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Experts and Financial Ties: Evidence from FDA Advisory Committees (Preliminary and Incomplete)*

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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

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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 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. Lurie et al. (2006) 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 (Walker (2014), Campbell et al. (2007), Zinner et al. (2009))).

We improve on earlier papers by including more information on both drug application and advisor characteristics. We develop a novel measure of financial ties using information disclosed in scientific publications authored by advisors. Consistent with prior work, we find that observable advisor characteristics explain very little of the variation in voting in a simple logit specification for votes. However, this approach assumes that votes across advisors are independent given drug and advisor characteristics, which amounts to ruling out unobserved quality. Since advisory committees exist in large part because quality is difficult to observe, this assumption is likely to be problematic.

We therefore use a structural model that imposes two key assumptions. First, signals of drug quality are positively correlated across advisors. Second, advisors are more likely to vote in favor of a good drug than a bad drug. These assumptions allow us to account for unobserved quality and to separately identify expert bias and ability. We can then 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.

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 (Gillis and Schwartz (2015)). In recent years, there has been increased pressure for academic economists to disclose their COI (Chan (2010)). 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]

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 3410[2] 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

[1] SEC Factsheet.
[2] http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM048297.pdf.

> 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." (US Food & Drug Administration (2008))

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

Lurie et al. (2006) 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%.

Lurie et al. (2006) 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, Ackerley et al. (2009) extended the original sample used by Lurie et al. (2006) 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), Ackerley et al. (2009) concluded that members tended to vote against their interests. A more recent analysis by Golec et al. (2013) 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. Li and Suen (2004) 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. Dewatripont and Tirole (1999) and Gromb and Martimort (2007) 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. Li and Madarász (2008) 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. Bourjade and Jullien (2011) 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.

Camara and Dupuis (2014) 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, Cohen et al. (2012) 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.

Li (2012) 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 Iaryczower and Shum (2012). As in our setting, there is no objective measure of the "correct" decision. Iaryczower and Shum (2012) 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. The payoffs are summarized in the following table:

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

Intuitively, if $\forall i, \pi_{it} = 1/2$, the model is one of pure common values. If $\pi_{it} \approx 0$ or 1, the expert is "biased." This bias, or disutility from voting against science, can reflect advisor i's inherent preference for Type I or Type II error. However, another component of this disutility can be financial ties to the sponsor of drug t, or to a competitor, or to the industry more generally. In our empirical analysis, we allow π to depend on all of these factors in a flexible way.

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:

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

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

$$\frac{\Pr(E \mid \omega_t = 1)}{\Pr(E \mid \omega_t = 0)} \geq \frac{\pi_{it}}{(1 - \pi_i)} \frac{1 - \rho_t}{\rho_t}$$

The approval threshold increases with the aversion of the expert for Type I error (approving a drug that does not meet the standard) relative to Type II error (rejecting a drug that meets the standards). The threshold can also vary with the expert's financial ties with the sponsor of the drug, a competing drug, or with other firms in the industry.

Above, we normalized the payoff to voting "with" science to 0. We could instead allow an advisor to receive some utility from voting in favor of a sponsor to which he has financial ties, regardless of the true state of science. In this case, his payoff from $v_{it} = 1$ includes an extra term S when $\omega_t = 0$ and when $\omega_t = 1$. Similarly, the advisor could receive extra utility C from voting against a drug when he has a tie to a competitor. The threshold voting conditions will be different, but the estimation approach we describe below will be the same.

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 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

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

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

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

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 ($\rho \approx 1/2$), and precise private information (θ large), 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. We allow for financial ties to affect θ as well as π, for two reasons. First, the industry may seek the most qualified researchers with whom to work, so that financial ties are correlated with quality

through selection. Second, working on industry-sponsored projects or trials may improve a researcher's ability to interpret information.

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 $\mathbf{Z}_i$. Characteristics specific to a drug-expert pair it, such as a financial tie to the sponsor or a competitor of i, are in $\mathbf{W}_{it}$.

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 export 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. $\gamma_{i,1} \geq \gamma_{i,0}$.

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

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

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:

$$\hat{\theta}_{it} = \Phi^{-1}(1 - \hat{\gamma}_{i,t,0}) - \Phi^{-1}(1 - \hat{\gamma}_{i,t,1}) \tag{5.1}$$

$$\hat{s}_{it} = \frac{\Phi^{-1}(1 - \hat{\gamma}_{i,t,0})}{\Phi^{-1}(1 - \hat{\gamma}_{i,t,0}) + \Phi^{-1}(\hat{\gamma}_{i,t,1})} \tag{5.2}$$

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

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

As discussed above, financial ties are part of $\mathbf{W}_{it}$ and therefore enter into our estimates of both θ and π. To determine the importance of financial ties as well as other characteristics, we estimate $\hat{\pi}_{it}$ and $\hat{\theta}_{it}$ as functions of $\mathbf{X}_t$, $\mathbf{Z}_i$ and $\mathbf{W}_{it}$. In our counterfactual simulations, we can evaluate how changes in industry ties would affect the bias of experts as well as their quality.

