Empirical Evidence on The Role of Public Warnings on Physicians Drug Prescriptions Behavior*

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Abstract:

We investigate how prescription behavior of physicians react to scientific information released by public authorities. Taking the example of antidepressant drugs, we use French panel data on exhaustive prescriptions of a representative sample of 386 general practitioners to more than 170,000 depressed patients, between 2000 to 2008. Changing scientific evidence on the efficacy and side effects of antidepressants during that period resulted in new official warnings and recommendations. Examples are the new results on the increase of suicidal thinking in children reported in 2004 for selective serotonin reuptake inhibitors (SSRI). After the warnings, physicians must update their risk perception on different drug treatments for the patients and physicians may react differently to these warnings. We use the official warnings and recommendations along the period to identify how they affected physicians' drug choices on the first visit the patient is diagnosed by depression. We find that physicians respond to the new information heterogeneously, providing evidence that heterogeneity of prescribing behavior is not simply due to heterogeneity of preferences towards different side effects but heterogeneity of knowledge or information acquisition. We find that antidepressant prescriptions decrease after 2004 for kids and adolescents. Even though the warning is only for kids and adolescents physicians change their prescription behavior for other age groups too.

Keywords: Physician behavior, prescription, drug efficacy, antidepressants, mixed logit

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1 Introduction

Understanding physicians prescription behavior is particularly important for public health and public finance. Physician prescription activity depends on physicians' judgment and continuous update of their medical knowledge through scientific information and public recommendation of health authorities. Moreover, prescription of treatments to patients is a difficult, partially subjective, choice that implies benefit-cost trade-offs depending on drugs efficacy, patient's condition and the evaluation of these by the physician. In this paper, we are interested in whether and how medical information and recommendation affect physicians' decisions through perceived efficacy of drugs and their perception of the patient's health state.

We investigate how prescription behavior of physicians react to scientific information release by public authorities in France. Taking the example of antidepressant drugs, we use some French panel data on exhaustive prescriptions of a representative sample of 386 general practitioners, between 2000 to 2008, to more than 170,000 depressed patients. We identify changes in the prescription behavior of physicians due to the changing scientific evidence on the efficacy and side effects of antidepressants during that period. As medical journals publish some new evidence, doctors may update their prescription behavior, and indeed, during the study period, important new evidence on antidepressants' efficacy and side effects were published and transmitted into new official recommendations to physicians. Examples are the new results on the increase of suicidal thinking in children reported in 2004 for selective serotonin reuptake inhibitors (SSRI). Physicians must update their risk perception on different drug treatments and also on no-drug treatment for the patient. Medical warnings affect those risk perceptions and physicians may react differently to these warnings.

We focus on the prescriptions when a patient is diagnosed by depression for the first time, that is, when the patient and the physician still do not have any specific information on patient's responsiveness to an antidepressant. Antidepressants are known to be experience products whose value must be assessed by individuals upon use, with varying ex ante efficacy belief depending on patients' characteristics. We use the public health authorities recommendations and warnings that appeared with new scientific evidence along the 2000-2008 period to identify how this knowledge affects the prescription decisions of physicians for inexperienced patients.

Using a simple model of prescription behavior with heterogeneity of physicians and patients, we show in Dubois and Tunçel (2014) that even with random matching of physicians and patients, we would not be able to separately identify physicians' individual specific knowledge from patients unobserved health state heterogeneity without changing scientific evidence. This implies that, without further assumption on changing scientific information, we cannot assess whether heterogeneity of treatments is due to different patients' preferences or states or due to heterogeneity of physicians preferences due to differences of knowledge (about drug efficacy or side effects for example). Using the changing scientific evidence and recommendations published during the period of study, and assuming that it did not change the distribution of severity of depression on the first diagnosis in the population, we are able to test not only whether changing scientific information affects physicians' prescriptions but also whether it affects physicians differently, providing evidence that heterogeneity of prescribing behavior is not only due to heterogeneity of patients (either in terms of states or in terms of preferences for example towards side effects) but also due to heterogeneity of knowledge or perception of prescribers.

The empirical literature on prescription behavior mostly addresses issues related to physician's induced demand (McGuire, 2000) and its relationship to drug prices, patients' copayments or availability of generic drugs. Only recently, some recent literature investigated the role of information processing by prescribers. For example, Coscielli and Shum (2004), and Crawford and Shum (2005) showed how to relevantly model the learning process of physicians with a dynamic discrete choice model on antiulcer drugs. But little has been done on the role of new scientific evidence on physicians prescriptions. Some have used drug withdrawal to evaluate how prescriptions change, like for example Collins, Simon and Tennyson (2013) with the Vioxx withdrawal that had both positive and negative effects for specific substitute drugs, and led to an overall increase in the usage of competitors. On the contrary, when a new drug is introduced, physicians need to learn their existence but also new scientific data on their efficacy. For example, 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. Concerning the learning process and its interaction with direct observation of treatment effects, Janakiraman, Sismeiro, Dutta (2009) show that physicians may learn in suboptimal way (salience effects) and put too much weight on patients switching molecules rather than those who stay with the same treatment. Finally, Dickstein (2012)

develops a model where physicians sequentially search for the best match between a patient and a drug allowing correlations across drugs in the learning process. In his model, a physician updates his priors on both the drug tried and drugs with similar characteristics. Dickstein (2013) focuses on the effects of interactions between patients, physicians and insurers on drug care spending, showing that inadequate reimbursement policies can reduce short-run costs, but increase patients relapses. Such trade-offs between short and long run efficacy can also be very important in prescription trade-offs. Risk perceptions and beliefs of physicians are crucial to explain their prescribing behavior and are also directly affected by both scientific knowledge and personal experience with their patients.

Our empirical results show that physicians behavior is very heterogenous in terms of propensity to prescribe some antidepressants and that government warnings have very heterogenous effects on prescription behavior of physicians. Physicians prescribe antidepressants to kids and adolescents less often after the warning but still much more than recommended as SSRI prescription is clearly not recommended by the warning but still happens quite a lot. It is possible that SSRIs are still considered as the safest options in terms of efficacy and/or side effects even though there is negative news about SSRIs. For kids and adolescents, choice probabilities of SSRIs decrease in favor of either no antidepressant drugs or of SNRI drugs. We also find that, after the warning, the probability of prescribing an SSRI responds very heterogeneously in young adults, adults and elderly, as if the 'bad' news about SSRIs for kids and adolescents, and no news for older age groups, some physicians interpret it as 'good' news for SSRIs in other age groups.

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

2 Institutional Background, Data and Stylized Facts

2.1 Depression and Antidepressants

Depression affects 20 % of French population during their lifetime. This illness is costly because it causes patients to suffer from a decrease in their productivity as 60% of depressed people have symptoms severe enough to keep them from performing daily tasks (Kessler et al. (2003)). It also

increases suicide attempts and hence mortality: the risk of suicide is 13-30 times higher among depressed people than among non-depressed people. Finally, it also increases health care expenditures. Depressed people visit their generalist for somatic complaints three times more often than non-depressed people. The cost of depression is estimated to increase: World Health Organization predicts that depression will be second most costly disease by 2020 (after cardiovascular diseases).

The medical literature groups antidepressants into two generations: first and second. Second generation antidepressants generally dominate the first generation. Of the antidepressant categories we are studying, only tricyclic antidepressants (TCAs) are in the first generation. French health authorities classify molecules of the second generation of antidepressants 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), serotonin-norepinephrine reuptake inhibitors (SNRIs) and "other antidepressants" which include mianserine, mirtazapine and tianeptine.

2.2 Scientific Information Release

Authorities such as the Federal Drug Authority in the US or other health authorities in other European countries monitor the use of drugs and outcomes in terms of public health in order to check and evaluate efficacy, scrutinize side effects or unintended effects of drugs, even after drugs are being 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 as ANSM (Agence Nationale de Sécurité du Médicament), is in charge of drug authorization and of regulating the use of prescription drugs by giving usage conditions and recommendations to physicians.

