

Experts and Financial Ties: Evidence from FDA Advisory Committees

Fanny Camara*

Margaret Kyle†

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Abstract

The use of expert committees is common in many settings. A key concern is the potential for conflict of interest, particularly for members of committees that oversee regulated firms. However, ties to industry may be correlated with relevant expertise. We examine the voting behavior of members of the Food & Drug Administration’s Advisory Committees, which make recommendations on new drug applications and other regulatory questions. We estimate a structural model of voting that allows us to recover each member’s skill and bias associated with financial ties to a drug’s sponsor or its competitors. Our work exploits a novel dataset that includes detailed information on each AC member, including their academic degrees, age, areas of expertise, and scientific contributions. We construct a measure of financial ties to industry using information disclosed in scientific publications authored by AC members, as well as those reported directly to the FDA and by the industry under the Sunshine Act. Finally, we consider the welfare effects of changes to conflict of interest policies.

1 Introduction

The use of expert committees is common in many settings. Boards of directors of firms, panels of judges, and referees for academic journals are all well-known examples. A challenge in the design of such committees is the potential for conflict of interest (COI). For instance, a referee at a journal may have a relationship (advisor/advisee, co-author) with the author of a paper under review. Such ties may be correlated with the quality of the expertise provided: a high-quality researcher may attract many co-authors. However, these ties may also introduce bias in the referee’s evaluation, or create a COI. This potential has particular salience in committees that directly affect regulatory policies. This paper empirically examines the importance of financial ties in the voting decisions of experts used by the US Food and Drug Administration (FDA).

The manufacturers of new drugs are required to win approval from the FDA in order to market their products in the US. Approval decisions are therefore critically important, both

*University of Frankfurt; fanny.camara@gmail.com.

†MINES ParisTech (CERNA), PSL Research University and CEPR; margaret.kyle@mines-paristech.fr

for the financial success of the manufacturers as well as for patient access to new treatments. Approval is based on an assessment of the drug’s safety and efficacy. Both may be difficult to assess for new technologies. The FDA often relies on committees of experts to provide advice on the approval of new drugs, as well as scientific guidance on the design of clinical trials, appropriate endpoints, and other issues. The medical experts who participate in these advisory committees may have financial ties to the firms whose products they are evaluating. For example, they may be researchers who have received financial support from pharmaceutical companies for clinical work, or who have received consulting or speaking fees. It is possible that experts with ties with the industry are leading researchers in their fields, who are therefore better able to review clinical evidence and make correct approval decisions.

The withdrawal of several prominent drugs, such as Vioxx in 2004, has increased scrutiny of potential COI by committee members. ? found that financial ties were weakly associated with votes for approval by committee members, for example, and media coverage revealed that 10 of the 32 FDA advisors who participated in the decision to approve Vioxx and similar drugs had some financial tie to the firms involved. Amid growing concerns that COIs corrupt the judgment of FDA advisors, the FDA introduced more stringent COI rules in 2008. Beyond the FDA, worries about the relationship between industry and doctors motivated the passage of the 2010 Physician Payments Sunshine Act, which requires disclosure of payments to physicians and teaching hospitals. However, critics contend that financial ties remain pervasive, and are underreported by the FDA (?, ?, ?).

We investigate (1) whether financial ties with the pharmaceutical industry affect the voting behavior of FDA advisors, and (2) whether the potential bias due to COI is offset by the higher level of expertise of advisors with ties with the industry. Rather than relying on data from the FDA on waivers granted to advisors with a potential financial COI, we develop a novel measure of financial ties using information disclosed in scientific publications authored by advisors. We estimate a structural model of voting by experts that allows us to recover each individual’s “quality” (defined below) and bias, controlling for observable characteristics of advisors (such as their publication record, degree, and experience on committees) as well as the question/issue under consideration. We allow the bias to be related to financial ties of the expert to the pharmaceutical industry in general, to the sponsor of a drug under consideration, and to competitors of that drug. We also consider how disclosure of a financial tie affects behavior.

Though we focus on a specific setting, the issues we consider are of general importance. For example, ties to the financial sector of potential cabinet members or governors of the Federal Reserve System receive considerable scrutiny. Scientists writing about climate change have been criticized for the potential bias introduced by receiving funds from corporate interests (?). In recent years, there has been increased pressure for academic economists to disclose their COI (?). The Securities and Exchange Commission in the US settled enforcement actions against 10 Wall Street firms in 2003 after investigating COI of research analysts.¹

¹SEC Factsheet.

2 Advisory Committees at the FDA

The FDA has more than 30 standing advisory committees (ACs) that evaluate products considered by its Center for Drug Evaluation and Research, which handles drugs; the Center for Biologics Evaluation and Research, which handles biotechnology and vaccine-related products; and the Center for Devices and Radiological Health, which handles medical devices. We focus on drugs and biologics, which have similar regulatory pathways for approval. Each advisory committee has 10-20 members that serve 3-year renewable terms as special government employees. In addition, the FDA may appoint temporary members as necessary. Committees are organized by expertise in a particular disease or technology type, such as oncology, anti-infectives, reproductive health, etc. Each committee meets several times per year on average at the request of the FDA. Meetings are typically 1-3 days in duration, with presentations by FDA staff, by the sponsors of products under evaluation, and by other interested parties. Often, following lengthy discussion, members vote on one or more questions provided to the committee in advance. Several weeks after a meeting, the transcripts of the discussion and votes are posted on the FDA's website, as well as other materials such as summaries of clinical evidence. The FDA does not request the advice of its ACs for all approval decisions, nor is it bound by law to follow their recommendations.

The FDA requires that committee members disclose any relevant "involvement or financial link with the meeting/task issues (including competing companies)" on Form 3410² prior to each meeting. Examples of such involvement are current or recent investments, employment, advising/consulting, research support, patents, expert witness, and speaking fees. Form 3410 is confidential, but if the FDA determines that the financial tie is sufficiently large, either the committee member will be excluded from the meeting or the committee chair will request a waiver from the FDA to allow the member to participate. Usually, the justification for the waiver is the importance of the committee member's expertise relative to the size of the financial tie. Committee members are also requested to disclose potential COIs at the start of each meeting.

Prior to the Vioxx withdrawal in 2004, the FDA did not provide information on the waivers granted to committee members. In 2008, the FDA revised its policy on conflict of interest as follows:

"Most recently, Congress enacted section 701 of FDAAA (section 712 of the Act), which, in addition to establishing a new conflict of interest prohibition and standard for assessing waivers, encourages FDA to focus efforts on recruitment of advisory committee members with fewer potential conflicts of interest and caps the numbers of waivers that the agency may grant in a given year. Section 712(c)(2)(C) requires that FDA reduce the rate of waivers the agency issues each year (total number of waivers issued per total number of members attending advisory committee meetings) by 5 percent, beginning with fiscal year 2008. By 2012, the agency may issue waivers at a maximum rate of 75 percent of the rate issued in 2007." (?)

In addition, the FDA now posts information about waivers granted on its webpage with other documents pertinent to AC meetings.

²<http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048297.pdf>.

? obtained information on COI waivers granted between 2001-2004 via a Freedom of Information Act request. Their data revealed that there was at least one COI waiver granted in 81% of AC meetings that discussed a specific product, and in 22% of these meetings, more than half of the advisors was granted a waiver. The size of the financial tie was more than \$100,000 of research support in almost a quarter of the cases, and speaking fees or honoraria of more than \$10,000 in 44%.

? found a weak relationship between financial ties were weakly associated with votes for approval by committee members, but also that these financial ties were not critical for the final outcome. In issuing a response to this study, the FDA noted that committee members did not necessarily vote in their own financial interests. Many members had ties to firms with competing products for the drug under review, and nevertheless voted to approve. At the request of the FDA, ? extended the original sample used by ? to more committees and a longer time period. This paper found results largely consistent with those of the earlier work when using similar definitions and methodology. However, when considering whether members vote in a way consistent with their financial interests (rather than whether having any financial tie to industry was related to voting), ? concluded that members tended to vote against their interests. A more recent analysis by ? using data on ACs from 1997-2012 concludes that COIs were largely unrelated to votes.

The papers cited above have limited data on the characteristics of the advisors themselves. The omission of variables that may be correlated with financial ties to industry as well as the ability to assess clinical data, both of which may affect voting, may lead to biased estimates of COI. Our first contribution is to include substantially more information about each advisor, including their age, academic credentials, board certifications, and contributions to the scientific literature. A second challenge is that the information provided by the FDA about financial ties is incomplete. We also address the potential problems associated with this limited information by using additional sources of data, particularly disclosures to scientific journals. Finally, unlike these reduced-form approaches that do not measure or estimate the ability of each advisor, our estimation enables us to identify three parameters of interest: ability, bias, and COI related to financial ties.