We tested the model using simulated datasets, and verified that our procedure yields reasonably precise, unbiased estimates of the "first-stage" conditional probabilities. We are currently experimenting with direct estimation of the structural parameters (without the intermediate step of estimating conditional voting probabilities) and with alternative estimation algorithms, in particular the EM algorithm.

6 Data

6.1 Advisory Committee meetings and voting outcomes

We obtained the data used in the Lurie et al. (2006) and Ackerley et al. (2009) papers from the Eastern Research Group, which conducted a study of voting and conflicts of interest for the FDA in 2009.[3] This dataset spans 2002-early 2008, and has information on which members attended each meeting; how each member voted; and which members received a COI waiver.

[3]We thank Nyssa Ackerley for sharing this data.

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 2. 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 1, 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 2).

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. 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

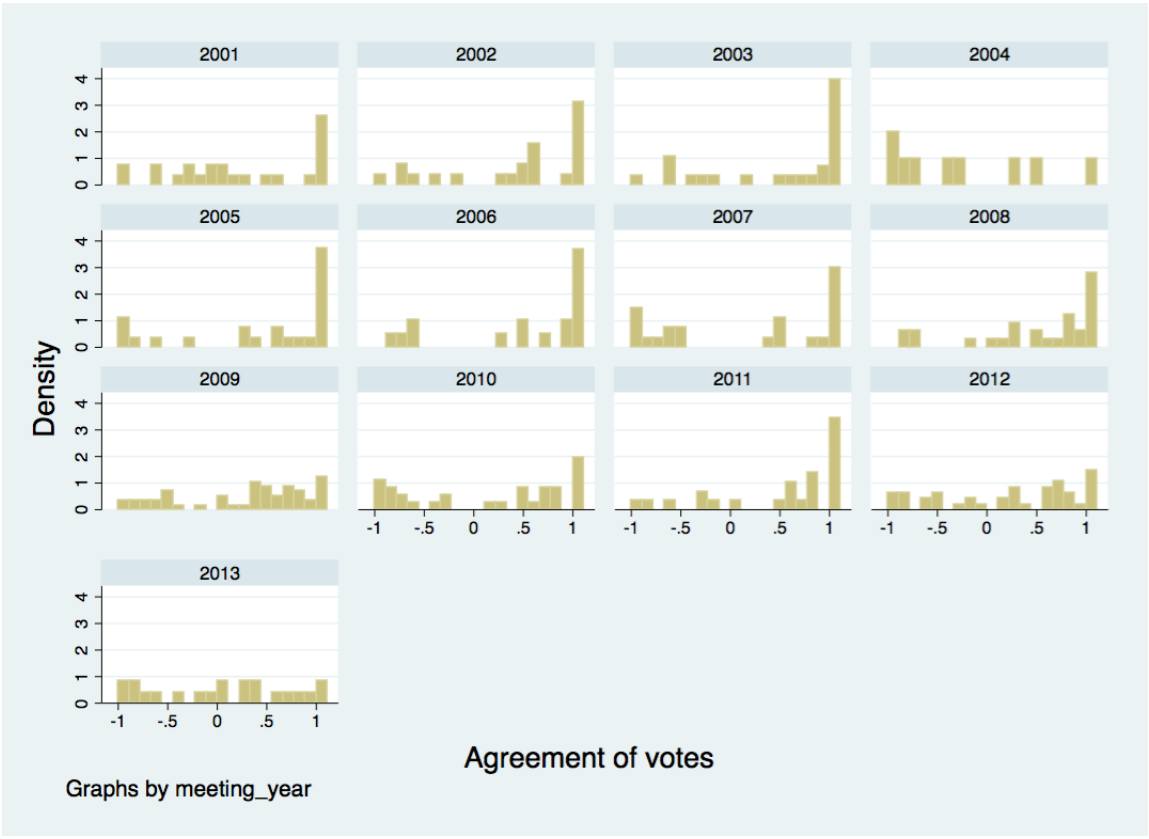

Figure 1: Votes by FDA ACs, 2001-2013

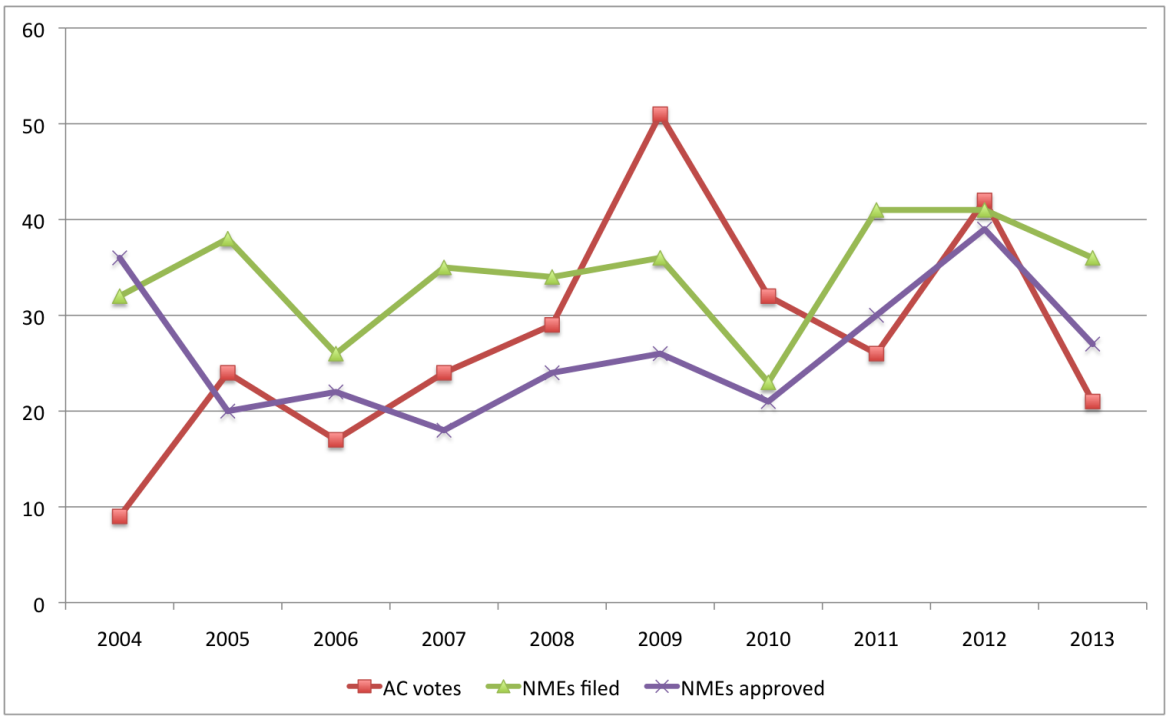

Figure 2: NME applications, approvals, and use of ACs

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 market[4] 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 Drug characteristics

Drugs reviewed by advisory committees vary in important ways. They treat different conditions, some affecting large numbers and others targeting orphan diseases. They also vary in novelty. New mechanisms of action, or the first drug developed in a therapeutic class, may arrive with more uncertainty or more diffuse priors. To capture this, we include several characteristics at the drug level. Orphan drug status indicates that the patient population is small but lacks existing treatments. We define "important" as a drug classified by the FDA for one of three regulatory patheways: priority review, accelerated approval, or breakthrough therapy. "Novel" is a drug with a new mechanism of action or the first in its therapeutic class.

6.6 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

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

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 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 (Ross et al. (2008)), 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.

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

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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 two additional sources. The first is Propublica's "Dollars for Docs" data, which includes payments voluntarily disclosed by pharmaceutical firms or revealed during litigation starting in 2009. In more recent years, we exploit 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.

6.7 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 3, 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 4). 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.

Descriptive statistics for the set of 1208 advisors participating in CDER committees 2008-2013 are presented in Table 1. 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 2. On average, these advisors have authored 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 5 and 6.

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 3, we present indicators of financial ties to