We collected all relevant information on recommendations of the French authority on antidepressant usage. We also examined the US FDA recommendations and warnings as well as the medical literature in order to check that the French health authority was giving all relevant information that could influence physicians. Recommendations and warnings between 2000 and 2008 are usually happening in France around the same time as they are in the US following closely the medical literature. All important scientific news are monitored by these agencies and processed into official

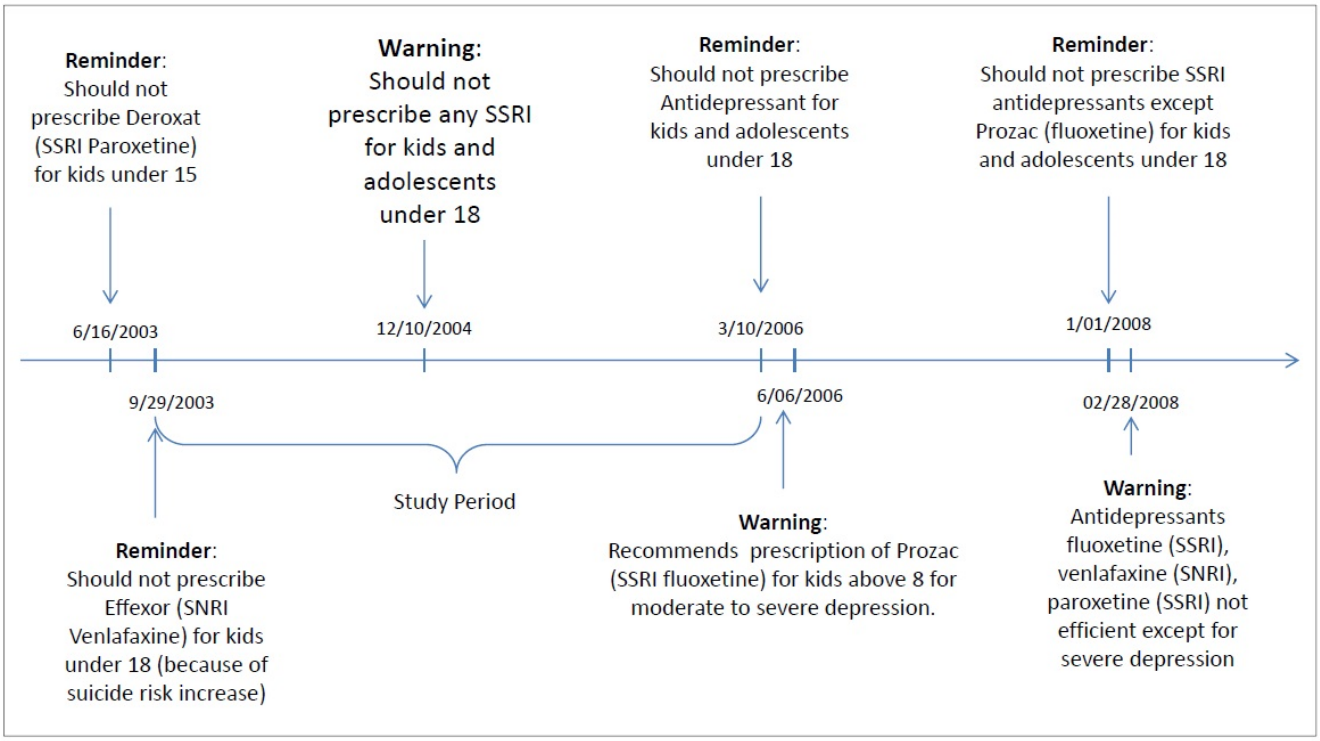

Figure 1: Timeline of Events on Antidepressants

warnings and recommendations. Among all the warnings during the study period, we consider two of them as the most important. The first one recommends not to use SSRI type antidepressants for kids and adolescents, and was issued in December 2004 in France. The second one, in June 2006, partially contradicts the 2004 warning by recommending Prozac, which is one of the SSRI molecule named fluoxetine, for adolescents and kids above 8 with moderate to severe depression. Finally at the end of our sample period, there is another warning in February 2008 concerning three different molecules that were not qualified as efficient enough to be prescribed except in the case of severe depression.

Figure 1 shows the timeline of warnings and reminders that were released by the French health authority. We are interested in the impact of the warning on December 2004, which informs the physicians that they should not prescribe SSRIs to kids and adolescents under 18 due to the increase in suicidal thinking at this age group. Because we do not want any contamination from other warnings/reminders we focus on the period starting from September 2003 (the timing of the reminder before our warning), ending in June 2006 (the timing of the reminder after our warning).

2.3 Data and Descriptive Statistics

We use a large panel data set on exhaustive prescriptions of 386 general practitioners to around 1.7 million patients in France between 2000 and 2008. These proprietary data is collected by CEGEDIM, a global technology and services company specializing in health care. The data contains information on physicians, patients and patient visits. At physician level, the data set includes age, gender and region of operation. At patient level, it includes socio-demographic information (age, gender, employment) and information on health (chronic diseases, height, weight). The data includes all information recorded at physician visits, including diagnosis, prescriptions, and also exam results automatically transmitted to the physician. Thus, we observe the diagnosis and all drugs and treatments that were prescribed by the physician on each visit. At drug level, we have information on the ATC code at the finest level, the price and the reimbursement level of the drug, and also whether the drug is generic or branded. For each physician visit, we have patient id, physician id, diagnosis and prescription details (drug, dosage, renewal).

The physician-patient pair may learn the value of a particular molecule for a patient through experience with usage (Crawford and Shum, 2005, Dickstein, 2013). To avoid the effect of this learning through usage,we study only the prescription choice at the physician visit on which the patient is diagnosed by depression for the first time, which is when the patient and the physician still do not have any specific information on patient's responsiveness to an antidepressant. Therefore, the unit of observation in our analysis is the physician visit on the first day of depression diagnosis.

Table 1 shows the percentages of antidepressant prescriptions on this first visit. Across all age groups, more than 50 % of patients do not get any antidepressant at depression diagnosis. The rate of no antidepressant ranges from 51 %, for the elderly, to 86 %, for kids and adolescents. SSRIs are the most prescribed antidepressants. The percentages of SSRI prescriptions is between 10 %, for kids and adolescents, and 32 %, for adults.

Table 1: Antidepressant Prescriptions Probabilities at Diagnosis

Antidep. Group	All Ages	Kids and Ado. (2-18)	Young Adults (19-25)	Adults (26-65)	Elderly (65+)
SSRI	29.4%	10.1%	23.8%	31.9%	29.1%
SNRI	5.5%	1.0%	4.1%	6.3%	4.6%
TCA	2.4%	1.1%	0.9%	2.4%	4.7%
Other	5.6%	1.7%	3.3%	5.4%	10.2%
None	57.1%	86.1%	67.9%	54%	51.4%
Patients	173,207	9,815	19,949	122,178	21,174

Table 2 shows the quantiles of prescriptions on the first visit of depression diagnosis. According to the table, there is a lot of heterogeneity across physicians. For instance, for kids and adolescents, more than 25 % of the physicians do not prescribe any SSRI on the first visit, whereas 50 % prescribe less than 7.7 % of the time and 75 % prescribe only up to 15 % of the times they diagnose depression. On the contrary, for adults and elderly, there are many more prescriptions of antidepressants and also more heterogeneity. For example, for elderly, 25% of physicians do not prescribe antidepressants more than 60.7% of the time while 25% do no prescribe antidepressants less than 42.1% of the time.

Table 2: Quantiles of Prescription Probability Across Physicians

Antidep. Group	Kids and Ado. (2-18)			Young Adults (19-25)			Adults (26-65)			Elderly (65+)		
	25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%
SSRI	0	7.7	15.4	14.3	22	32.4	24.4	31.3	38.7	20	28.5	37.1
SNRI	0	0	0	0	3	6.7	3.3	5.5	9.1	1.3	3.7	7.3
TCA	0	0	0	0	0	.6	1	1.9	2.9	0	3.6	6.4
Other	0	0	0	0	1.4	4.9	2.4	4.4	7.3	5.4	9.1	13.9
None	80	88.9	96.2	57.8	68.9	79.2	43.9	52.9	62.6	42.1	50	60.7

3 A Simple Discrete Prescription Choice Model

We develop a discrete choice model of antidepressant prescriptions by physicians on the first day of depression diagnosis with each patient. We assume that each physician i (where $i = 1, .., I$) receives patients with some depression state that the physician is able to observe. We will describe below the assumptions we make on the matching between patients and physicians. On a given sample period, a physician has J patients (J does not need to be the same across physicians) diagnosed with depression. We examine the physician prescription choices at the time $t(j)$ the depression is first diagnosed.

For each patient j who is in depression, the physician can choose among $C+1$ treatments indexed by each $c = 0, 1, .., C$. We assume that the welfare of each patient as perceived and maximized by the physician i can be written, for patient j who is prescribed treatment c, as

$$V_{cij} = \beta_{ci} - \theta_{cj} + \varepsilon_{cij} \tag{1}$$

where θ_{cj} increases with the depression severity of the patient and represents his responsiveness to the treatment c, and $\beta_{ci} + \varepsilon_{cij}$ is the physician's perception of how drug or treatment c will improve the welfare of the patient j. β_{ci} is the average health improvement provided by drug c as perceived

by the physician i and ε_{cij} is an individual idiosyncratic deviation provided by drug c as perceived by physician i and specific to patient j. We assume that θ_{cj} is known and observed by the physician who can assess all the patient's conditions when evaluating his depression state. Treatment 0 is by convention corresponding to no drug treatment and we normalize the mean welfare value of no drug treatment for the patient to zero such that $V_{0ij} = \varepsilon_{0ij}$. We then assume that the physician will choose the treatment that maximizes the welfare valuation of the patient for all $c = 0, .., C$.

