Evaluating the Mandatory Disclosure of Clinical Trial Results: Impact and Compliance

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I wish to examine how the recent policy adopted in the US to mandate the registration of clinical trials and the disclosure of their results has affected the amount of clinical research undertaken and disclosed by pharmaceutical companies. The theoretical literature on persuasion games establishes that mandatory disclosure can have ambiguous effects on the amount of information revealed to the market when information acquisition is costly. The gains in terms of transparency can be offset by the adverse effect on the incentives to acquire information: by suppressing the option to conceal unfavorable information, mandatory disclosure lowers the expected value of getting informed. Moreover, compulsory trials registration can create leakage of commercially valuable information to the competitors which further reduces the incentives of firms to invest in clinical research and drug development. Mandatory disclosure can then reduce the innovation rate in the pharmaceutical industry.

I also plan to determine the extent to which the policy has been enforced. The medical literature suggests that trials registered in ClinicalTrial.org after the adoption of the Food and Drug Administration Amendment Act (FDAAA) suffer from similar publication biases as previous trials. Andrew P Prayle et al. (2012) show that only 22 % of trials comply with the results disclosure requirement.

1 Legal Framework

Efficacy and safety of drugs are privately learned by pharmaceutical companies through the conduct of costly clinical trials. Clinical results serve as evidence to persuade regulatory agencies to grant marketing approval for drugs and to convince potential consumers to buy

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them. While some clinical studies are explicitly required for drugs to be approved, pharmaceutical firms have wide leeway to choose how much they want to invest in drug testing. Firms have the legal obligation to disclose the results of all clinical trials to the agencies but they are free to select the clinical outcomes that they wish to disclose to the market via medical publications.

Selective reporting of clinical trials results have been of growing concern in the medical community. Turner et al. (2008) study publications of FDA-registered clinical trials for antidepressant drugs from 1987 to 2004. They find that clinical trials whose outcomes are judged as unfavorable by the FDA are much less likely to be published than those yielding outcomes deemed as favorable.

In 2005, in order to tackle the issue of selective publication, the International Committee of Medical Journal Editors (ICMJE) adopted a new policy requiring prospective registration of all interventional clinical studies to investigators in order to be eligible for publication. In September 2007, the Food and Drug Administration Amendment Act (FDAAA) imposed mandatory registration of all interventional clinical studies above stage I as well as the disclosure of their results.

2 Data

I collected a nearly exhaustive data set describing the clinical trials and the medical publications for drugs that reached at least the second phase of clinical development in the US (i.e. 5454 drugs distributed over 242 three digit Anatomical Therapeutic Classes (ATC)). I collected information from three sources: the IMS drugs development focused database, the clinical trials registry maintained by the US National Institutes of Health (NIH) , and publications on drugs registered in PubMed.

The IMS database provides rich information on drugs' characteristics such as molecule names, brand names, ATCs, and companies developing and marketing the drugs.

The clinical trials registry provides precise information on trials including titles, the lists of drugs under clinical investigation, sponsors, the phases of the clinical development, and patient enrollment. I match data on clinical trials with the IMS sample of drugs to measure the research effort exerted by the drug sponsor.

Data on publications collected on PubMed provide, for each drug, all medical publications of randomized clinical trials results mentioning the name (generic name, brand name or lab code) of the drug in their title and funded by the industry. I use these publications to measure the quantity of information on drugs disclosed by pharmaceutical companies.

3 Empirical Strategy

In order to estimate how the FDAAA has affected the production of clinical knowledge on drugs by pharmaceutical companies, I intend to regress the number of publications on each drug on a time dummy indicating the year of the FDAAA adoption and controlling for various confounding factors. These controls include the ATC (which corresponds to the drug's market), the number of competitive drugs, and the innovativeness of the drug measured by the number of citations of the drug's patent.

Evaluating the degree of enforcement of the mandatory disclosure policy is methodologically more challenging. I plan to estimate a dynamic oligopoly game with finite horizon given by the length of the patent. At each period, firms observe their own state, which is the prior on the quality of their drug and the privately observed results of their completed trials, and the state of the market, which is the number of competitive drugs and the priors on their qualities. Given these state variables, they choose their research effort as given by the number of clinical trials they run and the size of these trials and the disclosure rule, i.e. the probability to disclose the result of a trial given the state variables, so as to maximize their expected sum of future profits. I can estimate directly from the data before the introduction of mandatory disclosure the expected disclosure rule. Using the structural assumption that forward-looking firms choose the level of research effort and the disclosure rule that maximize their profits, I can infer the expected return on research effort net of the research cost under selective disclosure from the observed equilibrium research effort and disclosure rule.

Using the estimation of the expected return on research effort, I can then compute the equilibrium research effort chosen by firms under mandatory disclosure. By comparing the simulated research efforts to the ones that are observed after the adaption of mandatory disclosure we can evaluate whether the policy is enforced and whether the departure from perfect enforcement are large or small.

References

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