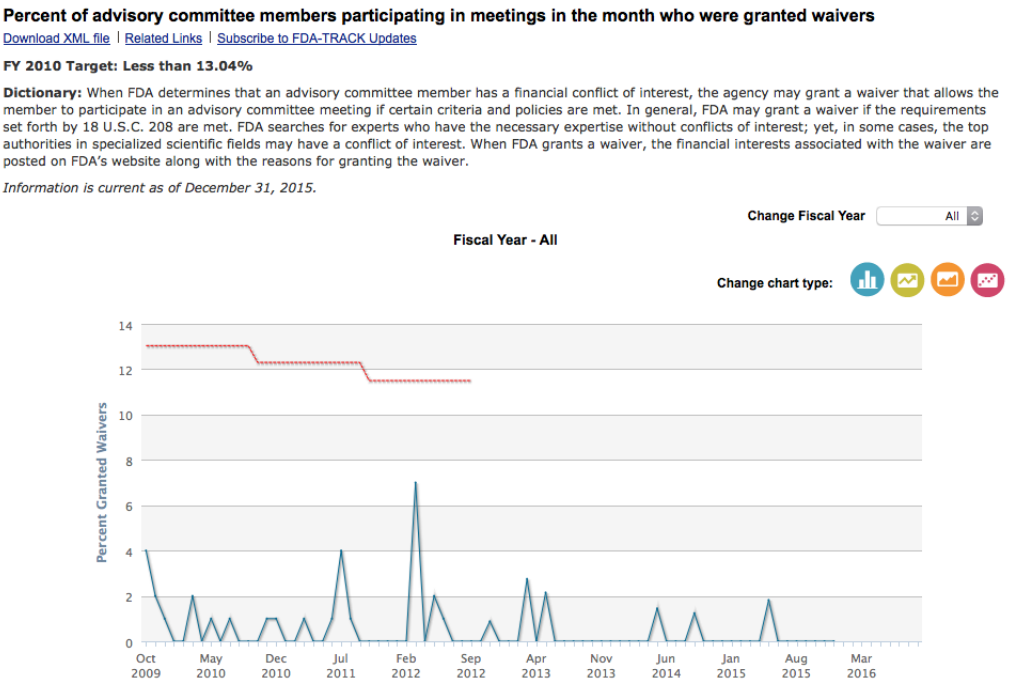

Figure 3: Conflict of interest waivers issued by the FDA.
Source: http://www.accessdata.fda.gov

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 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 4. 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 5 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:

Table 1: Advisor demographics

Variable	Mean	Std. Dev.	Min.	Max.	N
Has academic affiliation	0.64	0.48	0	1	983
MD	0.75	0.43	0	1	1090
PhD	0.23	0.42	0	1	1090
PharmD	0.04	0.19	0	1	1090
MPH	0.07	0.26	0	1	1090
Female	0.33	0.47	0	1	1090
Age	54.2	9.72	26	87	854

Table 2: Advisor research output

Variable	Mean	Std. Dev.	Min.	Max.	N
Total publications (as of 2014)	62.43	73.19	0	566	1090
Percentage of papers as last author	0.13	0.13	0	1	1090
Percentage of papers as first_author	0.2	0.19	0	1	1090
Ever received NIH grant	0.55	0.5	0	1	1090
Number of clinical trials	1.48	3.18	0	32	1090

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	1090
Number of industry-sponsored clinical trials	0.3	0.92	0	14	1090
Ever received a waiver for COI	0.17	0.38	0	1	1090
Advisor ever reported financial support from industry in publication	0.14	0.35	0	1	676
Number of firms advisor reported financial support from in publications	0.34	1.6	0	23	1090