Before observing diagnosis and prescriptions on a match couple of physician and patient, we assume that some assortative process between physicians and patients takes place and satisfies mild restrictions on the joint distribution of $(\beta_{ci}, \theta_{cj})_{c=1,.,C}$. Actually, we assume that the cumulative distribution function of $(\theta_{1j}, .., \theta_{Cj})$ given $(\beta_{1i}, .., \beta_{Ci})$ satisfies:

$$F(\theta_{1j}, .., \theta_{Cj}|\beta_{1i}, .., \beta_{Ci}) \text{ is weakly increasing in each } \beta_{ci} \tag{2}$$

This assumption means that for any $\beta_c^+ > \beta_c^-$ the cumulative distribution function $F\left(\theta_{1j}, .., \theta_{Cj}|\beta_{1i}, ., \beta_c^-, ., \beta_{Ci}\right)$ first order stochastically dominates (FOSD) the cumulative distribution function $F\left(\theta_{1j}, .., \theta_{Cj}|\beta_{1i}, ., \beta_c^+, ., \beta_{Ci}\right)$. One example of such distribution is for example when the p.d.f. would satisfy

$$F(\theta_{1j}, .., \theta_{Cj}|\beta_{1i}, .., \beta_{Ci}) = F(\theta_{1j} + \lambda_1\beta_{1i}, .., \theta_{Cj} + \lambda_C\beta_{Ci})$$

where $\lambda_c \geq 0$. The case where $\lambda_1 = .. = \lambda_C = 0$ corresponds to independence of the joint distribution of $(\theta_{1j}, .., \theta_{Cj})$ and $(\beta_{1i}, .., \beta_{Ci})$ that would be obtained with random matching of physicians and patients. The case where some $\lambda_c > 0$ means that there is positive assortative matching between the physician taste of treatment c and the patient valuations for this treatment. The large the λ_c the more important is positive assortative matching.

3.1 Binary Antidepressant Prescription Choice

Let's consider for now the case where we consider only the decision to prescribe antidepressants or not, namely the binary choice between $c = 1$ or 0. Denoting $y_{ij} \in \{0, 1\}$ the choice of physician i for patient j, assuming that choices are based on valuations (1) and that all ε_{cij} are i.i.d. distributed extreme value, the probability that physician i chooses to give antidepressants to patient j is

$$\begin{aligned} P(y_{ij} = 1|\beta_{1i}, \theta_{1j}) &= P(V_{1ij} \geq V_{0ij}|\beta_{1i}, \theta_{1j}) \\ &= P(\varepsilon_{0ij} - \varepsilon_{1ij} \leq \beta_{1i} - \theta_{1j}|\beta_{1i}, \theta_{1j}) \\ &= \frac{\exp(\beta_{1i} - \theta_{1j})}{1 + \exp(\beta_{1i} - \theta_{1j})} \end{aligned}$$

However, as econometrician, we don't observe β_{1i} and θ_{1j}, but with enough patients per physician, we can still identify the expected probability $P(y_{ij} = 1|\beta_{1i})$ that a given physician i prescribes antidepressants.

Then, using the assumption that the distribution of θ_{1j} is either independent of β_{1i} or depends on β_{1i} according to the weakly positive assortative matching assumption (2), we show in Dubois and Tunçel (2014) that $P(y_{ij} = 1|\beta_{1i}) = \psi(\beta_{1i})$ is an increasing function of β_{1i} with

$$\psi(\beta) = \int \frac{\exp(\beta - \theta_{1j})}{1 + \exp(\beta - \theta_{1j})} f(\theta_{1j}|\beta)\, d\theta_{1j}$$

As mentioned before, the assumption (2) will be satisfied for example if physicians and patients match randomly from the point of view of the patient's unobserved depression state or from the point of view of the physicians' preferences to prescribe antidepressants or if there is positive assortative matching meaning that it's more likely that patients with high θ_{1j} will match with physicians having high β_{1i}. It means that the distribution of unobserved heterogeneity of patients in terms of drugs responsiveness and thus in terms of severity of depression is either independent of the physician's identity or stochastically dominating the one of physicians with higher β_{1i}.

We also show in Dubois and Tunçel (2014) that the quantiles of the distribution function of prescription probability, $P(y_{ij} = 1|i)$, identify the quantiles of the distribution of β_{1i}.

Let's now introduce the time period of diagnostic such that V_{cij} is the indirect utility for the prescription of drug c to patient j by physician i at the diagnostic time $t(j)$. New scientific information release is at time t_1, we assume that potentially all values change at t_1. As we study only the decision for each patient appears on the first day of depression diagnosis, we don't need to add a time subscript to random variables whose draw is at the patient level. We now have the general random utility

$$V_{cij} = \beta^0_{ci} 1_{t(j) \leq t_1} + \beta^1_{ci} 1_{t(j) > t_1} - \theta_{cj} + \varepsilon_{cij}$$

where the previous random variable representing the physician perception of the drug improvement effect can have two different values before and after t_1.

Then, assuming that the distribution of patients health states θ_{1j} is the same before and after the warning for each physician, Dubois and Tunçel (2014) show that the sign of $\beta^1_{1i} - \beta^0_{1i}$ is equal to the sign of $\psi\left(\beta^1_{1i}\right) - \psi\left(\beta^0_{1i}\right)$, where ψ is the increasing function defined above.

Thus, using the prescriptions of physicians before and after the public health authority warning

in t_1, we can identify how scientific information will change the quantiles of the distribution of heterogeneity of physicians, identifying changes from quantile to quantile but also identifying which quantiles of the distribution of physician's preference parameter β_{1i} increase or decrease.

3.2 Multiple Treatments Choice

We now turn to the analysis of treatments choice by the physician, looking not only at whether or not the physician chooses to prescribe some antidepressants but also at the type of antidepressants prescribed. We adopt another approach by adding parametric restrictions on the distribution of $\beta_{ci} - \theta_{cj}$ in order to identify their distribution and their change with the release of new government recommendations. Thus, for the $C+1$ distinct treatment choices we are considering, we first condition the random utilities on patients' observables X_j, such that

$$V_{cij} = \beta^0_{ci}(X_j)\, 1_{\{t(j)\leq t_1\}} + \beta^1_{ci}(X_j)\, 1_{\{t(j)>t_1\}} - \theta_{cj}(X_j) + \varepsilon_{cij}$$

and then, denoting $\alpha^\tau_{cij} = \beta^\tau_{ci}(X_j)\, 1_{\{t(j)\leq t_1\}} + \beta^\tau_{ci}(X_j)\, 1_{\{t(j)>t_1\}} - \theta_{cj}(X_j)$ for $\tau = 0, 1$, we assume that $\alpha^\tau_{cij} \sim N(\overline{\alpha}^\tau_c(X_j), \sigma^2_{c\tau}(X_j))$.

Assuming again that ε_{cij} is i.i.d. extreme value, we obtain then a random coefficient logit model with normally distributed coefficients. Actually, using the extreme value distribution for individual deviation ε_{cij}, individual choice probabilities are

$$P\left(y_{ij} = c | \left\{\alpha^0_{cij}, \alpha^1_{cij}\right\}_{c=1}^{C}\right) = \frac{\exp\left(\alpha^0_{cij} 1_{t(j)\leq t_1} + \alpha^1_{cij} 1_{\{t(j)>t_1\}}\right)}{1 + \sum_{c'=1}^{C} \exp\left(\alpha^0_{c'ij} 1_{t(j)\leq t_1} + \alpha^1_{c'ij} 1_{\{t(j)>t_1\}}\right)}$$

where $y_{ij} \in \{0, 1, .., C\}$ denotes the drug prescription choice for patient j made by physician i.

Then, conditional choice probability that physician i chooses $(y_{i1} = c_1, y_{i2} = c_2, .., y_{iJ} = c_J)$ for his J patients is

$$\int \left[\prod\nolimits_{j=1}^{J} P\left(y_{ij} = c | \left\{\alpha^0_{cij}, \alpha^1_{cij}\right\}_{c=1}^{C}\right)\right] dF\left(\alpha^0_{cij}, \alpha^1_{cij} | \theta\right) \tag{3}$$

where $\theta = \left(\left\{\overline{\alpha}^\tau_c(X_j), \sigma^2_{c\tau}(X_j)\right\}_{c=1}^{C}, \tau = 0, 1\right)$.

Estimating directly this random coefficient logit model allows us to identify directly the (normal) distribution of α^τ_{cij} that is of $\beta^\tau_{ci}(X_j)\, 1_{\{t(j)\leq t_1\}} + \beta^\tau_{ci}(X_j)\, 1_{\{t(j)>t_1\}} - \theta_{cj}(X_j)$.