3 Literature Review

3.1 Theory

In considering the FDA's use of ACs, we draw on the theoretical literature that examines delegation to experts. ? focus on the selection of experts by a decision-maker. The key insight is that the information value of committees of experts with extreme opposing views is low, and a decision-maker should select experts who are less partisan than himself. ? and ? consider delegation to experts with contracts that include transfers. These papers assume that the acquisition of information is costly, so agents need some reward for that acquisition (and correct reporting). The FDA does not provide outcome-based or report-based rewards, and is relying on experts to interpret information rather than to acquire it, which might be less costly to experts. However, these features might affect the types of experts willing to participate. If participation

is costly, and experts only participate if they have an interest in advancing a particular agenda that exceeds the cost of participation, then committee membership may include experts with “extreme” views.

A number of papers examine the role of disclosure. ? focus on information transmission with and without disclosure of conflicts/bias by experts. They find that under some conditions, the expert can report with less noise under nondisclosure. ? is the most relevant to our application. In their model, experts care about their reputation. Truth-telling is more likely when there are multiple experts if their individual contributions (votes in our case) are observed by the market. Transparency, or disclosure of bias, doesn’t always improve the information. Experts in the above papers are heterogeneous in their biases or conflicts, but not in their ability (assuming they incur the cost of acquiring information, but these costs are identical).

3.2 Empirics

The empirical literature in this area is relatively sparse, given the volume of theoretical work and the policy relevance of the economic questions. This reflects an inherent challenge: if bias or financial ties are difficult for the market to observe, they are also difficult for the econometrician. Several recent papers have tackled the problem in a variety of settings.

? use a structural model based on reputational cheap-talk to estimate the bias of experts (movie reviewers) with career concerns. A key feature of their setting is that reviewers influence the quantity of signals about the true quality of the movie through their effect on demand for a film. However, the true quality is gradually revealed over time through consumer reviews. Their results suggest that reviewers do behave strategically in this context, and write reviews that do not fully reveal their true signal (or opinion) about a film.

In the financial sector, ? consider the selection of experts (directors) to corporate boards. They find that existing board members appoint sell-side analysts who exhibit a positive bias in their recommendations for the appointing firm, and that these analysts are relatively poor performers. Following the appointment of sell-side analysts as board members, firms are more likely to take actions that are favorable to management than to shareholders. In this case, the selection of biased experts comes at a cost.

? examines the behavior of members of grant review committees at the National Institutes of Health. She considers the tradeoff between expertise and bias: experts who review grant applications may have a preference for projects in their own areas of research, but are also informed about such research. An advantage of her setting is the ability to measure the quality of projects following a funding decision. Assuming that the projects on which applications are based are generally already advanced enough to yield publications, she uses bibliometric data on citations to those publications to assess the true quality of an application. Her findings suggest that the selection of higher quality projects by better-informed experts outweighs the costs of bias.

In our setting, the true quality of a drug is unobservable, both to the advisors and to the econometrician. Measures such as post-approval sales are endogenous: advisor votes influence whether a drug is marketed, and with what restrictions. Approval in other countries is also likely to be endogenous, since those regulators may factor in the FDA’s decision. For specific

cases with unambiguous clinical endpoints, it may be possible to use the results of subsequent clinical studies as a measure of quality. However, such cases are probably rare, and follow-on clinical study may also be influenced by advisory committee opinions. We therefore take an empirical approach that does not require a measure of quality.

Our approach builds on an adaptation of the spatial voting model used to study voting by Supreme Court Justices by ?. As in our setting, there is no objective measure of the “correct” decision. ? assume that justices vary in their ability to interpret the law as well as in their ideological biases. The cases they hear vary in informational content. Unlike in the pure spatial voting model, where ideology alone determines votes, this set-up allows for both common values and dispersed information. It yields structural estimates of ideological bias and the value of information provided during court deliberations.

4 Model

We estimate an expert’s ability and bias due to COI. In our application, experts with common values and potential COIs vote on whether to recommend approval of a new drug candidate. The committee’s deliberations result in public information. Experts also receive private signals of the quality of the candidate drug that they review based on their understanding of the clinical evidence collected by the sponsor and the committee’s deliberations. We define *quality* as the scientific or clinical benefits provided by the drug, including any side effects or adverse interactions, etc. Higher *ability* experts have a better understanding of clinical research and therefore receive more precise signals about quality. Experts use their private information to make their approval recommendations, possibly applying a lower threshold to sponsors with which they have strong financial ties and a higher threshold for sponsors that compete with a firm with which they have ties.

Each Advisory Committee has n experts, indexed by i , and reviews a total of T drugs, indexed by t . In general, the AC considers whether to recommend approval of drug t . Each expert votes $\nu_i^t \in \{0, 1\}$, where $\nu_i^t = 0$ is a vote against approval and $\nu_i^t = 1$ is a vote for. The AC’s recommendation to the FDA is based on the majority of the aggregated votes of its experts, denoted as $\nu^t \in \{0, 1\}$.

4.1 Information structure

Prior to voting, each expert receives a private signal $s_{it} = \omega_t + \sigma_{it}\epsilon_t$, with $\epsilon \sim \mathcal{N}(0, 1)$. $\omega_t \in \{0, 1\}$ is an indicator variable for drug t ’s true quality justifies approval; this is unobservable to both the expert and to the econometrician. We define $\theta_{it} = \frac{1}{\sigma_{it}}$ as the precision of expert i ’s signals. The Monotone Likelihood Ratio Property is satisfied for this parameterization of the information structure. Experts share a common prior of the unobserved state ω_t , denoted as $\rho_t \equiv \Pr(\omega_t = 1)$.

4.2 Payoffs

An advisor i receives payoffs that depend on the truth (ω_t) and his vote (ν_{it}). We assume that experts receive some disutility from voting “against” science, and this varies across experts and

drugs. This disutility is parameterized by $\pi_{it} \in [0, 1]$, and normalized to 0 when $\nu_{it} = \omega_t$. If the true state of science does not justify approval but expert i votes in favor, he receives $-\pi_{it}$: this is the cost of recommending a bad drug. Similarly, i receives $-(1 - \pi_{it})$ if he votes against approving a drug whose true quality is high, i.e. it is the cost of blocking a good drug.

Our model differs from ? in that experts have other components to their payoffs. Specifically, an expert with a financial tie to the sponsor of a drug receives extra utility from voting in favor of approval.³ For example, a favorable vote may improve the advisor’s chances of receiving future funding. We denote this extra payoff as $\alpha_{it}FT_{it}$, where FT_{it} is a dummy variable for the existence of a financial tie between the expert and the drug sponsor. In theory, α_{it} could be negative: if an advisor wants to establish a reputation for honesty, for example, he might vote against a firm to which he has a financial tie in order to signal his independence, although we don’t explicitly model dynamic considerations here. The payoffs are summarized in the following table:

| | $\omega_t = 0$ | $\omega_t = 1$ |
|--------------|---------------------------------|----------------------|
| $v_{it} = 0$ | 0 | $-(1 - \pi_{it})$ |
| $v_{it} = 1$ | $\alpha_{it}FT_{it} - \pi_{it}$ | $\alpha_{it}FT_{it}$ |

Intuitively, if there are no COIs and $\forall i, \pi_{it} = 1/2$, the model is one of pure common values. If $\pi_{it} \approx 0$ or 1, the expert is “biased” (or has an inherent preference for Type I or II error). If α_{it} is close to 1, voting is very sensitive to financial ties; if close to 0, financial ties have less importance.

Expert i votes in favor of approval of drug t if his expected payoff, given his information E , exceeds that from voting against. That is, iff:

$$\alpha_{it}FT_{it} - \pi_{it} \Pr(\omega_t = 0|E) \geq -(1 - \pi_{it}) \Pr(\omega_t = 1|E)$$

Equivalently, expert i approves the drug if the likelihood ratio exceeds the approval threshold, or:

$$\frac{\Pr(E | \omega_t = 1)}{\Pr(E | \omega_t = 0)} \geq \frac{\pi_{it} - \alpha_{it}FT_{it}}{(1 - \pi_{it})} \frac{1 - \rho_t}{\rho_t}$$

The approval threshold increases with the aversion of the expert for Type 1 error (approving a drug that does not meet the standard) relative to Type 2 error (rejecting a drug that meets the standards). The threshold is lower when the expert has financial ties with the sponsor of the drug.