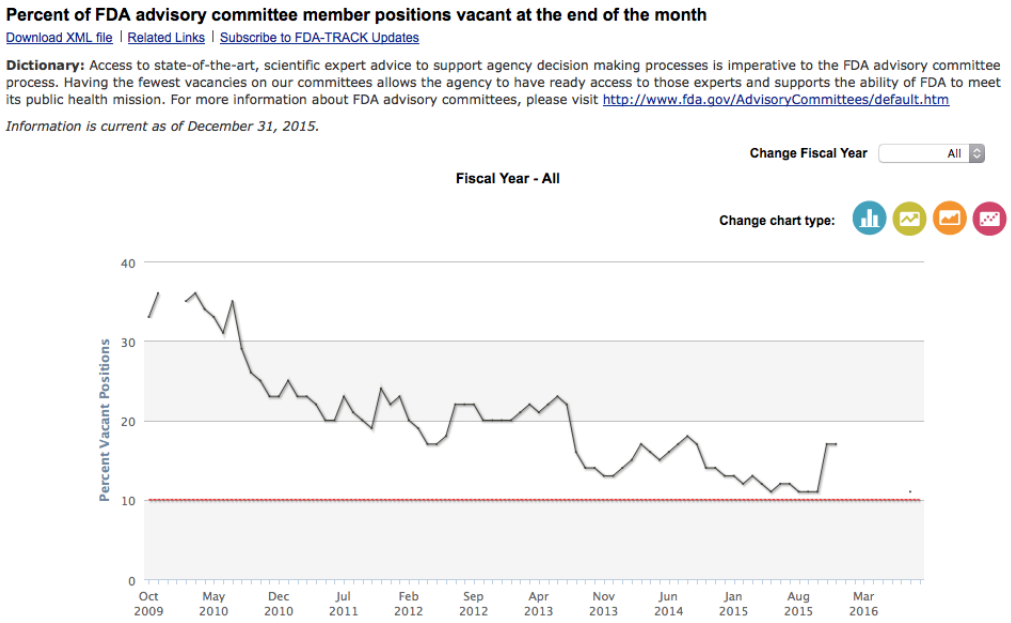

Figure 4: Committee vacancies.
Source: http://www.accessdata.fda.gov

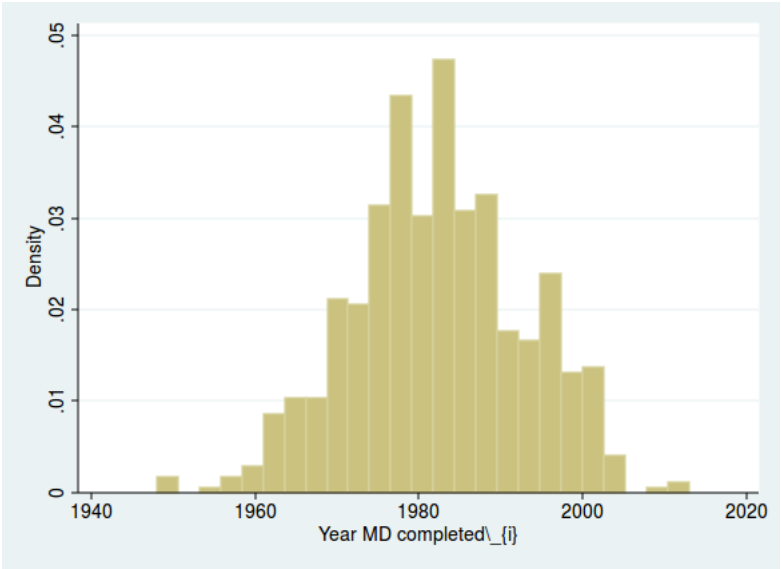

Figure 5: Distribution of MD completion year

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

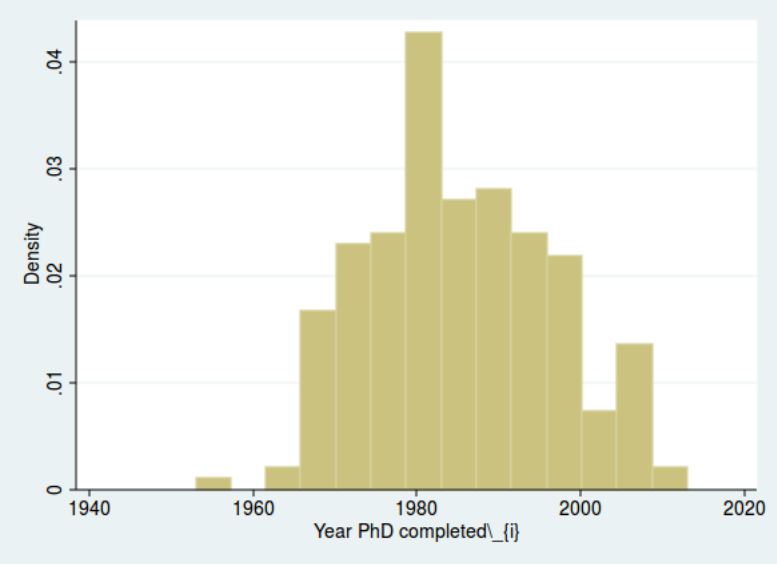

Figure 6: Distribution of PhD completion year

also higher.

The distribution of voting questions and their outcomes is provided in Table 6, and table 7 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 4: Summary statistics for CDER meetings, 2008-2013

Variable	Mean	Std. Dev.	Min.	Max.	N
Number of committee members present	15.43	4.71	4	35	217
Number of standing members present	7.5	2.78	2	15	217
Number of temporary members present	7.92	4.39	0	25	217
Number of members with MD	11.19	4.22	0	26	217
Number of members with PhD	4.45	2.57	0	15	217
Number of members with observable tie to industry	10.57	5.41	0	35	217
Orphan drug	0.31	0.46	0	1	164
Important drug	0.38	0.49	0	1	217
Novel drug	0.32	0.47	0	1	164