4 Econometric Estimation and Empirical Results

4.1 Prescribing Antidepressants

We first look at the estimation of the antidepressants prescription choice probability $P(y_{ij} = 1|\beta_{1i})$ for each physician i for the two different periods of study, before the warning on the negative side effects of antidepressants prescription for kids and adolescents in 2004 and after this warning. As we will see later, we will also study the effect of this warning that targeted specially SSRI drugs on the choice probability of each treatment. However, as a first analysis, it is interesting to see if this warning has changed the probability that each physician chooses to treat the depression with drugs or not.

Figure 2 shows a scatter plot as well as fractional polynomial regression of the probability of antidepressant prescription of each physician after the warning in the vertical axis versus the antidepressant prescription of each physician before the warning on the horizontal axis. We also have drawn the 45 degree line in order to see whether this probability increases or decreases with the warning. We can see that more data points are below the 45 degree line, meaning that many physicians decrease their probability of antidepressant prescription. The fractional polynomial regression line shows that this decrease exists mostly for physicians having an initial prescription probability larger than 40% and that this decrease is larger for physicians initially prescribing with higher probability. However physicians prescribing more antidepressants remain prescribing more after the warning.

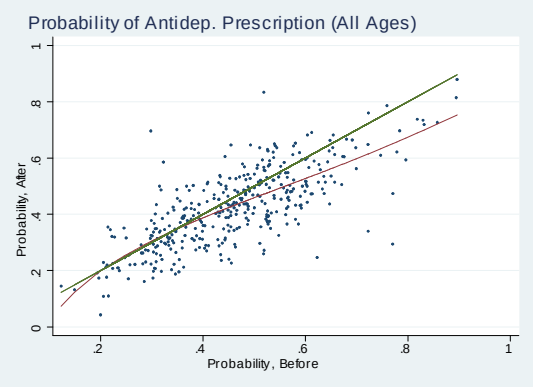

Figure 2: Change in Antidepressant Prescription Probabilities

Figure 3 then shows the same graph but by age category of patients. We can see that the prescription probability for kids and adolescents is much lower and that it decreases after the warning

for almost all physicians whose prescription probability is above 10 % before the warning. The probabilities change much less for young adults, adults and elderly. For young adults, the prescription probabilities seem to decrease for those with a probability above 40 % before the warning, while it slightly increases for those prescribing very little antidepressants before the warning. For the elderly, the antidepressant prescription probabilities decrease for those above 50% and increase for those below 50%, thus reducing the heterogeneity of prescription probabilities across physicians after the warning. For adults, there is a small effect but a slight decrease for the physicians prescribing antidepressants the most often.

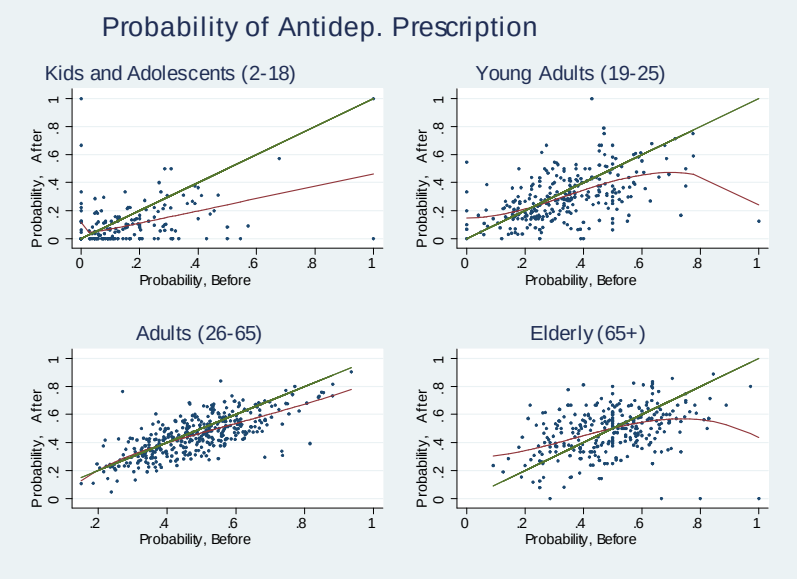

Figure 3: Change in Antidepressant Prescription Probabilities (by age category)

As mentioned before, these changes in probabilities of prescriptions, $\psi\left(\beta_{1i}^{1}\right)-\psi\left(\beta_{1i}^{0}\right)$, do identify the sign of the change in the physician preferences to prescribe antidepressants, $\beta_{1i}^{1}-\beta_{1i}^{0}$, but not their magnitude because $\psi(.)$ is increasing but can be very non linear (actually without heterogeneity of patients, $\psi(.)$ is S shaped with a convex part when $\psi<1/2$ and concave for $\psi>1/2$; with heterogeneity, ψ is likely to be very non linear). Thus, it is possible that the larger downward change in antidepressants prescription for high initial probabilities corresponds either to very large reaction of physicians or to small reaction of physicians, depending on the heterogeneity distribution of patients states θ_{1j}. We thus look at the quantiles of prescription probabilities that, according to our model in section 3.1, allow to identify the quantiles of physicians tastes β_{1i}. Figure 4 shows a scatter plot with fractional polynomial regression of the quantile of each physician after

the warning on the vertical axis and the one before the warning on the horizontal axis, with a 45 degree line allowing to see whether the quantile of each physician increases or decreases. Figure 4 shows that physicians who are for example at the 20% lower quantile of prescribing antidepressants before the warning are approximately at the 30% lower quantile after the warning. Figure 5 shows the correspondence between probabilities of prescription and their quantiles. We can see that 20 % lower quantile before the warning corresponds to a probability of prescribing an antidepressant of 35 % while after the warning it is 30 % lower quantile that corresponds to a probability of 35 %. It shows that physicians that are at this particular quantile did not change (on average) a lot their prescription probability. However, according to Figure 4, on average, physicians whose prescribing probability is on the median are still on the median after the warning but it implies a decrease of their prescription probability by approximately 5 percentage points according to Figure 5. Finally physicians who are at the 80% quantile before the warning are, on average, at the 70% quantile of prescription probability after the warning. According to the inverse cumulative distribution functions of prescription probabilities of Figure 5, their prescription probability decreases from approximately 55% to 50%. Figure 5 also shows that the prescription probability decreases for each and every quantile of prescription probability, even though changes are very heterogenous, as shown initially in Figure 2.

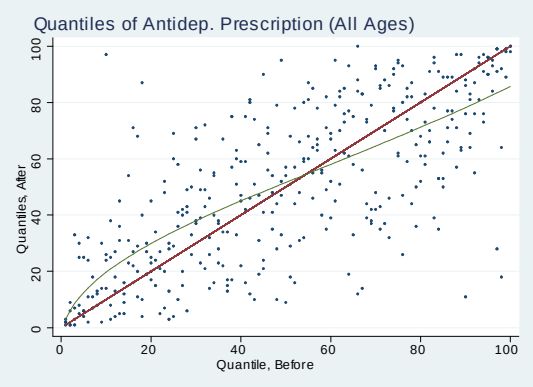

Figure 4: Change in Antidepressant Prescription Quantiles

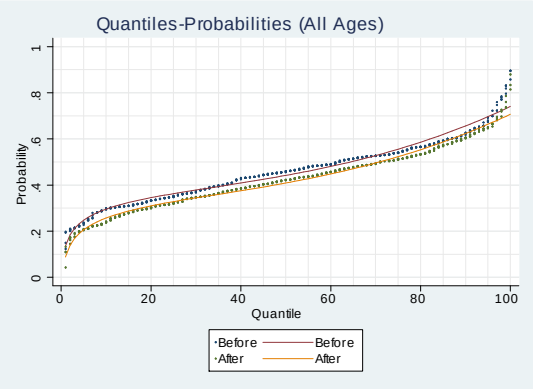

Figure 5: Antidepressant Prescription Quantiles and Prescription Probabilities

Figure 6 shows the changes of quantiles of physicians' probability of antidepressant prescriptions for each age category. The graph for kids and adolescents of Figure 3 shows that quite an important part of physicians switch to zero probability, strictly following the public health authority recommendation. According to Figure 7, more than 50% of physicians stop prescribing antidepressants to kids and adolescents while they were only around 25% before the warning. For young adults, adults and elderly, we can see, in Figure 6, that physicians that are on average above the median before the warning have a lower quantile after, while those below the median before have a higher quantile after. It means that there are more physicians in upper quantiles going down than in other quantiles and more physician in lower quantiles going up than in other quantiles. Moreover, Figure 7 shows that the distribution of prescription probabilities of antidepressants after the warning is stochastically dominated at first order by the distribution before the warning (curves in Figure 7 are inverse cumulative distribution functions of prescription probabilities). This first order stochastic dominance is larger for kids and adolescents than for young adults which is also larger than for adults and elderly.

