI}\}} \exp(\omega_{\tilde{d}ij}^0 + \omega_{\tilde{d}ij}^1 \tau(j))} \prod_{\{\tilde{d} \neq \text{SSRI}\}} dF(\omega_{\tilde{d}ij}^0, \omega_{\tilde{d}ij}^1) \quad (5.1)$$

Table 5.5 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 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 5.5); 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 post-warning 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 a quite 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 5.5: *Effects of an SSRI Ban versus the Warning on Physician Prescription Probabilities (Kids and Adolescents (2-18))*

Drug	With Prewarning Preferences			With Postwarning Preferences			Warning Only
	No Ban	With Ban	Change	No Ban	With Ban	Change	Change
	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 kid 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.

6 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 estimate a model that allows us to infer the effect of the warning on the full distribution of each physician’s preferences over her patients. We use 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. By 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.

In the case of antidepressant drugs, new evidence on the increase in suicidal thinking in kids were reported in 2004 for selective serotonin reuptake inhibitors (SSRIs). 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 to estimate the effect of an official warning. We find that SSRI-type antidepressant prescriptions decreased after 2004 for kids and adolescents, but the physicians responded to the new information very heterogeneously. 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 kids 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. Using counterfactual simulations that our discrete choice model estimation allows us to perform, we compare the effect of the SSRI warning with a strict compliance with the recommendation (a ban) to not prescribe SSRIs by kids and adolescents. The results show that in the case of a warning, physicians who

follow the recommendation by not prescribing SSRIs to kids and adolescents substitute more towards other antidepressant classes (SNRIs in particular) than what they would do if there was a strict ban in which case they substitute more towards drugs that are not antidepressants. This shows that the warning has, perhaps unexpectedly, positive spillover effects on preferences for other antidepressants compared to a strict removal of SSRIs. 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 Balancing Tests Before and After the Warning

This section provides descriptive statistics at physician level on patient observables (age, gender) before and after the warning. For each physician we compute the average age of patients and share of female patients, before and after the warning in order to compare those characteristics and see if observable differences seem to be important. The mean across physicians of the average patients' age went slightly up from 52.4 years before the warning to 54.1 years after. However, the mean age of kids and adolescents did not significantly change, which was 14.9 years before the warning and 14.8 years after. The average of gender composition by physician stayed stable for all age groups. It was 71% females both before and after the warning. For kids and adolescents, it was 69% females both before and after the warning.

In Table A.1, we present the regression results of the mean age of patients and share of female patients at physician level before and after the warning on a warning dummy variable. We thus have two observations of these statistics by physician, one before and one after the warning. In columns (1) and (2) the mean age and gender at physician level are calculated including all the patients. Columns (3) and (4) are for the mean age and gender of kids and adolescents, and columns (5) and (6) are across the adult patients only. The results show no significant change in those characteristics for kids and adolescents but a significant increase in age for adults by a bit more than 1.5 years.

Table A.1: *Testing for Change in Patient Observables Before and After the Warning*

Patients Variables	All		Kids/Adolescents		Adults	
	Age (1)	Gender (2)	Age (3)	Gender (4)	Age (5)	Gender (6)
Warning	1.699*** (0.391)	-0.001 (0.010)	-0.096 (0.308)	0.000 (0.046)	1.639*** (0.385)	-0.001 (0.010)
Constant	52.403*** (0.276)	0.707*** (0.007)	14.904*** (0.218)	0.689*** (0.033)	52.597*** (0.272)	0.707*** (0.007)
Observations	772	772	248	248	772	772

Notes: OLS regressions of mean age of patients and share of female patients by physician before and after the warning on a warning dummy variable.

A.2 Full Model Estimates Table

Table A.2 reports the distribution of all coefficient estimates of the model across the 386 physicians.