We use the expressive voting model, i.e. the expert votes based on her private information and individual preferences and does not care about the decision taken by the committee. In doing so, we are assuming that an expert’s financial position is affected more by his own vote rather than by the vote of the committee. For example, an expert receiving research support

³This will be extended to allow for utility of voting against approval if the advisor has a financial tie to a competing firm.

from a drug’s sponsor may risk losing that support if *he* votes against the sponsor’s drug, but the sponsor is unlikely to reduce his research support if the *committee* votes against. This is less likely to be the case if the expert receives a large financial payoff conditional on the drug’s approval, such as through holding substantial stock in the sponsoring firm. In this case, there is a unique cutoff point s_{it}^{exp} that solves

$$\begin{aligned} \frac{\Pr^i(s_{it}|\omega_t = 1)}{\Pr^i(s_{it}|\omega_t = 0)} &= \frac{\phi(\theta_{it}[s_{it} - 1])}{\phi(\theta_{it}s_{it})} \\ &\geq \frac{\pi_{it} - \alpha FT_{it}}{(1 - \pi_{it})} \frac{1 - \rho_t}{\rho_t} \end{aligned} \quad (4.1)$$

This ratio is increasing in s . Using the MLRP, if i receives a signal $s_{it} > s_{it}^{\text{exp}}$, i votes 1. The likelihood of votes by experts for a specific drug t is

$$\Pr(v_t) \equiv \sum_{\omega_t} \Pr(\omega_t) \prod_{i=1} N[1 - \Phi(\theta_{it}[s_{it}^{\text{exp}} - \omega_t])]^{\nu_{it}} \Phi(\theta_{it}[s_{it}^{\text{exp}} - \omega_t])^{1-\nu_{it}} \quad (4.2)$$

Identification is based on the following intuition. Experts share a common value for each question or application they evaluate, and this common value induces correlation of their votes. With no bias ($\pi \approx 1/2$), an uninformative prior ($\rho \approx 1/2$), good information (θ large), and no COI, we should observe unanimous recommendations, evenly split between approval/rejection. A biased expert will have low variability in votes. In other words, i will more consistently vote for (or against), rather than splitting his votes evenly. An expert with low ability to interpret information will tend to have more variable voting and to be on the losing side. Finally, COI will mean that an expert is more likely to vote for the sponsor, all else equal.

Note that in a strategic voting model, in which experts behave as if their vote is pivotal given the equilibrium strategy profile followed by the rest of the committee members, there are multiple equilibria, also characterized by cutoff points. Estimation results are therefore valid only if the same equilibrium is played in all the meetings we observe in our data. We focus for now on the expressive model.

5 Estimation

Let \mathbf{X}_t contain data on the characteristics of a drug application (e.g., what disease it treats; whether it is a biologic or a small molecule product; etc.). The experts voting on drug t have characteristics \mathbf{Z}_i .

We parameterize the prior ρ , the probability that drug is good $\Pr(\omega_t) = 1$, as function of drug characteristics as follows:

$$\rho(\mathbf{X}_t; \beta) \equiv \frac{\exp(\mathbf{X}_t' \beta)}{1 + \exp(\mathbf{X}_t' \beta)} \in [0, 1]$$

We assume a similar parameterization for the conditional vote probabilities as functions of drug and expert characteristics. Let $\gamma_{i,0}$ be the probability of expert i voting for a bad drug ($\Pr(v_{it} = 1|\omega_t = 0)$), and $\gamma_{i,1}$ be the probability of voting for a good drug ($\Pr(v_{it} = 1|\omega_t = 1)$). We assume that experts are more likely to vote in favor of a good drug than a bad drug, i.e. $\gamma_{i,1} \geq \gamma_{i,0}$.

$$\begin{aligned}\gamma_{i,0}(\mathbf{X}_t, \mathbf{Z}_i; \zeta, \eta) &\equiv \Pr(\nu_{it} = 1|\omega_t = 1) \\ &= \frac{\exp(\mathbf{Z}'_i \zeta + \mathbf{X}'_t \eta)}{1 + \exp(\mathbf{Z}'_i \zeta + \mathbf{X}'_t \eta)} \in [0, 1]\end{aligned}$$

$$\begin{aligned}\gamma_{i,1}(\mathbf{X}_t, \mathbf{Z}_i; \zeta, \eta, \mu, \xi) &\equiv \Pr(\nu_{it} = 1|\omega_t = 0) \\ &= \frac{\gamma_{i,0} + \exp(\mathbf{Z}'_i \mu + \mathbf{X}'_t \xi)}{1 + \exp(\mathbf{Z}'_i \mu + \mathbf{X}'_t \xi)} \in [\gamma_{i,0}(\zeta, \eta), 1]\end{aligned}$$

Estimation takes place in two stages. First, we maximize the reduced-form likelihood function for votes to obtain estimates of $\hat{\gamma}_{i,t,1}$ and $\hat{\gamma}_{i,t,0}$:

$$\max_{\alpha, \beta, \zeta, \eta, \delta} \sum_t \log \rho \prod_{i=1}^n (\gamma_{i,1})^{\nu_{it}} (1 - \gamma_{i,1})^{1-\nu_{it}} + (1 - \rho) \prod_{i=1}^n (\gamma_{i,0})^{\nu_{it}} (1 - \gamma_{i,0})^{1-\nu_{it}}$$

In the second stage, we use these estimates to solve for the expert's ability θ_{it} and voting cutoff s_{it}^* . Using $s_{it} = \omega_t + (1/\theta_i)\epsilon_{it}$, we have:

$$\begin{aligned}\gamma_{i,1} &\equiv \Pr(\nu_{it} = 1|\omega_t = 1) \\ &= 1 - \Pr(1 + (1/\theta_i)\epsilon_{it} > s_i^*) \\ &= 1 - \Pr(\epsilon_{it} > \theta(s_i^* - 1)) \\ &= 1 - \Phi(\theta(s_i^* - 1)) \\ \gamma_{i,0} &= 1 - \Phi(\theta_i s_i^*)\end{aligned}$$

Solving these equations for θ_{it} and s_{it}^* yields:

$$\begin{aligned}\hat{\theta}_{it} &= \Phi^{-1}(1 - \hat{\gamma}_{i,t,0}) - \Phi^{-1}(1 - \hat{\gamma}_{i,t,1}) \\ \hat{s}_{it} &= \frac{\Phi^{-1}(1 - \hat{\gamma}_{i,t,0})}{\Phi^{-1}(1 - \hat{\gamma}_{i,t,0}) + \Phi^{-1}(\hat{\gamma}_{i,t,1})}\end{aligned}$$

To recover the bias π_{it} and COI parameter α_{it} , we use the equilibrium voting condition, which is:

$$\frac{\phi(\hat{\theta}_{it}[\hat{s}_{it} - 1])}{\phi(\hat{\theta}_{it}\hat{s}_{it})} = \frac{\pi_{it} - \alpha_{it}FT_{it}}{(1 - \pi_{it})} \frac{1 - \hat{\rho}_t}{\hat{\rho}_t}$$

Since we have two unknowns, π_{it} and α_{it} , we need an additional functional form assumption to identify both. First, we select the observations for which there is no financial tie to the sponsor, so that $FT_{it} = 0$. From this subset, we can calculate π_{it} from the equilibrium voting condition just provided. We then let π_{it} be a function of drug and advisor characteristics, $f(\mathbf{X}_t, \mathbf{Z}_i; \tau)$. With estimates of the coefficients $\hat{\tau}$, we can compute $\hat{\pi}_{it}$ for the observations where $FT_{it} = 1$, and $\hat{\alpha}_{it}$ follows once we plug these in to the equilibrium voting condition with the other parameter estimates.

While we estimate a structural parameter for COI that is associated with a *direct* tie to the sponsoring firm, we can include ties to the industry more broadly as an element of advisor characteristics \mathbf{Z}_i . Such ties enter into the estimates of both advisor quality θ_{it} as well as bias π_{it} . In our counterfactual simulations, we can evaluate how changes in industry ties would affect both.

5.1 Simulation results

We begin by testing the model using simulated datasets, to verify that our procedure yields reasonably precise, unbiased estimates of the structural parameters. We choose a set of true structural parameters, draw random values for advisor and drug characteristics 100 times, and simulate votes given these parameter values and data. We then use our two-step approach that first estimates a set of “reduced-form” parameters using maximum likelihood, and then recover estimates of the structural parameters given these reduced-form estimates.