Table 5: Comparison of advisors with and without financial ties

	No Tie	Any Tie	Difference
Number of previous meetings attended	6.11	8.03	-1.92***
Years since completing MD or PhD	26.20	27.87	-1.67***
Number of years serving as expert	2.46	3.61	-1.15***
Cumulative publications	25.87	41.34	-15.47***
Ever received NIH grant	0.45	0.66	-0.21***
Average status in publications	0.26	0.30	-0.04***
Number of clinical trials	0.64	2.08	-1.44***
Number of board certifications	0.41	0.70	-0.29***
Number of advanced degrees	1.09	1.22	-0.13***

Table 6: Summary statistics for CDER votes, 2008-2013

	Outcome for drug			
Category	For	Against	Tie	Total
Safety	56	25	4	85
Efficacy	86	32	4	122
Safety+efficacy or risk/benefit	59	30	1	90
Approval	75	35	0	110
Withdrawal	1	3	0	4
Restriction	5	2	0	7
Relabeling	3	7	0	10
OTC switch	1	0	0	1
Other	36	56	2	94
Total	322	190	11	523

Table 7: Summary statistics at meeting-advisor level

Variable	Mean	Std. Dev.	Min.	Max.	N
Cumulative industry trials led	0.23	0.73	0	14	8036
Any payment disclosed in 2013	0.25	0.43	0	1	8036
Ever received a waiver for COI	0.19	0.39	0	1	8036
Advisor ever reported financial support from industry in publication	0.18	0.38	0	1	5718
Number of firms advisor reported financial support from in publications	0.49	1.79	0	23	8036
Number of previous meetings attended	7.32	9.15	1	80	8036
Years since completing MD or PhD	27.34	10.36	-5	62	6233
Number of years serving as expert	3.19	3.23	0	12.78	8036
Cumulative publications	35.63	44.11	0	443	8036
Ever received NIH grant	0.58	0.49	0	1	8036
Average status in publications	0.29	0.13	0	1	8036
Number of clinical trials	1.55	3.13	0	29	8036
Number of board certifications	0.59	0.75	0	5	8036
Number of advanced degrees	1.17	0.57	0	3	7698

7 Reduced-form results

Preliminary reduced-form results are 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 the only explanatory variable is a measure of financial ties. Table 8 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 8: Regression results, simplest specification

	Model 1	Model 2	Model 3	Model 4
	b/se	b/se	b/se	b/se
Financial tie	0.002			
	(0.011)			
Ever received a waiver for COI		−0.011		
		(0.014)		
Any payment disclosed in 2013			0.040∗	
			(0.013)	
Advisor ever reported financial support from industry in publication				−0.015
				(0.017)
N	8036	8036	8036	5718
R^2	0.0000	0.0001	0.0012	0.0001
Adj. R^2	−0.0001	−0.0000	0.0011	−0.0000

Table 9 includes observable advisor characteristics and drug characteristics in addition to measures of financial ties. The addition of these controls improves the fit of the regression, although most coefficients are only marginally statistically significant at best. 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). Patient representatives show less inclination to vote in favor of the industry. Voters appear to view novel drugs more positively than orphan drugs or important drugs. For the latter two categories, clinical trial information may be more limited.

Orphan drugs are tested using small samples, as there is only a small population of potential patients. Important drugs that have been fast-tracked also might arrive with preliminary data or results based on a short-term horizen.

Finally, in Table 10, we consider differences across categories of voting questions. Again, we find very little that is statistically significant, although the relationship with financial ties and pro-industry voting is weaker for votes on safety versus efficacy or risk/benefit questions.

Table 9: Regression results with advisor characteristics

	Model 1	Model 2	Model 3	Model 4
	b/se	b/se	b/se	b/se
Financial tie	0.025	0.032+		
	(0.015)	(0.015)		
Any tie (publication)				0.026
				(0.027)
Any sponsor tie			0.039	0.180
			(0.026)	(0.163)
Any competitor tie				−0.155
				(0.163)
Number of previous meetings attended	−0.004∗	−0.003∗	−0.003∗	−0.004∗
	(0.001)	(0.001)	(0.001)	(0.001)
Age	0.001+	0.002+	0.002+	0.002
	(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	−0.000	0.001	0.002	−0.000
	(0.003)	(0.003)	(0.003)	(0.003)
Ever received NIH grant	−0.005	−0.003	−0.002	−0.001
	(0.015)	(0.015)	(0.015)	(0.018)
MD	0.006	0.032	0.036	0.080∗
	(0.024)	(0.024)	(0.024)	(0.028)
PhD	−0.023	−0.001	−0.002	0.040
	(0.019)	(0.019)	(0.019)	(0.023)
Female	−0.014	−0.006	−0.005	−0.006
	(0.015)	(0.015)	(0.015)	(0.018)
Patient representative	−0.101∗	−0.078+	−0.078+	−0.062
	(0.039)	(0.039)	(0.039)	(0.043)
Standing member	0.009	0.001	−0.001	−0.030
	(0.014)	(0.014)	(0.014)	(0.016)
Orphan drug	−0.042+	−0.020	−0.017	−0.038
	(0.017)	(0.018)	(0.018)	(0.022)
Important drug	0.013	−0.047∗	−0.049∗	−0.050+
	(0.014)	(0.016)	(0.016)	(0.019)
Novel drug	0.077∗	0.066∗	0.067∗	0.058∗
	(0.014)	(0.016)	(0.016)	(0.019)
Intercept	0.533∗	0.156+	0.161∗	0.062
	(0.048)	(0.062)	(0.062)	(0.076)
Year fixed effects	No	Yes	Yes	Yes
Committee fixed effects	No	Yes	Yes	Yes
N	5606	5606	5606	4076
R^2	0.0171	0.0573	0.0569	0.0725
Adj. R^2	0.0146	0.0517	0.0513	0.0647