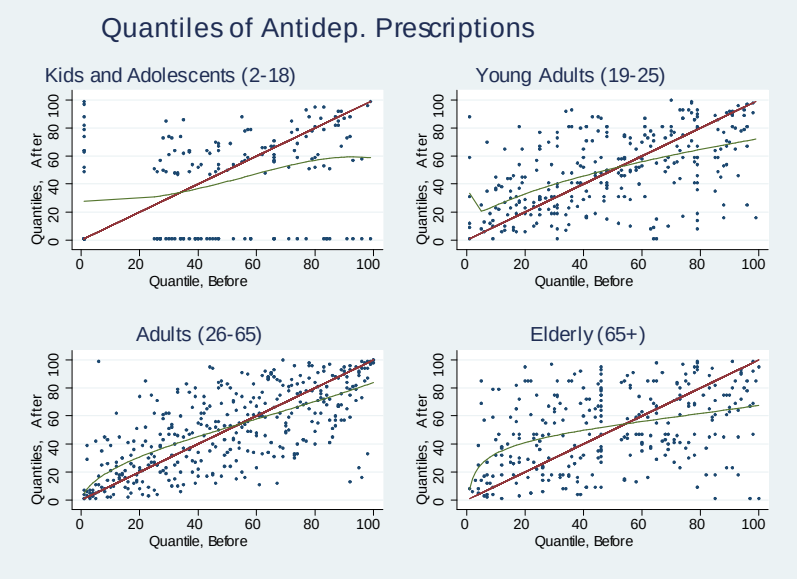

Figure 6: Change in Antidepressant Prescription Quantiles

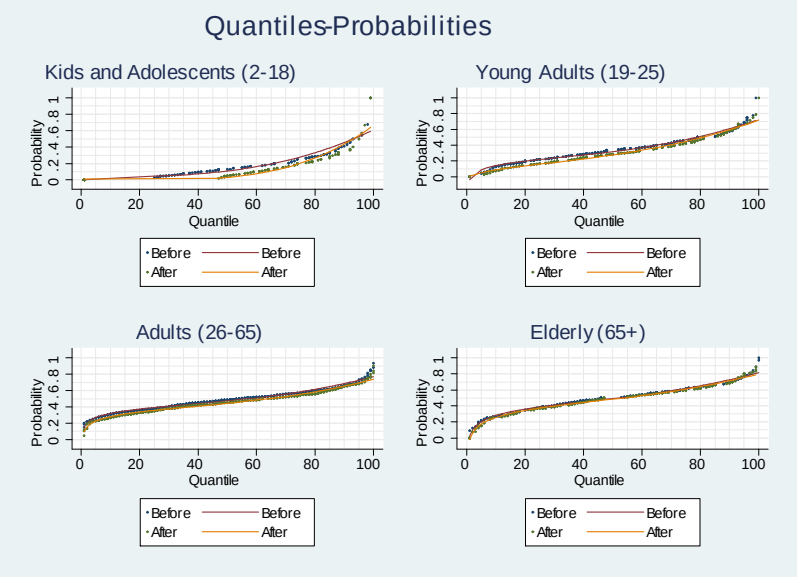

Figure 7:Antidepressant Prescription Quantiles - Probabilities

4.2 Antidepressants Choice

We have seen in the previous section how antidepressant prescriptions have been affected by the warning of public health authority in 2004. We now turn to the analysis of the more precise choice of treatment given the fact that the warning targeted more precisely SSRI type antidepressants in addition to targeting specially kids and adolescents. The warning has reduced the prescription probability of antidepressants overall but this could hide a larger effect on SSRI with substitutions away from SSRI drugs to other antidepressant drugs.

Table 3 shows the first, second and third quantiles of prescription probabilities of the four categories of antidepressants and of no antidepressant prescription, before and after the warning. From section 3.2, we know that the change of the prescription probability of a given quantile shows that there is a change in the distribution of heterogeneity of physicians perceptions of treatments. Table 3 shows that on the whole population, the quartiles of the probability of SSRI prescriptions all decrease. However, concerning kids, we find small effects on quartiles of SSRI prescriptions but we find stronger effects on young adults where the median prescription probability of SSRI drugs goes down from 25% to 21%.

Table 3: Heterogeneity Across Physicians before and after the Warning

Antidep. Group	Before/After Warning	All Ages			Kids and Ado. (2-18)			Young Adults (19-25)			Adults (26-65)			Elderly (65+)		
		Quantiles			Quantiles			Quantiles			Quantiles			Quantiles		
		25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%	25%	50%	75%
SSRI	Before	.24	.31	.38	.08	.14	.24	.17	.25	.36	.26	.32	.41	.20	.30	.40
	After	.19	.27	.36	.08	.15	.25	.13	.21	.33	.21	.30	.38	.20	.29	.39
SNRI	Before	.02	.04	.07	.04	.06	.13	.03	.05	.09	.02	.05	.08	.04	.05	.10
	After	.03	.06	.10	.05	.09	.14	.05	.08	.13	.04	.07	.11	.05	.08	.13
TCA	Before	.01	.02	.04	.04	.09	.14	.02	.03	.06	.01	.02	.04	.04	.07	.10
	After	.01	.02	.03	.04	.07	.18	.03	.04	.06	.01	.02	.03	.04	.07	.11
Other	Before	.03	.05	.09	.04	.08	.13	.03	.06	.11	.03	.05	.09	.06	.11	.16
	After	.02	.04	.07	.06	.09	.13	.04	.07	.13	.02	.04	.07	.07	.11	.19
None	Before	.46	.54	.65	.70	.82	.89	.53	.65	.76	.43	.51	.62	.38	.50	.61
	After	.49	.58	.68	.69	.80	.90	.57	.70	.81	.45	.55	.65	.40	.50	.63

We now look at the SSRI prescription decisions using the same binary discrete choice model as for the probability of prescription of any antidepressant. Given the warning targeted SSRI drugs, recommending not to use them for kids and adolescents, we estimate, for each physician, the probability of prescribing an SSRI drug on the first day of depression diagnostic. We estimate the probability before and after the warning and Figure 8 shows these probabilities with a scatter plot including a fractional polynomial regression of the prescription probability of each physician after the warning on the same probability before the warning, together with a 45-degree line allowing to see if the probability increases or decreases. We can see that on average, physicians prescribing SSRI drugs with the highest probability before the warning are the ones decreasing their prescriptions the most after the warning but that they still prescribe more than others.

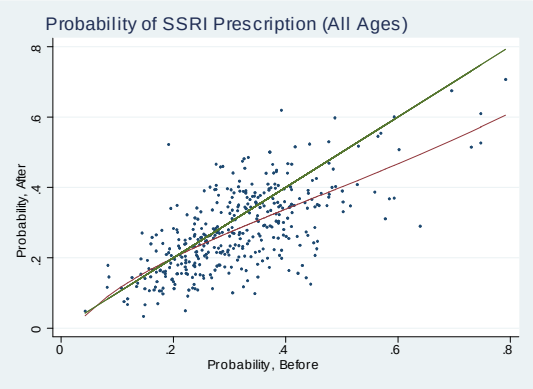

Figure 8: Change in SSRI Prescription Probabilities

Figure 9 shows the same probabilities before and after by age category of patients. We can see that the probabilities of prescribing SSRI drugs are much lower for kids and adolescents than for young adults, adults or elderly and that it goes down on average after the warning but with some heterogeneity. There is also a decrease in these probabilities for older ages for physicians whose prescription rate is initially above 40%, while the warning did not target those age categories.

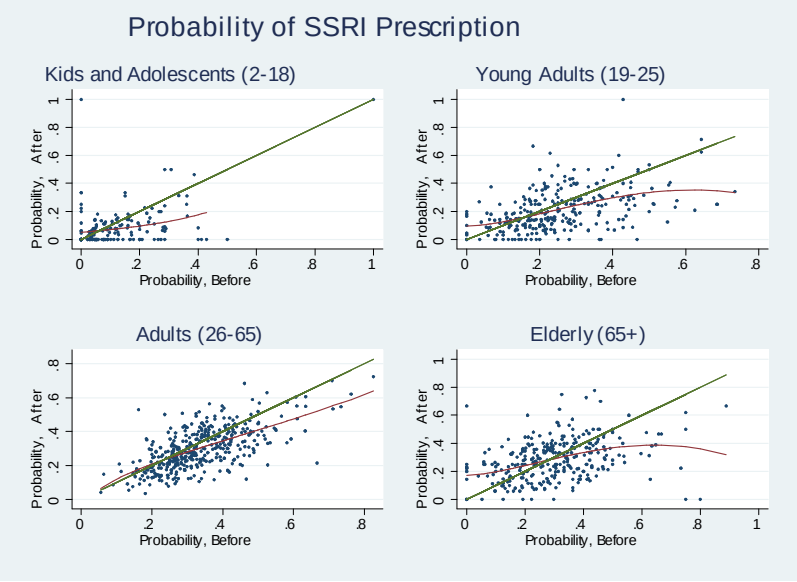

Figure 9: Change in SSRI Prescription Probabilities (by age)

As these probabilities do not show the multiple treatment choices made by physicians, we now turn to the estimation of the multiple discrete choice model outlined in 3.2, allowing to take into account the effect of the warning on the different treatment choices. As shown in appendix 3.2, identifying individual physician preferences in multiple prescription choices is not possible non parametrically. While bounds on quantiles of the distribution of physicians preferences are

still identified, we prefer to restrict our attention to the parametric but still very flexible logit model. Another advantage of the logit and mixed logit approach is that we can also condition choice probabilities on observable variables without having to cope with the problem of curse of dimensionality in the nonparametric quantile estimates.