Results from these simulations are summarized below, using a sample size of 100 drug applications and 100 advisors. We assume that there are 4 observable application characteristics and 3 advisor-level variables, and that there is a financial tie in one-third of the observations. For each draw of data, we try 10 different starting values for the reduced-form parameters in case the minimization routine gets stuck at local minima, and we try both the Nelder-Mead and quasi-Newton search algorithms to verify robustness.

A challenge in our data, described in the following section, is that we observe a large number of advisors relative to the number of votes, and only a subset of advisors vote on each application. In a second set of simulations, we assume that only 10 experts vote on each application, and each expert is observed for only 10 votes.

6 Data

6.1 Advisory Committee meetings and voting outcomes

We obtained the data used in the ? and ? papers from the Eastern Research Group, which conducted a study of voting and conflicts of interest for the FDA in 2009.⁴ This dataset spans

⁴We thank Nyssa Ackerley for sharing this data.

2002-early 2008, and has information on which members attended each meeting; how each member voted; and which members received a COI waiver. While all meetings are recorded in this data, only a subset of the questions on which committees voted is included, typically the question most directly related to a drug's approval.

We then collected the same information for committee meetings from 2008-2013 ourselves, using the minutes of AC meetings posted on the FDA's website. In addition to votes on new drug approvals, we recorded all votes taken. Often, advisors vote on separate questions related to safety, efficacy, and the use of a drug in a specific population. They also occasionally vote on questions related to clinical endpoints or other regulatory guidelines. This diversity of questions helps us tease out bias versus risk aversion. We augmented the 2002-2007 dataset to include information on all questions as well.

While most of our analysis will focus on the 2008-2013 period, we describe here some changes over time. Of course, these patterns permit only limited inference. There was also a change in president and in the political party of the executive branch, which oversees the FDA. Politics may change how the FDA uses experts or the agency's risk aversion. The FDA changed its COI policy in 2008, as noted in section ???. In addition, the ACs gradually moved from sequential oral voting to simultaneous electronic voting during 2007-08.

6.2 Patterns

The 2002-2007 dataset contains a total of 246 votes on approval. Excluding the 91 votes on medical devices, we have 155 vote outcomes. The vote was unanimous in 73 cases, 61 of which were recommendations to approve. In 134 votes, there were no abstentions. On average, about 16 members voted (including abstentions), with a range of 7 to 29.

For the data we collected ourselves from 2008-2013, we have a total of 242 votes on approval. The majority voted to recommend approval in 169 cases, against in 70, and tied in 3. The vote was unanimous in 80 cases, 68 of which were recommendations to approve. In 174 votes, there were no abstentions. On average, about 13 voting members participated in meetings (including abstentions), but the total number of voting members varied from 4 to 36.

The average number of experts per vote declined over time, which is consistent with the idea that a change in COI policy led to greater difficulty in finding experts to participate. There appears to be increased disagreement in the later period, as unanimous votes account for a lower share of the total (33% vs. 47%). The evolution of the degree of consensus is shown in Figure ??, where -1 indicates a unanimous negative vote and +1 is a unanimous vote to approve.

The FDA is not required to seek the advice of an AC, nor to follow it. Both decisions should depend on the quality of the AC, accounting for any COI introduced by financial ties. There is some variation in the use of ACs over time that appears unrelated to the volume of applications for new molecular entities (NMEs) (Figure ??).

6.3 Advisor data

For each advisor who participated in a meeting in the 2008-2013 period, we collect measures of their observable quality, expertise, and other characteristics, as well as their ties to industry.

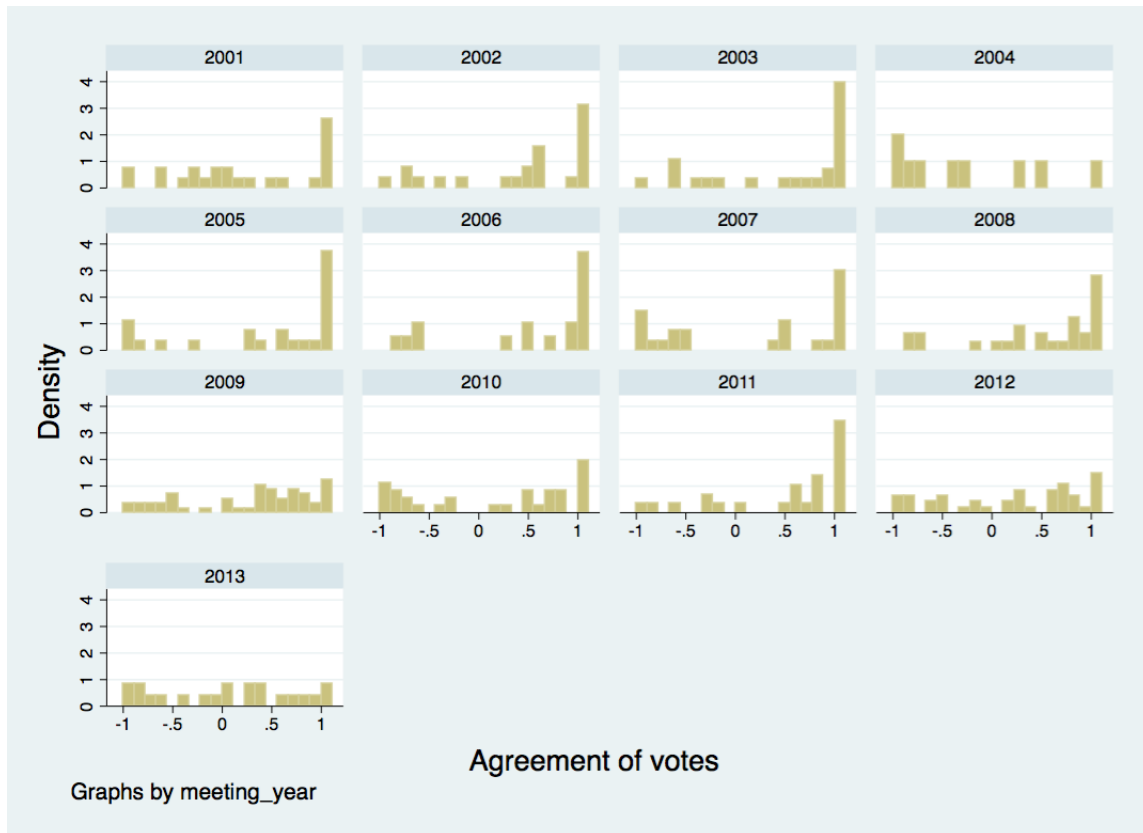


Figure 1: Votes by FDA ACs, 2001-2013

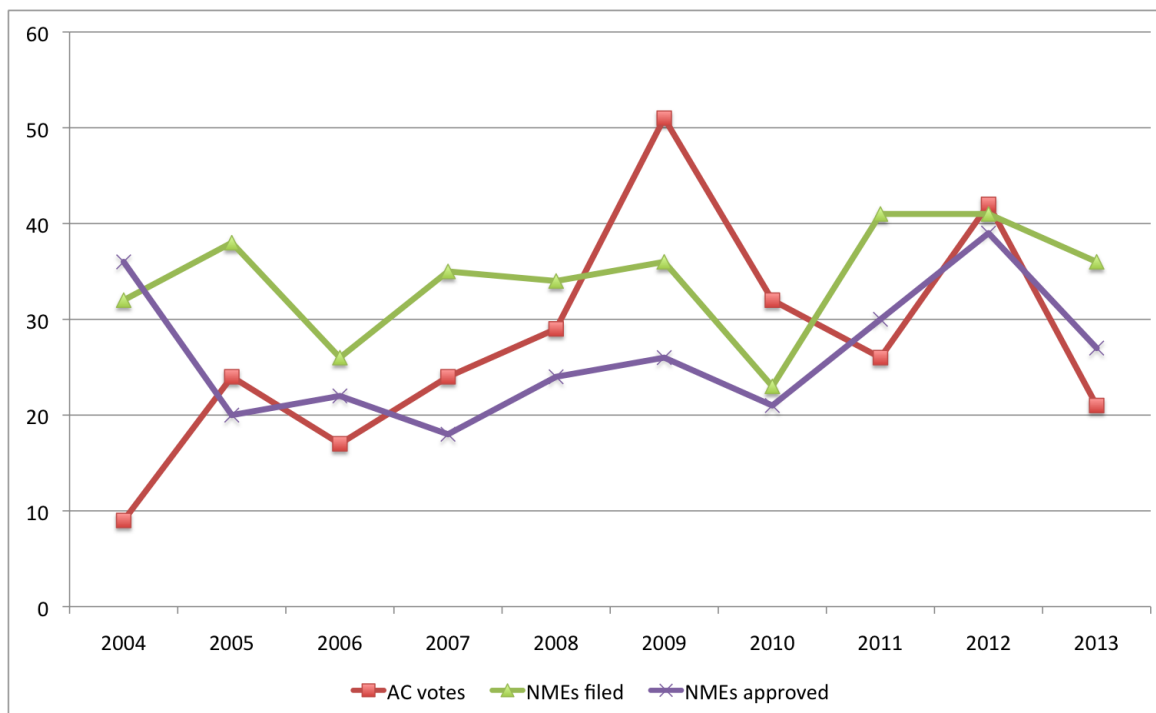


Figure 2: NME applications, approvals, and use of ACs

We focus on more recent years primarily because more data is available for these advisors. In particular, advisors who have retired since the 2002-2007 period are difficult to find. We derive these measures from several sources.