Table 10: Regression results by question category

	Safety	Efficacy	Risk-benefit
	b/se	b/se	b/se
Financial tie	0.026	0.050	0.051+
	(0.036)	(0.028)	(0.022)
Number of previous meetings attended	−0.007∗	−0.005∗	−0.003∗
	(0.002)	(0.001)	(0.001)
Age	0.002	−0.001	0.003∗
	(0.002)	(0.001)	(0.001)
Cumulative publications	−0.000	−0.001	−0.000
	(0.000)	(0.000)	(0.000)
Cumulative trials led	−0.001	−0.001	0.002
	(0.008)	(0.006)	(0.004)
Ever received NIH grant	−0.018	−0.029	0.018
	(0.035)	(0.029)	(0.023)
MD	0.100	0.069	−0.013
	(0.056)	(0.045)	(0.037)
PhD	0.034	0.026	−0.041
	(0.045)	(0.036)	(0.030)
Female	−0.044	0.024	−0.022
	(0.036)	(0.029)	(0.023)
Patient representative	0.047	−0.069	−0.127
	(0.101)	(0.072)	(0.065)
Standing member	−0.020	0.040	0.023
	(0.032)	(0.026)	(0.021)
Orphan drug	−0.225∗	0.094+	0.026
	(0.052)	(0.038)	(0.029)
Important drug	0.015	−0.143∗	−0.088∗
	(0.051)	(0.036)	(0.027)
Novel drug	0.005	0.084+	0.096∗
	(0.045)	(0.033)	(0.024)
Intercept	−0.029	0.352∗	0.189+
	(0.160)	(0.118)	(0.093)
Year fixed effects	Yes	Yes	Yes
Committee fixed effects	Yes	Yes	Yes
N	957	1350	2139
R^2	0.1325	0.1383	0.1460
Adj. R^2	0.1044	0.1188	0.1330

8 Structural results

Below we present some very preliminary results from estimating the structural model. The specification used is parsimonious, and does not include committee or year fixed-effects. Standard errors will be bootstrapped and included in the next draft. We tried 10 different starting values for the reduced-form parameters in case the minimization routine gets stuck at local minima, and we use both the Nelder-Mead and quasi-Newton search algorithms to verify robustness.

We begin with a description of the first-stage results for ρ (the prior for the drug being good) and the conditional choice probabilities γ. Table 11 contains the coefficients for meeting characteristics that affect the prior. We include whether a vote concerned safety, efficacy, or approval (the omitted category includes everything else, such as relabeling). The results suggest that the priors for these three critical questions are lower than for arguably less important issues. Larger committees are associated with a slightly higher prior.

Table 12 contains the coefficients for determinants of γ_0, the probability that an advisor votes for a "bad" drug, and γ_1, the probability of voting for a "good" drug. The difference between these two identifies an expert's quality (see 5.1): intuitively, a small difference means that an advisor is equally likely to vote in favor of a drug, whether it is good or bad. We focus on advisor characteristics. Medical doctors and PhDs are less likely to vote for a bad drug and more likely to vote for a good one, suggesting that they are capable of understanding and interpreting the scientific evidence rather well. We see a similar pattern for experience running clinical trials. In contrast, patient representatives, whose background is generally less scientific, appear somewhat less likely to vote in favor of a good drug. Members with financial ties are more likely to vote in favor of both types of drugs. However, they are more favorable towards good ones.