Table 4 shows the results of multinomial logit regressions. The omitted category is "no antidepressants". The regressions include group specific fixed effects which show that the probability of not prescribing an antidepressant is higher than probability of prescribing an antidepressant for all age groups. The variable "severe" is 1 if it is severe depression and 0 otherwise. The interactions of "severe" with each antidepressant category shows that, for all age groups, the probability of prescribing an antidepressant for severe depression is higher than the probability of not prescribing one. The variable "mild" is 1 if the depression is mild and 0 otherwise.

We have a dummy variable for the warning, which is 0 for the visits before the warning and 1 for the visits after. The results show that after the warning, the probability of prescribing an SSRI for mild depression decreases for all age groups. For severe depression the probability of prescribing an SSRI also decreases for all age groups except the elderly. The probability of prescribing other types of antidepressants does not change after the warning.

Table 4: Multinomial Logit

Logit	All	Kids and Ado. (2-18)	Young Adults (19-25)	Adults (26-65)	Elderly (65+)
SSRI	-1.223***	-2.595***	-1.483***	-1.071***	-1.167***
	(0.019)	(0.106)	(0.055)	(0.022)	(0.058)
SNRI	-2.784***	-4.857***	-3.135***	-2.552***	-3.187***
	(0.037)	(0.317)	(0.115)	(0.042)	(0.142)
TCA	-4.035***	-4.857***	-5.019***	-3.973***	-3.309***
	(0.068)	(0.317)	(0.290)	(0.082)	(0.150)
OTHER	-2.923***	-4.215***	-3.573***	-2.859***	-2.225***
	(0.039)	(0.231)	(0.142)	(0.048)	(0.090)
Severe*SSRI	2.244***	3.190***	2.374***	2.099***	2.402***
	(0.035)	(0.188)	(0.105)	(0.041)	(0.110)
Severe*SNRI	2.097***	2.084***	2.213***	1.918***	2.681***
	(0.058)	(0.605)	(0.182)	(0.065)	(0.196)
Severe*TCA	2.350***	3.000***	2.152***	2.199***	2.574***
	(0.094)	(0.465)	(0.435)	(0.112)	(0.209)
Severe*OTHER	2.176***	2.135***	2.314***	2.004***	2.446***
	(0.059)	(0.440)	(0.214)	(0.072)	(0.143)
Mild*Warning*SSRI	-0.222***	-0.415**	-0.526***	-0.187***	-0.209**
	(0.028)	(0.174)	(0.088)	(0.033)	(0.086)
Mild*Warning*SNRI	-0.021	-0.369	-0.117	-0.019	0.048
	(0.054)	(0.518)	(0.168)	(0.059)	(0.199)
Mild*Warning*TCA	-0.005	-0.369	-0.387	0.016	0.051
	(0.098)	(0.518)	(0.458)	(0.117)	(0.211)
Mild*Warning*OTHER	-0.196***	-0.500	-0.225	-0.193***	-0.192
	(0.060)	(0.393)	(0.214)	(0.072)	(0.135)
Severe*Warning*SSRI	-0.235***	-0.640***	-0.486***	-0.233***	0.037
	(0.043)	(0.233)	(0.132)	(0.049)	(0.136)
Severe*Warning*SNRI	-0.096	-0.348	-0.357*	-0.069	-0.033
	(0.063)	(0.783)	(0.215)	(0.071)	(0.197)
Severe*Warning*TCA	-0.101	-1.265*	-0.357	-0.100	0.086
	(0.093)	(0.681)	(0.504)	(0.111)	(0.208)
Severe*Warning*OTHER	-0.083	0.163	-0.151	-0.151*	0.154
	(0.064)	(0.505)	(0.234)	(0.078)	(0.159)
Observations	238,925	14,825	28,915	167,335	27,775

Note: ***, **, * mean respectively significance at 1%, 5% and 10% level.

Because there is a lot of heterogeneity in physicians' antidepressant prescriptions, we would expect heterogeneous response from physicians to the warning. Thus, we have results from mixed logit regressions in Table 5. In the last part of Table 5 (effect of warning on SSRI in 2004), we have significant standard deviations for all age groups, except elderly, which means there is heterogeneity across physicians' response to the warning. Table 6 shows the means of marginal effects of the warning across age groups and antidepressant categories. The probability of no-antidepressant prescription increases slightly by 2.2 and 1.6 percentage points for all kids for mild

and severe depression respectively. The increase for mild depression is a bit larger. The change comes mostly from a decrease in SSRI prescription for kids after the warning: -4.3 percentage points for severe depression and -2.5 for mild depression. The rate of prescription of SSRI remains high for kids with severe depression even after the warning and is still at more than 14% even for mild depression. A surprising result is that, after the warning, the probability of prescribing an SSRI increases by 1.3% points for mild depression in young adults. Potential explanation for this could be that since the 'bad' news about SSRIs is only for kids and adolescents, some physicians take it as 'good' news for SSRIs in other age groups; hence they increase SSRI prescriptions.

Table 5: Mixed Logit Results

	Kids		Young Adults		Adults		Elderly	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
SSRI	-2.990***	1.043***	-1.665***	0.785***	-1.179***	0.744***	-1.334***	0.654***
	(0.150)	(0.123)	(0.0732)	(0.0686)	(0.0348)	(0.0268)	(0.0691)	(0.0561)
SNRI	-5.631***	1.263***	-3.246***	0.691***	-2.833***	0.791***	-3.325***	0.648***
	(0.597)	(0.451)	(0.133)	(0.148)	(0.0513)	(0.0353)	(0.143)	(0.139)
TCA	-5.706***	1.425***	-5.642***	1.108***	-4.097***	0.769***	-3.454***	-0.525***
	(0.488)	(0.302)	(0.374)	(0.251)	(0.0810)	(0.0553)	(0.146)	(0.116)
Other	-6.053***	-2.107***	-3.959***	0.864***	-3.165***	0.814***	-2.600***	0.811***
	(0.554)	(0.325)	(0.176)	(0.141)	(0.0616)	(0.0367)	(0.107)	(0.0808)
Additive Effect of Severe Depression								
SSRI	3.583***		2.661***		2.388***		2.782***	
	(0.193)		(0.0947)		(0.0343)		(0.0912)	
SNRI	2.225***		2.201***		2.186***		2.791***	
	(0.505)		(0.149)		(0.0530)		(0.152)	
TCA	2.959***		2.111***		2.191***		2.653***	
	(0.439)		(0.350)		(0.0843)		(0.154)	
Other	3.123***		2.535***		2.241***		2.839***	
	(0.431)		(0.178)		(0.0589)		(0.116)	
Effect of Warning on SSRI in 2004								
SSRI	-0.710***	0.894***	-0.508***	0.263**	-0.209***	-0.163***	-0.168**	-0.209
	(0.192)	(0.226)	(0.0788)	(0.134)	(0.0289)	(0.0411)	(0.0753)	(0.139)
SNRI	-0.579	0.705	-0.434**	0.710***	-0.116*	0.615***	-0.214	-0.627**
	(0.685)	(0.869)	(0.185)	(0.248)	(0.0601)	(0.0699)	(0.180)	(0.264)
TCA	-1.678*	1.450*	-0.340	0.314	-0.0472	-0.007	-0.144	0.631***
	(0.941)	(0.848)	(0.385)	(0.646)	(0.0810)	(0.134)	(0.180)	(0.222)
Other	-0.576	-0.740**	-0.634***	1.118***	-0.178***	-0.135	-0.0644	0.234
	(0.394)	(0.370)	(0.233)	(0.203)	(0.0534)	(0.0987)	(0.105)	(0.198)
Observations	14,825		28,915		167,335		27,775	

Note: ***, **, * mean respectively significance at 1%, 5% and 10% level.