First, we use information from FDA records. We record each expert’s tenure on the committee and the number of meetings in which each has participated. Greater experience should improve the precision of the expert’s signal, or the expert’s ability to evaluate the scientific evidence. FDA rosters also provide the degrees held by each advisor and their current affiliations.

For the set of advisors holding PhDs, we obtain data on the year they completed their doctoral studies and the specific subjects of their dissertations from the ProQuest Dissertations & Theses Database. For those holding MDs, we use two additional sources. The first is the Medicare Official Physician Compare Data, which includes information on all physicians providing treatments reimbursed by Medicare. The second is the [Healthgrades](#) website, from which we extracted information on the age, specialties, and board certifications of individual advisors. We have yet to identify a comprehensive source of information on advisors holding PharmDs or MPH degrees.

For objective measures of research-related expertise, we use three sources. Research-active experts, particularly those working in academic settings, are likely to apply for funding from the National Institutes of Health. We record the level of NIH funding each advisor in our data received in each year. The registry of clinical trials maintained by the National Library of Medicine, [clinicaltrials.gov](#), provides information on principal investigators and sponsors.

We record the number of trials for which each advisor has acted as principal investigator, and whether those trials were funded by industry, the US government, or another sponsor. Lastly, we use PubMed, a database of scientific publications in the life sciences, to determine the research output of each advisor. Specifically, we record the number of publications on which an advisor is listed as an author in each year, the number of co-authors on each paper, and the advisor's position in the list of co-authors.

All of the above require considerable effort to deal with name disambiguation. The current version of our data matches on the full author name in PubMed, which is only possible for publications from 2002-present. Our publication-based measures should therefore be interpreted as indicating recent research activity, rather than that over the full career of an advisor. In general, we use middle initials and information on affiliations or specialties to ensure that our matches are correct. However, some potential for error remains in the case of very common names.

6.4 Sponsor and competitor data

For each drug considered by an advisory committee, we identify all firms involved in its clinical development using IMS R&D Focus, which provides development histories on all new drug candidates since the early 1990s. This definition includes not only the firm responsible for the FDA application, but all licensors and licensees. Firms with marketing rights in other countries, or which receive royalties or other licensing payments, also have a clear interest in committee's recommendation.

We identify competitors from the same source. We treat all firms involved in the development of a drug with the same indication that has reached the market or is close to market⁵ as a direct competitor. It is possible to use a broader market definition as well, although doing so would likely dilute the impact of a committee's recommendation.

6.5 Measures of financial ties

AC members disclose financial ties on Form 3410, but this disclosure is generally confidential. Based on this information, the FDA determines whether a COI exists, and whether to grant a COI waiver that allows the expert to participate in the AC meeting. We therefore directly observe only financial ties that meet three conditions. First, the advisor must disclose a financial tie. Second, this tie must exceed the FDA's threshold for conflict of interest. Third, the FDA must issue a waiver for the advisor. As discussed above, the FDA is now limited to a small number of waivers each year. It is therefore difficult to know whether advisors post-2008 have fewer conflicts, whether they recuse themselves voluntarily from meetings for which a waiver might otherwise be required, or whether the FDA uses a different (higher) threshold for determining whether a waiver is needed.

We therefore use an alternative source of information on financial ties. Driven by the same concerns about COI that triggered changes in FDA practices, many medical journals have

⁵Specifically, if the competing drug candidate has reached Phase III, the final stage of development prior to approval, we consider it close to market.

introduced policies requiring disclosure of financial ties. Not all of these disclosures constitute a COI for the purpose of Form 3410 and the FDA: for example, receiving industry funding for a study that does not concern the drug under review or one of its direct competitors is generally permitted by FDA guidelines. While the disclosure to journals is probably imperfect (?), we believe it nevertheless provides a more complete picture than FDA COI waivers alone.

We use the PubMed database described earlier to identify publications authored by each FDA advisor. We then search the full-text of each article for the disclosure of a tie to industry. For example, an author might acknowledge research support from a pharmaceutical firm, or state that they own stock in a firm whose product was the subject of study, etc. We use this information to quantify the strength of financial ties, at least as a percentage of total publications, and the nature of these ties (research funding, travel, speaking fees, etc.).

Below is a specific example corresponding to an advisor in our data: Julia B. Lewis, who was a member of the Cardiovascular and Renal Drugs Advisory Committee during the period covered by our dataset. Her authorship of this and all other publications contributes to our measure of her scientific contribution. The publication provides additional information about her industry ties, which include funding from five pharmaceutical firms: Bristol-Myers-Squibb, Sanofi-Aventis, Nephrogenix, Keryx Biopharmaceuticals, and Eli Lilly. These ties did not constitute a COI as defined by the FDA, so no waiver was issued for her participation in AC meetings. Note that we do not claim *a priori* that these ties constitute a conflict of interest either: the fact that she receives funding from many firms may be indicative of her expertise. We also include ties to industry as measured by sponsorship of clinical trials for which an advisor served as principal investigator. As with the publications information, this is a useful source for advisors who are active in clinical research.

Cardiorenal Med. Feb 2012; 2(1): 1–10.

PMCID: PMC3318932

Published online Oct 26, 2011. doi: [10.1159/000333249](https://doi.org/10.1159/000333249)

Renal Dysfunction in the Presence of Normoalbuminuria in Type 2 Diabetes: Results from the DEMAND Study

[Jamie P. Dwyer](#),^{a,*} [Hans-Henrik Parving](#),^{b,c} [Lawrence G. Hunsicker](#),^d [Moti Ravid](#),^e [Giuseppe Remuzzi](#),^f and [Julia B. Lewis](#)^a, for the DEMAND Investigators

Disclosure Statement

Go to: 

J.P.D. reports research and travel support from Keryx Biopharmaceuticals, Inc, and Eli Lilly, Inc., and H.-H.P consultancy and speaker's fees from Sanofi-Aventis, Merck, Bristol-Myers-Squibb, and Novartis. L.G.H received research support from Bristol-Myers-Squibb, Sanofi-Aventis, and Eli Lilly. G.R. obtained speaker's fees from Astra-Zeneca and Novartis, and has acted as a consultant to Pharmanet. M.R. reports speaker's fees from Sanofi-Aventis and has acted as consultant for Novo-Nordisk. J.B.L. confirmed research and travel support from Bristol-Myers-Squibb, Sanofi-Aventis, Nephrogenix, Keryx Biopharmaceuticals, and Eli Lilly.

The sponsors of the study (Bristol-Myers Squibb and Sanofi-Aventis) contributed to the study design, data collection, and reviewed and commented on drafts of the original DEMAND report, but had no role in data analysis (performed by J.P.D. and L.G.H.), interpretation or writing the report, or reviewing drafts of this current study. The corresponding author had full access to all data in the study and had final responsibility for the decision to submit for publication.

We complement our measure of financial ties using payment information (“Open Payments”) required by the Sunshine Act. From Open Payments, we know that the same Dr. Lewis received \$11.20 for food and beverages from Amgen Inc. in 2014, for example. This dataset includes

only payments made in 2013 and 2014, and only covers physicians, so our publication disclosure-based measure has better time coverage. However, the Open Payments data includes financial ties to physicians who are not active publishers of scientific papers or engaged in clinical trial activity.

6.6 Descriptive statistics

As we noted earlier, the FDA’s COI policy changed in 2008 to limit the number of waivers granted. As is evident from Figure ??, the policy has succeeded in reducing the number to close to zero. During the same period, the number of committee vacancies has remained higher than the FDA’s target level (see Figure ??). This pattern provides some support for the idea that the COI policy has made filling committee seats more difficult, although other factors could also explain it, and vacancies have declined over time.