Table A.2: *Distribution of Coefficient Estimates Across Physicians*

Drugs	Baseline parameters		Quantiles		
			25 %	50 %	75 %
SSRIs	Age	α_{di}^g	-0.04	-0.01	0.01
	Gender	α_{di}^a	-0.62	0.07	0.81
	Constant	α_{di}^0	0.30	1.55	3.06
	Std Deviation	σ_{di0}	2.41	3.12	4.10
SNRIs	Age	α_{di}^g	-0.05	-0.01	0.02
	Gender	α_{di}^a	-1.31	0.01	1.19
	Constant	α_{di}^0	-5.60	-2.75	-0.66
	Std Deviation	σ_{di0}	2.64	3.43	5.04
TCAs	Age	α_{di}^g	0.01	0.04	0.09
	Gender	α_{di}^a	-1.54	0.03	1.77
	Constant	α_{di}^0	-12.8	-7.73	-4.13
	Std Deviation	σ_{di0}	2.92	4.15	6.12
Other Antidep.	Age	α_{di}^g	-0.02	0.02	0.06
	Gender	α_{di}^a	-1.48	-0.35	0.58
	Constant	α_{di}^0	-6.81	-3.32	-0.95
	Std Deviation	σ_{di0}	2.50	3.46	4.74
SSRIs	Warning effects				
	Mean	α_{di}^1	-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_{di}^1	-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_{di}^1	-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_{di}^1	-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.

A.3 Correlation Between Physician Observables and Prescription Probabilities

In this section, we report the correlations between physician observables and physician-level prescription probabilities. We regress physician-level prescription probabilities for each drug on physician observables. Tables A.3, A.4, and A.5 show the correlations between physician observables and prescription probabilities before the warning, after the warning and the change in probabilities, respectively.

Table A.3: *Correlation of Physician Observables with Before Warning Prescription Probabilities*

VARIABLES	(1) SSRI	(2) SNRI	(3) TCA	(4) Other Antidep.	(5) Other Drugs
Female Physician	-0.0262 (0.0164)	0.0227** (0.0096)	-0.0003 (0.0077)	-0.0092 (0.0102)	0.0155 (0.0137)
Physician's Age	-0.0010 (0.0009)	-0.0001 (0.0005)	0.0005 (0.0004)	-0.0002 (0.0005)	0.0008 (0.0007)
Number of Patients	0.0002 (0.0001)	-0.0001 (0.0001)	0.0001* (0.0001)	0.0000 (0.0001)	-0.0003** (0.0001)
Constant	0.5056*** (0.0428)	0.1144*** (0.0249)	0.0432** (0.0201)	0.1303*** (0.0265)	0.2065*** (0.0357)
Observations	338	338	338	338	338
R-squared	0.0139	0.0226	0.0151	0.0026	0.0220

Notes: Significance levels: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Table A.4: *Correlation of Physician Observables with After Warning Prescription Probabilities*

VARIABLES	(1) SSRI	(2) SNRI	(3) TCA	(4) Other Antidep.	(5) Other Drugs
Female Physician	-0.0203 (0.0174)	0.0079 (0.0150)	0.0054 (0.0112)	-0.0065 (0.0136)	0.0143 (0.0155)
Physician's Age	-0.0007 (0.0009)	-0.0002 (0.0008)	0.0003 (0.0006)	0.0002 (0.0007)	0.0007 (0.0008)
Number of Patients	0.0003* (0.0002)	-0.0003* (0.0001)	0.0001 (0.0001)	-0.0001 (0.0001)	-0.0003* (0.0001)
Constant	0.4316*** (0.0454)	0.1770*** (0.0393)	0.0523* (0.0289)	0.1206*** (0.0354)	0.2286*** (0.0404)
Observations	338	337	332	337	330
R-squared	0.0137	0.0119	0.0036	0.0024	0.0148

Notes: Significance levels: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.

Table A.5: *Correlation of Physician Observables with the Change in Prescription Probabilities*

VARIABLES	(1) SSRI	(2) SNRI	(3) TCA	(4) Other Antidep.	(5) Other Drugs
Female Physician	0.0061 (0.0142)	-0.0129 (0.0157)	0.0209 (0.0157)	0.0106 (0.0124)	-0.0124 (0.0126)
Physician's Age	0.0003 (0.0007)	0.0002 (0.0008)	-0.0008 (0.0008)	0.0010 (0.0006)	-0.0005 (0.0007)
Number of Patients	0.0001 (0.0001)	-0.0002 (0.0001)	-0.0000 (0.0001)	0.0000 (0.0001)	0.0000 (0.0001)
Constant	-0.0759** (0.0370)	0.0477 (0.0409)	0.0294 (0.0406)	-0.0485 (0.0324)	0.0386 (0.0328)
Observations	338	337	332	337	330
R-squared	0.0027	0.0069	0.0124	0.0075	0.0038

Notes: Significance levels: *** $p < 0.01$, ** $p < 0.05$, * $p < 0.1$.