Finally, we take our estimates of advisor bias π and quality θ and regress them on advisor and meeting characteristics. Table 13 presents the results for bias, with the lower and upper bounds of the 95% confidence interval for each coefficient. Recall that $-\pi$ is the disutility an advisor realizes from voting for a bad drug, while $-(1-\pi)$ is the disutility from voting against a good drug. Positive coefficients on the variables below imply greater disutility from voting for a bad drug and smaller disutility from voting against a good one; overall, a positive coefficient pushes an advisor away from voting in favor of a drug. The results suggest that PhDs and patient representatives are generally more skeptical, i.e. less likely to vote in favor, relative to MDs and others. Standing committee members, and those with more experience in committee

	ρ
Intercept	-0.1026
Safety	-0.6243
Efficacy	-0.5122
Approval	-0.3322
Committee size	0.0653

Table 11: Determinants of ρ

	γ_0	γ_1
Intercept	-2.4894	1.4606
Safety	1.2167	-0.3348
Efficacy	0.7864	-0.0510
Approval	0.2617	0.1565
Committee size	0.0774	-0.0206
MD	-0.1936	0.4345
PhD	-0.3830	0.2703
Patient rep	-0.0793	-0.3659
Financial tie	0.2119	0.2803
Standing member	-0.1086	-0.1804
Experience (meetings)	-0.0516	-0.0347
Trials	-0.0523	0.0617
Publications	-0.0007	-0.0022

Table 12: Determinants of γs

meetings, are also less favorable. The coefficient on financial ties is negative, which implies that advisors with such ties have a smaller disutility from voting for a bad drug and a larger aversion to voting against a good one.

Finally, we come to the determinants of advisor quality, or ability to interpret the scientific evidence. Large θs mean that an advisor has relatively informative signals, or small σs, of a drug's true quality. Table 14 contains the coefficients on meeting and advisor characteristics for a linear regression of $\hat{\theta}_{ij}$. Positive coefficients are associated with higher quality. Advisors with MDs and/or PhDs have more informative signals, which is reassuring. Patient representatives, often lacking in scientific training, receive noisier signals. Experience with committee meetings and clinical trials is also associated with higher quality, although status as a standing committee member and publications are not. The coefficient on financial ties is positive. This is consistent with the idea that the industry selects high quality researchers to fund, or with an alternative interpretation that experience with the industry improves an advisor's ability to interpret information.

To be estimated: models that allow for direct financial ties to the sponsor and competitors of the sponsor; committee fixed effects; additional information on drug quality, such as the number or size of clinical trials, first in class, etc.

	Coef.	LB	UB
Intercept	0.4070	0.4011	0.4130
Safety	-1.1979	-1.2022	-1.1936
Efficacy	-0.9877	-0.9916	-0.9837
Approval	-0.5971	-0.6009	-0.5934
Committee size	0.0292	0.0289	0.0294
MD	-0.0986	-0.1020	-0.0953
PhD	0.0930	0.0899	0.0961
Patient rep	0.1492	0.1404	0.1580
Financial tie	-0.2816	-0.2843	-0.2789
Standing member	0.1653	0.1628	0.1677
Experience (meetings)	0.0497	0.0494	0.0500
Trials	-0.0018	-0.0024	-0.0013
Publications	0.0016	0.0016	0.0017

Table 13: Determinants of π

	Coef.	LB	UB
Intercept	2.3588	2.3571	2.3605
Safety	-0.6921	-0.6934	-0.6909
Efficacy	-0.3703	-0.3714	-0.3692
Approval	-0.0333	-0.0343	-0.0324
Committee size	-0.0441	-0.0442	-0.0441
MD	0.3113	0.3103	0.3123
PhD	0.3047	0.3038	0.3056
Patient rep	-0.1701	-0.1726	-0.1677
Financial tie	0.0536	0.0528	0.0544
Standing member	-0.0431	-0.0438	-0.0424
Experience (meetings)	0.0031	0.0030	0.0031
Trials	0.0548	0.0546	0.0550
Publications	-0.0009	-0.0009	-0.0008

Table 14: Determinants of θ

9 Counterfactuals

Work in progress....

We will simulate the effects of removing experts with financial ties, which changes both bias and quality.

10 Conclusion

Using reduced-form methods, we find a small positive association between financial ties and the tendency to vote in favor of a drug. In some sense, the size of the relationship 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. Our data includes much more information about both the advisors and the drugs considered by each committee than previous work on this topic. In particular, we show that financial ties are also correlated with observable measures of advisor quality.

Our structural results suggest that there is indeed a trade-off associated with financial ties. Advisors with ties are more likely to vote in favor of industry interests, but they also have somewhat higher estimated ability. Counterfactual simulations suggest that....

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