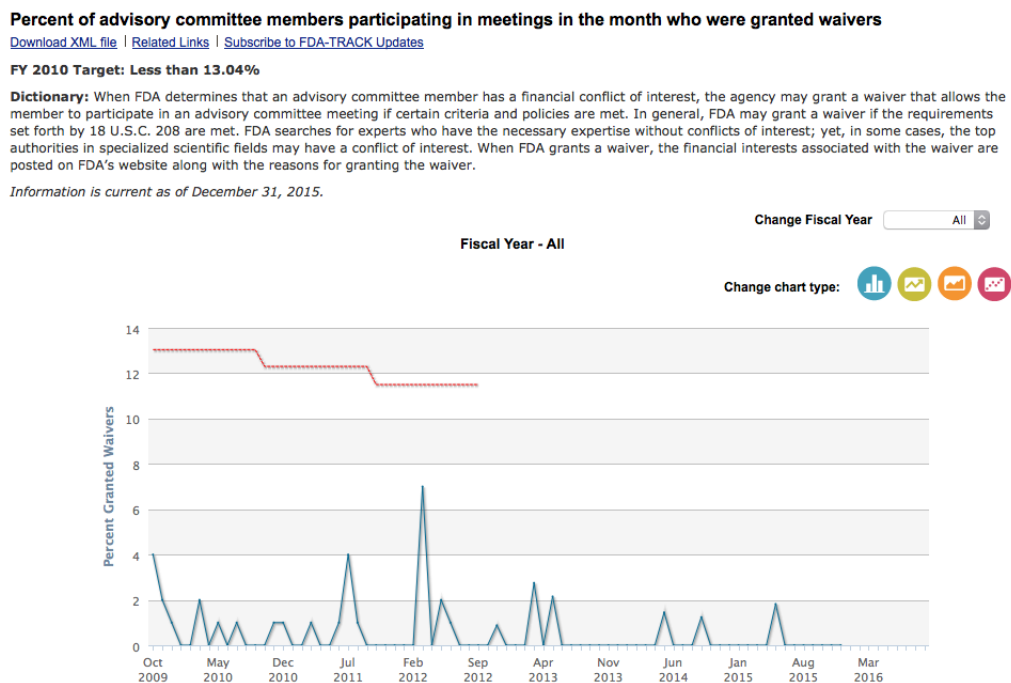


Figure 3: Conflict of interest waivers issued by the FDA.

Source: <http://www.accessdata.fda.gov>

Descriptive statistics for the set of 1208 advisors participating in CDER committees 2008-2013 are presented in Table ?. More than half report an academic affiliation in the rosters provided by the FDA, although this includes both tenure-track faculty as well as clinical positions. About three-quarters hold MDs, and about one-quarter have PhDs (some have both). A smaller number have PharmDs or a master’s in public health (MPH), and there are a few lawyers and veterinarians.

Research activities are summarized in Table ?. On average, these advisors have authored

Percent of FDA advisory committee member positions vacant at the end of the month

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Dictionary: Access to state-of-the-art, scientific expert advice to support agency decision making processes is imperative to the FDA advisory committee process. Having the fewest vacancies on our committees allows the agency to have ready access to those experts and supports the ability of FDA to meet its public health mission. For more information about FDA advisory committees, please visit <http://www.fda.gov/AdvisoryCommittees/default.htm>

Information is current as of December 31, 2015.

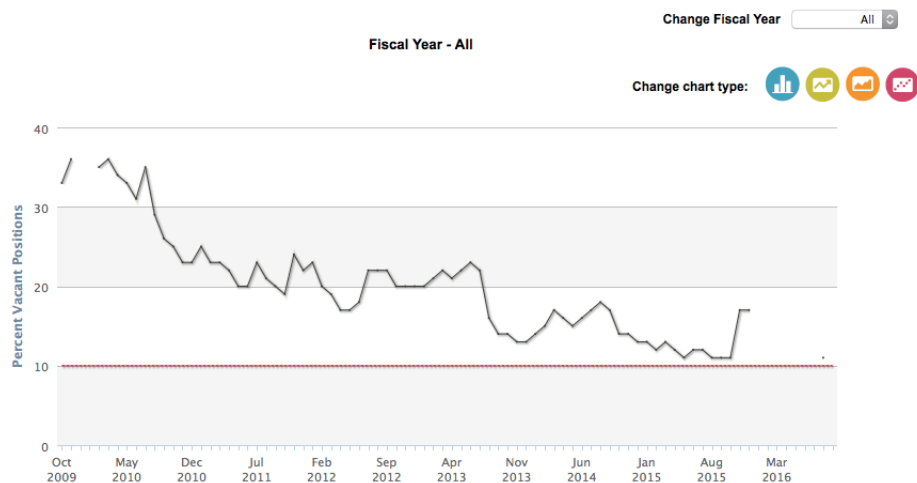


Figure 4: Committee vacancies.
Source: <http://www.accessdata.fda.gov>

about 60 scientific papers, and more than half have received an NIH grant. Advisors without postgraduate degrees are typically patient representatives. The distribution of the years at which MDs and PhDs completed their degrees is presented in Figures ?? and ??.

Table 1: Advisor demographics

| Variable | Mean | Std. Dev. | Min. | Max. | N |
|--------------------------|-------|-----------|-------|-------|------|
| Has academic affiliation | 0.62 | 0.49 | 0 | 1 | 1096 |
| MD | 0.75 | 0.43 | 0 | 1 | 1208 |
| PhD | 0.23 | 0.42 | 0 | 1 | 1208 |
| PharmD | 0.04 | 0.19 | 0 | 1 | 1208 |
| MPH | 0.08 | 0.26 | 0 | 1 | 1208 |
| Female | 0.34 | 0.47 | 0 | 1 | 1208 |
| Age | 54.18 | 9.9 | 27.67 | 85.06 | 905 |

As we explained earlier, the number of COI waivers issued after 2008 has dropped considerably. Even when issued, a COI is narrowly defined by the FDA: it includes financial interests from the previous 12 months only, and from specific firms (the sponsor of the drug reviewed by the committee or a direct competitor). In table ??, we present indicators of financial ties to industry using different sources and definitions. About one-fifth of the advisors in our sample received a payment disclosed in the Open Payments data, as required by the Sunshine Act. This data corresponds to only 6 months in 2013, and covers only physicians. About 17% of the

Table 2: Advisor research output

| Variable | Mean | Std. Dev. | Min. | Max. | N |
|--------------------------------------|-------|-----------|------|------|------|
| Total publications (as of 2014) | 64.48 | 76.94 | 0 | 606 | 1208 |
| Percentage of papers as last author | 0.13 | 0.13 | 0 | 1 | 1208 |
| Percentage of papers as first author | 0.19 | 0.19 | 0 | 1 | 1208 |
| Ever received NIH grant | 0.55 | 0.5 | 0 | 1 | 1208 |
| Number of clinical trials | 1.55 | 3.23 | 0 | 32 | 1208 |

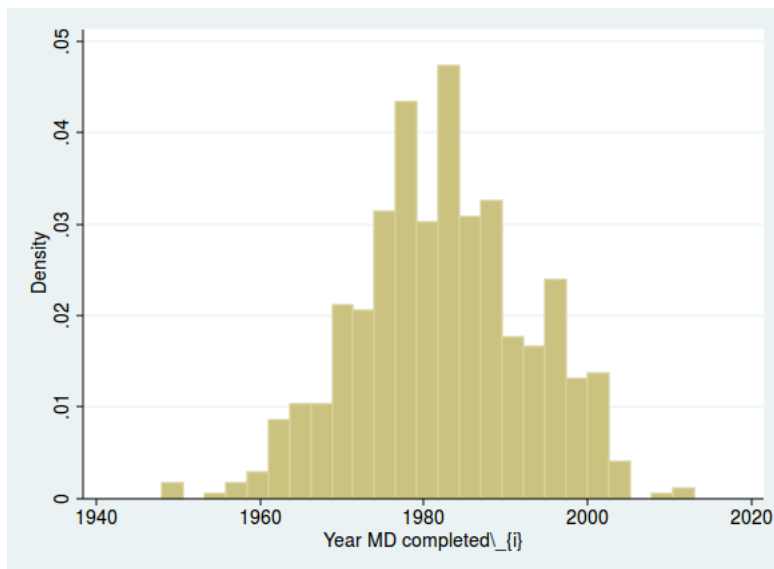


Figure 5: Distribution of MD completion year

advisors in 2008-2013 received a COI waiver at some point during their tenure on FDA committees. Most of these were issued prior to 2008. About 14% of these advisors disclosed financial support in a paper published within a 5-year window $(-4, +1)$ of a committee meeting in which they participated. This can be measured only for advisors who are active in publishing. Two other measures related to industry connections are the number of industry-sponsored trials for which an advisor has been an investigator and the total number of firms the advisor has noted in publication disclosures. Some advisors have ties to many firms (more than 20), and are very active in industry-sponsored trials; many others have report no activity of this sort.