Table 6: Means of Marginal Effects (Mixed Logit)

Depression		Mild			Severe		
		Prob. (%)		Change	Prob. (%)		Change
Prescription	Age group	Before	After	(% points)	Before	After	(% points)
No Antidepressant							
	Kids (2-18)	70.6	72.8	2.2	14.3	15.9	1.6
	Young Adults	17	14.6	-2.3	1.9	1.7	-0.2
	Adults	17.9	15	-3.0	2.3	1.9	-0.3
	Elderly	15.9	11.1	-4.8	1.2	.8	-0.4
SSRI							
	Kids (2-18)	16.7	14.2	-2.5	47.5	43.2	-4.3
	Young Adults	18.4	19.7	1.3	26.9	26.9	-0.1
	Adults	20.1	18.4	-1.7	26.9	23.6	-3.3
	Elderly	20.4	20.9	0.5	24.2	23.8	-0.5
SNRI							
	Kids (2-18)	3.3	3.7	0.4	10.6	12.4	1.7
	Young Adults	20.8	22.6	1.8	21.2	23.1	1.9
	Adults	20.4	22.9	2.5	22.3	24.6	2.3
	Elderly	21.9	22.5	0.6	27	26.2	-0.9
TCA							
	Kids (2-18)	2.6	2.7	0.1	7.2	7.9	0.7
	Young Adults	21.1	21.7	0.6	21.5	22.3	0.8
	Adults	22.8	22	-0.8	25.8	24.4	-1.4
	Elderly	19.2	22	2.8	20	22.3	2.3
Other							
	Kids (2-18)	6.8	6.5	-0.2	20.3	20.6	0.2
	Young Adults	22.7	21.3	-1.3	28.5	26.1	-2.4
	Adults	18.8	21.7	2.9	22.7	25.4	2.8
	Elderly	22.6	23.6	0.9	27.5	26.9	-0.6

Note: Number of observations are 238 925 for all age categories, and respectively 14 825, 28 915, 167 335, 27 775 by age category.

Figure 10 shows the histograms of choice probabilities for not prescribing an antidepressant with and without the warning both for mild and severe depression across age categories. For kids, although there is a warning physicians continue prescribing an antidepressant in case of both mild and severe depression but with lower slightly probability as shown on average in Table 6. Figure 10 shows that there is still heterogeneity but the distribution of these probabilities after the warning first order stochastically dominates the one before the warning as shown in Figure 11 with cumulative distribution functions. This shows that there is a clear move to prescribing less antidepressants for kids, but Figures 10 and 11 show that the contrary happens for young adults, adults and elderly with mild depression. Nothing significant seems to happen for these age categories with severe depression.

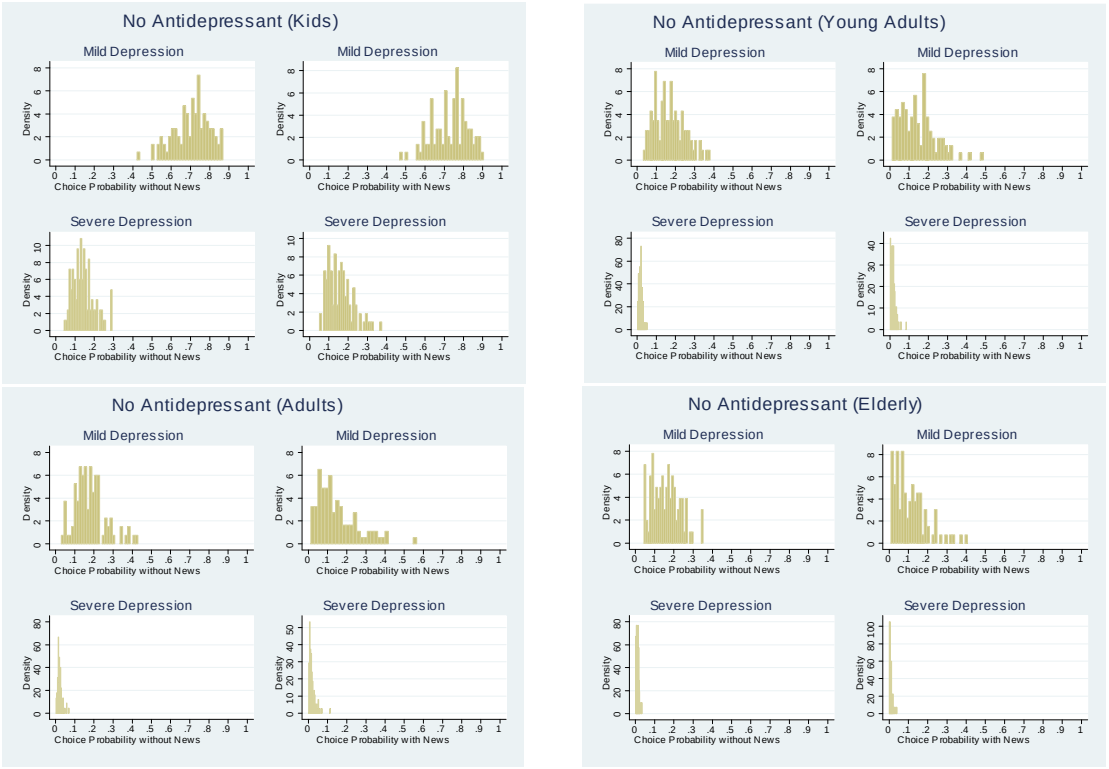

Figure 10: Change in no-antidepressant category

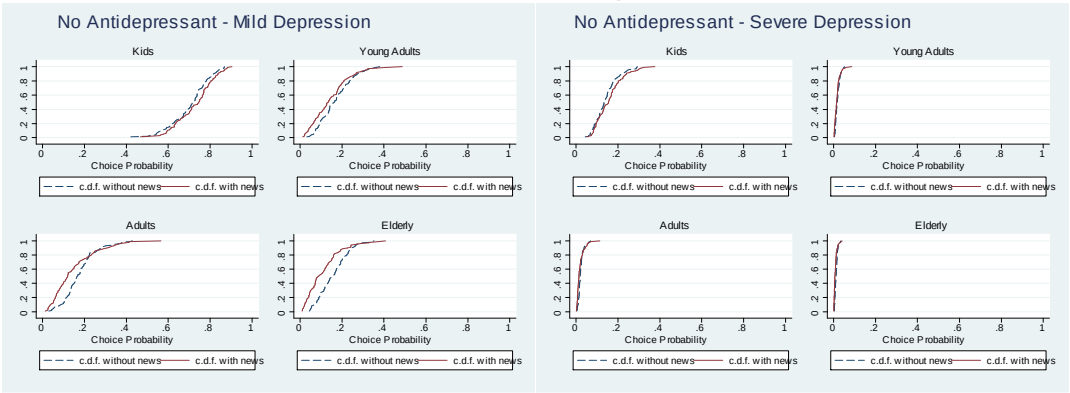

Figure 11: Change in no-antidepressant category (cumulative distribution functions)

Figure 12 shows the choice probabilities for SSRI prescriptions and Figure 13 shows the cumulative distribution functions. It is only for the age category of kids that we can observed a clear stochastic dominance at first order of the distribution of prescription probability of SSRI before than after the warning. For mild and severe depression, for all older age groups, physicians respond very heterogeneously as the distribution moves to the right and left, increasing the heterogeneity of prescribing probabilities, specially for young adults. One potential explanation for this is that since the 'bad' news about SSRIs is only for kids and adolescents, some physicians take it as 'good'

news for SSRIs in other age groups; hence they increase SSRI prescriptions for young adults, adults and elderly, while others understand it as 'bad' news for older age groups too.

Figure 12: Change in SSRI category

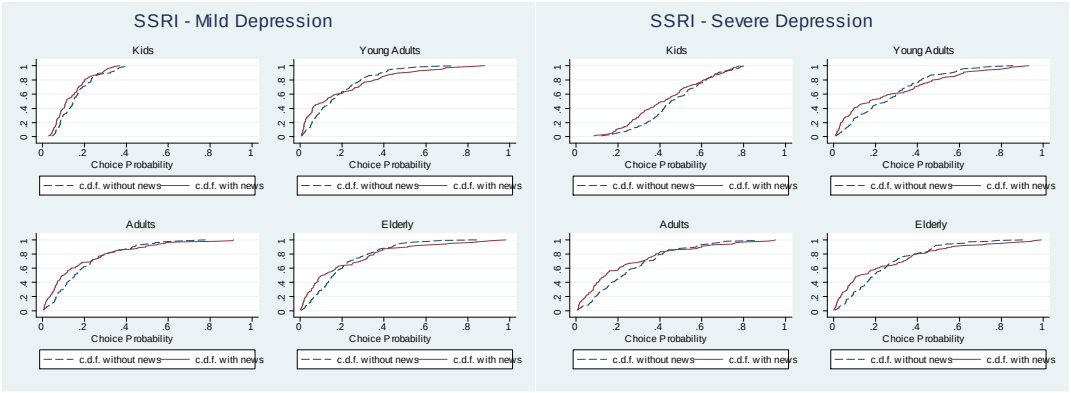

Figure 13: Change in SSRI category (cumulative distribution functions)

Figure 14 shows the choice probabilities for SNRI prescriptions and figure 15 the cumulative distributions. We can see that, with the warning, physicians prescribe an SNRI more often for kids, probably because of the 'bad' news about SSRI leading to substitution to SNRI. However, for all older age groups, the distribution of prescribing probabilities of SNRI seems also to widen as for SSRI. One potential explanation for this result could be that some physicians react to the negative

information about SSRI by substitution SSRI with SNRI while others decrease their prescriptions also in categories other than SSRI because they interpreted the warning as good news for older age categories than kids.

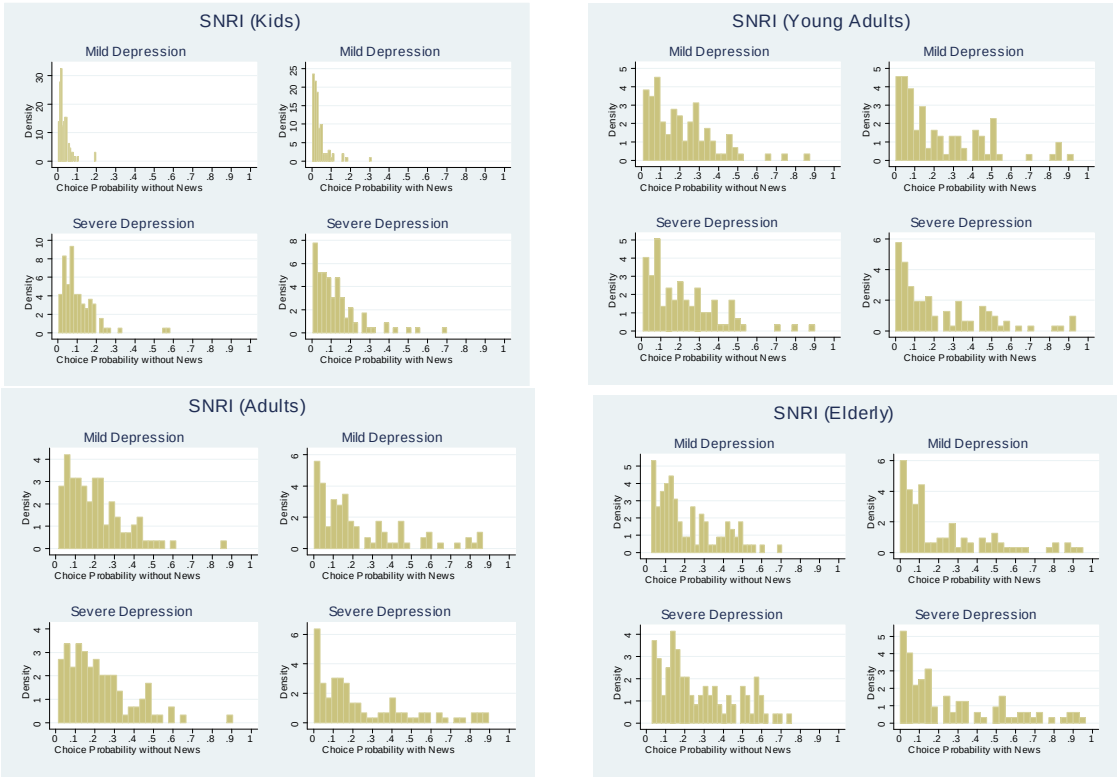

Figure 14: Change in SNRI category

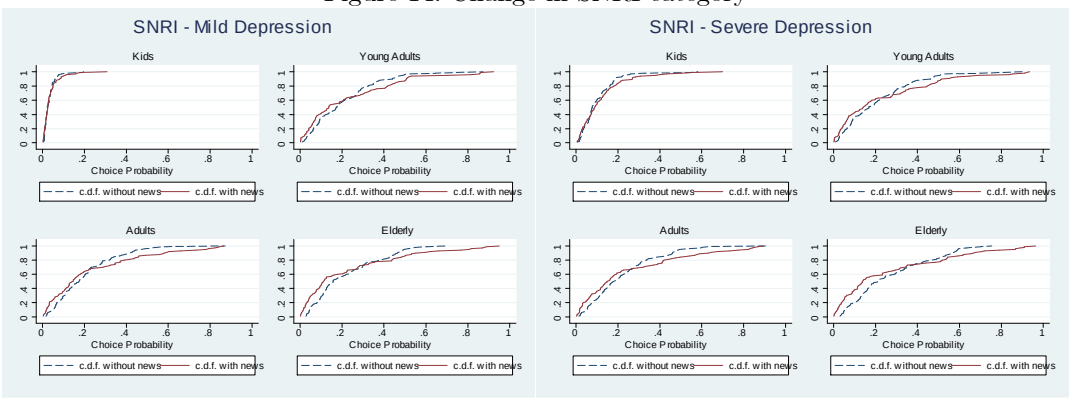

Figure 15: Change in SNRI category (cumulative distribution functions)

5 Conclusion

We study how prescription behavior of physicians react to scientific information release on the efficacy and side effects of drugs. More precisely,we examine how physicians react to the warning

about the increase of suicidal thinking in kids and adolescents in 2004 for SSRI type antidepressants. We focus on the prescriptions when a patient is diagnosed by depression for the first time, that is when the patient and physician still do not have any specific information on patient's responsiveness to a drug.

The results show that, for both mild and severe depression, physicians prescribe an antidepressant to kids and adolescents less often after the warning, much less often for mild depression than for severe depression, but with a decrease that is larger in percentage points for severe depression. This decrease in antidepressant prescriptions for kids and adolescents is expected since the warning is about kids and adolescents. However, some surprising results happen for older age categories, where there are very heterogenous responses with some increase and some decrease.

For kids and adolescents, we see a decrease in choice probabilities of SSRIs in case of both mild and severe depression, both to no antidepressants at all but also to SNRI drugs. For older age groups, there are very heterogenous responses that cannot be seen in the average effects. The prescription probabilities distribution seem to spread out. One potential explanation for this surprising result is that for some physicians, the warning on SSRI for kids and adolescents (which is clearly a 'bad' news about SSRIs for kids and adolescents) is associated with 'no news' for other age groups that some physicians interpret as 'good' news for SSRIs in other age groups (they may think if there was bad news for other age groups they would be informed). For other physicians, it is the contrary and they over-interpret the warning on kids and adolescents as also a bad news for the usage of SSRI drugs in older age categories. Thus some physicians increase SSRI prescriptions for adults and older people while others decrease, and decrease prescriptions in other categories.

We observe that physicians respond to the warning heterogeneously. As future work, we will investigate what are the determinants of these different responses of physicians by looking at physician characteristics. We will also include dynamics into the model using the panel structure of the data to see how the response to the warning changes depending on the experience physician-patient pair has on the value of antidepressants they tried.

References

Berndt, E. R., A. Bir, S. H. Busch, R. G. Frank, and S.-L. T. Normand (2002) "The medical

treatment of depression, 1991-1996: productive inefficiency, expected outcome variations, and price indexes" *Journal of Health Economics*, 21,373-396.

Ching, A. (2010a) ""A Dynamic Oligopoly Structural Model for the Prescription Drug Market After Patent Expiration," *International Economic Review*, vol. 51(4), 1175-1207

Ching A. (2010b) "Consumer Learning and Heterogeneity: Dynamics of Demand for Prescription Drugs After Patent Expiration" *International Journal of Industrial Organization*, 28(6), 619-638

Collins J. M. , K. Simon and S. Tennyson (2013) "Drug withdrawals and the utilization of therapeutic substitutes: The case of Vioxx" *Journal of Economic Behavior and Organization*, 86, 148–168

Coscielli A. and M. Shum (2004) "An empirical model of learning and patient spillovers in new drug entry", *Journal of Econometrics* 122, 213 – 246

Crawford, G. S. and M. Shum (2005) "Uncertainty and Learning in Pharmaceutical Demand", *Econometrica*, 73, 4, 1137-1173

Dickstein, M. (2012) "Efficient Provision of Experience Goods: Evidence from Antidepressant Choice" *mimeo* Stanford University

Dickstein, M. (2013) "Physician vs. Patient Incentives in Prescription Drug Choice" *mimeo* Stanford University

Dubois P. and T. Tunçel (2014) "Identifying the Effects of Scientific Information and Recommendations on Physicians Prescribing Behavior", Toulouse School of Economics

Ferreyra M. M. and G. Kosenok (2011) "Learning about new products: An empirical study of physicians' behavior" *Economic Inquiry*, Vol. 49, No. 3, 876–898

Janakiraman R., C. Sismeiro, S. Dutta (2009) "Perception Spillovers Across Competing Brands: A Disaggregate Model of How and When" *Journal of Marketing Research*, 467 Vol. XLVI, 467–481

Kessler, R. C., P. Berglund, O. Demler, R. Jin, D. Koretz, K. R. Merikangas, A. J. Rush, E. E. Walters, and P. S. Wang (2003) "The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R)", *JAMA*, 289, 3095.

McGuire T.G. (2000) "Physician Agency" *Handbook of Health Economics*, Volume 1, Part A, 2000, Pages 461–536, Edited by A.J. Culyer and J.P Newhouse

Pauly M. (1980) *Doctors and Their Workshops: Economic Models of Physician Behavior,* National Bureau of Economic Research, http://papers.nber.org/books/paul80-1