We now turn to meeting-level variables, summarized in table ???. On average, meetings have about 13 voting participants, split evenly between standing members and temporary members. The distribution of MDs and PhDs is similar to that observed in the advisor-level data. Note that nearly half of the participants have some observable tie to industry. That is, either we see a Sunshine Act payment, or a conflict-of-interest waiver at some point, or a role as investigator of an industry-sponsored clinical trial, or a disclosure in a publication. This is a broad definition of industry ties, but illustrates their overall prevalence.

Table 3: Industry ties

| Variable | Mean | Std. Dev. | Min. | Max. | N |
|---|-------------|------------------|-------------|-------------|----------|
| Any payment disclosed in 2013 under Sunshine Act | 0.21 | 0.41 | 0 | 1 | 1208 |
| Number of industry-sponsored clinical trials | 0.31 | 0.91 | 0 | 14 | 1208 |
| Ever received a waiver for COI | 0.17 | 0.37 | 0 | 1 | 1208 |
| Advisor ever reported financial support from industry in publication | 0.14 | 0.35 | 0 | 1 | 1208 |
| Number of firms advisor reported financial support from in publications | 0.59 | 2.17 | 0 | 23 | 1208 |

Table 4: Summary statistics for CDER meetings, 2008-2013

| Variable | Mean | Std. Dev. | Min. | Max. | N |
|---|-------------|------------------|-------------|-------------|----------|
| Number of committee members present | 13.13 | 4.56 | 0 | 31 | 156 |
| Number of standing members present | 6.56 | 2.69 | 0 | 13 | 156 |
| Number of temporary members present | 6.57 | 3.89 | 0 | 23 | 156 |
| Number of members with MD | 9.56 | 3.62 | 0 | 22 | 156 |
| Number of members with PhD | 3.53 | 2.26 | 0 | 14 | 156 |
| Number of members with observable tie to industry | 6.37 | 2.99 | 0 | 17 | 156 |

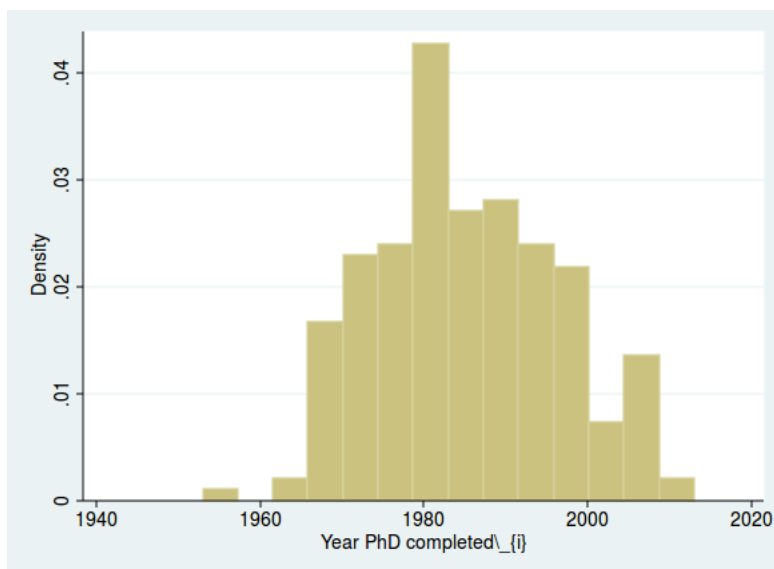


Figure 6: Distribution of PhD completion year

Table ?? compares observable advisor characteristics between those with no financial tie and those with any tie that we observe. On average, advisors with financial ties are more experienced: they are about 2 years older, have participated in about 2 additional meetings, and have more than 1 additional year of service on advisory committees. In addition, advisors with financial ties have published more papers, are more likely to have received a grant from the NIH, and have more advanced degrees and board certifications. Their average status in publications is also higher.

Advisors may opt-out of participating in meetings for which they have a COI, or the FDA may avoid using people with conflicts as either standing or temporary members of committees. We are unable to observe whether an advisor requested a waiver and was denied, or whether the advisor recuses himself pre-emptively. In Table ??, we compare two measures of financial ties for the set of advisors who were present for a meeting and those that were not. The “absent” set includes all advisors who participated in at least one meeting for a specific committee; we consider this the potential pool of experts. The measures of financial ties are based on publication disclosures, and include indirect ties through co-authors. We do not observe a difference in the likelihood of having a financial tie between the set of advisors present and potential participants who did not attend. This pattern suggests that any selection based on conflicts may be more likely for committee membership rather than for specific meetings.

The distribution of voting questions and their outcomes is provided in Table ??, and table ?? presents summary statistics for data at the advisor-meeting level. As noted previously, some meetings include multiple voting questions, and the language varies. We classify the outcome as favoring the index drug based on the exact phrasing of the question. In some cases, the vote does not concern a specific drug.

Table 5: Comparison of advisors with and without financial ties

| | No Tie | Any Tie | Difference |
|--------------------------------------|--------|---------|------------|
| Number of previous meetings attended | 4.30 | 6.49 | -2.19*** |
| Years since completing MD or PhD | 26.19 | 28.07 | -1.89*** |
| Number of years serving as expert | 1.86 | 3.25 | -1.39*** |
| Cumulative publications | 25.97 | 46.79 | -20.82*** |
| Ever received NIH grant | 0.45 | 0.69 | -0.24*** |
| Average status in publications | 0.26 | 0.31 | -0.05*** |
| Number of clinical trials | 0.64 | 2.52 | -1.88*** |
| Number of board certifications | 0.40 | 0.75 | -0.35*** |
| Number of advanced degrees | 1.09 | 1.23 | -0.14*** |

Table 6: Financial ties comparison

| Variable | Present | | Absent | |
|---|----------------|----------|---------------|----------|
| | Mean | N | Mean | N |
| Advisor received financial support from sponsor within 5 years | 0.08 | 2048 | 0.07 | 16650 |
| Advisor received financial support from competitor within 5 years | 0.08 | 2048 | 0.07 | 16650 |
| Co-author received financial support from sponsor within 5 years | 0.16 | 2048 | 0.14 | 16650 |
| Co-author received financial support from competitor within 5 years | 0.16 | 2048 | 0.15 | 16650 |

Table 7: Summary statistics for CDER votes, 2008-2013

| Category | Outcome for drug | | | |
|---------------------------------|------------------|---------|-----|-------|
| | For | Against | Tie | Total |
| Safety | 42 | 18 | 4 | 64 |
| Efficacy | 66 | 30 | 4 | 100 |
| Safety+efficacy or risk/benefit | 55 | 26 | 1 | 82 |
| Approval | 54 | 26 | 0 | 80 |
| Withdrawal | 0 | 2 | 0 | 2 |
| Restriction | 3 | 1 | 0 | 4 |
| Relabeling | 1 | 5 | 0 | 6 |
| Other | 25 | 38 | 1 | 64 |
| Total | 246 | 146 | 10 | 402 |
| Total | 301 | 177 | 9 | 487 |

Table 8: Summary statistics at meeting-advisor level

| Variable | Mean | Std. Dev. | Min. | Max. | N |
|---|-------|-----------|------|-------|------|
| Cumulative industry trials led | 0.22 | 0.74 | 0 | 14 | 5504 |
| Any payment disclosed in 2013 | 0.24 | 0.42 | 0 | 1 | 5504 |
| Ever received a waiver for COI | 0.19 | 0.39 | 0 | 1 | 5504 |
| Advisor ever reported financial support from industry in publication | 0.18 | 0.38 | 0 | 1 | 5504 |
| Number of firms advisor reported financial support from in publications | 0.68 | 2.09 | 0 | 23 | 5504 |
| Number of previous meetings attended | 5.35 | 5.9 | 1 | 50 | 5504 |
| Years since completing MD or PhD | 27.21 | 10.34 | -3 | 60 | 4276 |
| Number of years serving as expert | 2.53 | 2.87 | 0 | 12.04 | 5504 |
| Cumulative publications | 35.95 | 44.4 | 0 | 399 | 5504 |
| Ever received NIH grant | 0.56 | 0.5 | 0 | 1 | 5504 |

7 Reduced-form results

At this stage, we have only preliminary reduced-form results, summarized below. In all specifications, we classify votes as “pro-industry” if a positive vote favored the index drug under review. The unit of analysis is an advisor-vote. Although the dependent variable is discrete, we estimate linear probability models for simplicity. The mean of the dependent variable is about .5, so predicted values outside the [0,1] range are unlikely, and results from a logit model are very similar. Statistical significance is indicated by + for $p < .05$ and * for $p < .01$.

We begin with the simplest possible specification, essentially that of the earlier papers that have examined COI at the FDA, where only explanatory variable is a measure of financial ties. Table ?? presents the results using four different measures of financial ties. (Too few COI waivers were issued post-2008 to attempt to replicate the previous papers’ specifications exactly.) Earlier studies found little relationship between COI and pro-industry voting, and we obtain similarly economically small and statistically insignificant results with these alternative measures.

Table 9: Regression results, simplest specification

| | Model 1 | Model 2 | Model 3 | Model 4 |
|--|------------------|-------------------|------------------|-------------------|
| | b/se | b/se | b/se | b/se |
| Advisor has any observable financial tie | 0.013 (0.013) | | | |
| Ever received a waiver for COI | | -0.013 (0.017) | | |
| Any payment disclosed in 2013 | | | 0.028 (0.016) | |
| Advisor ever reported financial support from industry in publication | | | | -0.020 (0.017) |
| N | 5504 | 5504 | 5504 | 5504 |
| R^2 | 0.0002 | 0.0001 | 0.0006 | 0.0002 |
| Adj. R^2 | -0.0000 | -0.0001 | 0.0004 | 0.0001 |

Table ?? includes observable advisor characteristics in addition to measures of financial ties. Few of these additional variables prove important in explaining votes. The probability of voting favorably for the industry declines somewhat as advisors accumulate committee experience, measured as the number of previous meetings in which they have participated. Physicians are more likely to vote in favor of a drug than are PhDs, who in turn are more positive than the omitted category (PharmDs and others).

Since variation in observable characteristics across advisors provides little explanatory power, we next include advisor fixed effects to control for unobservable differences. Since many of the observable characteristics are fixed across time and committee, the set of explanatory variables

Table 10: Regression results with advisor characteristics

| | Model 1 | Model 2 | Model 3 | Model 4 |
|--|--------------------|--------------------|--------------------|--------------------|
| | b/se | b/se | b/se | b/se |
| Advisor has any observable financial tie | 0.027 (0.016) | 0.045* (0.016) | | |
| Advisor ever reported financial support from industry in publication | | | | -0.005 (0.025) |
| Advisor received financial support from sponsor within 5 years | | | 0.038 (0.026) | 0.086 (0.156) |
| Advisor received financial support from competitor within 5 years | | | | -0.043 (0.155) |
| Number of previous meetings attended | -0.006* (0.001) | -0.007* (0.001) | -0.006* (0.001) | -0.006* (0.001) |
| Age | 0.001 (0.001) | 0.001 (0.001) | 0.001 (0.001) | 0.001 (0.001) |
| Cumulative publications | -0.000 (0.000) | -0.000+ (0.000) | -0.000+ (0.000) | -0.000+ (0.000) |
| Cumulative trials led | -0.002 (0.003) | 0.001 (0.003) | 0.002 (0.003) | 0.002 (0.003) |
| Ever received NIH grant | -0.015 (0.016) | -0.005 (0.016) | -0.003 (0.016) | -0.003 (0.016) |
| MD | 0.065+ (0.028) | 0.080* (0.027) | 0.086* (0.027) | 0.086* (0.027) |
| PhD | 0.023 (0.022) | 0.040 (0.022) | 0.036 (0.022) | 0.036 (0.022) |
| Female | -0.010 (0.017) | -0.003 (0.017) | -0.003 (0.017) | -0.003 (0.017) |
| Patient representative | -0.021 (0.129) | -0.037 (0.128) | -0.036 (0.128) | -0.036 (0.128) |
| Standing member | -0.020 (0.015) | -0.021 (0.015) | -0.024 (0.015) | -0.024 (0.015) |
| Intercept | 0.524* (0.052) | 0.077 (0.074) | 0.075 (0.074) | 0.076 (0.075) |
| Year fixed effects | No | Yes | Yes | Yes |
| Committee fixed effects | No | Yes | Yes | Yes |
| N | 4448 | 4448 | 4448 | 4448 |
| R^2 | 0.0102 | 0.0691 | 0.0679 | 0.0680 |
| Adj. R^2 | 0.0078 | 0.0629 | 0.0618 | 0.0614 |

is smaller. In particular, the broad measures of financial ties used in previous specifications don't vary within an advisor. Therefore, we include ties to the sponsor and the sponsor's competitors within the same drug class, as derived from publication disclosures. These do vary within an advisor and across meetings. Results are presented in Table ???. The measures of fit are much improved as a result of advisor fixed effects, although other variables remain statistically insignificant. However, the signs of the coefficients on ties to the sponsor and to competitors are consistent with advisors voting in their financial interest.

Table 11: Regression results with advisor fixed effects

| | No controls | With controls |
|---|-------------|---------------|
| | b/se | b/se |
| Advisor received financial support from sponsor within 5 years | 0.106 | 0.122 |
| | (0.153) | (0.155) |
| Advisor received financial support from competitor within 5 years | -0.063 | -0.079 |
| | (0.146) | (0.148) |
| Number of previous meetings attended | | 0.004 |
| | | (0.004) |
| Cumulative publications | | -0.001 |
| | | (0.001) |
| Standing member | | -0.009 |
| | | (0.025) |
| Intercept | 0.365* | 0.381* |
| | (0.081) | (0.085) |
| Year fixed effects | Yes | Yes |
| Committee fixed effects | Yes | Yes |
| N | 5504 | 5504 |
| R^2 | 0.2527 | 0.2529 |
| Adj. R^2 | 0.1306 | 0.1302 |

Finally, in Table ??, we consider differences across categories of voting questions, without advisor fixed effects but controlling for observable characteristics. Again, we find very little that is statistically significant.

Table 12: Regression results by question category

| | Safety | Efficacy | Risk-benefit |
|--|--------------------|--------------------|--------------------|
| | b/se | b/se | b/se |
| Advisor has any observable financial tie | 0.043 (0.041) | 0.063+ (0.031) | 0.043 (0.025) |
| Number of previous meetings attended | -0.011* (0.004) | -0.008* (0.003) | -0.006* (0.002) |
| Age | -0.000 (0.002) | -0.002 (0.001) | 0.003+ (0.001) |
| Cumulative publications | -0.000 (0.000) | -0.000 (0.000) | -0.000 (0.000) |
| Cumulative trials led | -0.006 (0.010) | -0.000 (0.007) | 0.001 (0.004) |
| Ever received NIH grant | -0.045 (0.042) | -0.059 (0.032) | 0.018 (0.025) |
| MD | 0.200* (0.069) | 0.114+ (0.053) | 0.003 (0.041) |
| PhD | 0.098 (0.056) | 0.078 (0.042) | -0.022 (0.033) |
| Female | -0.054 (0.045) | 0.044 (0.033) | -0.016 (0.026) |
| Patient representative | -0.245 (0.207) | -0.084 (0.211) | 0.262 (0.272) |
| Standing member | -0.015 (0.039) | 0.020 (0.029) | 0.016 (0.023) |
| Intercept | -0.016 (0.208) | 0.441* (0.133) | 0.041 (0.113) |
| Year fixed effects | Yes | Yes | Yes |
| Committee fixed effects | Yes | Yes | Yes |
| N | 676 | 1084 | 1810 |
| R^2 | 0.1186 | 0.1585 | 0.1461 |
| Adj. R^2 | 0.0832 | 0.1370 | 0.1322 |

8 Conclusion

Using reduced-form methods, we find little association between financial ties and the tendency to vote in favor of a drug. In some sense, this is not particularly surprising: even with some financial tie to the industry, an advisor is unlikely to benefit directly from the outcome of a particular vote. In addition, the increased scrutiny of conflicts-of-interest following the Vioxx scandal and others may have induced different voting behavior, or different types of advisors. These specifications include no controls for drug characteristics, which (in an ideal world) should be the most important factors in voting.

It is important to bear in mind that these specifications tell us nothing about whether a vote is “correct.” In order to infer anything about an advisor’s ability to assess a drug candidate’s quality accurately, we need to estimate a structural model derived from the assumptions described in section ??.