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Tripartite Conflicts of Interest and High Stakes Patent Extensions in the DSM-5

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Abstract

Background: The revision process for and recent publication of the *DSM-5* initiated debates about the widening of diagnostic boundaries. The pharmaceutical industry had a major financial stake in the outcome of these debates. This study examines the three-part relationship among *DSM* panel members, PIs of clinical trials for new *DSM-5* diagnoses, and drug companies.

Methods: Financial conflicts of interest (FCOI) of *DSM* panel members responsible for some new diagnoses in the *DSM-5* and PIs of clinical trials for related drug treatments were identified. Trials were found by searching ClinicalTrials.gov. Patent and revenue information about these drugs was found using the FDA Orange Book and manufacturer Annual Reports.

Results: Thirteen trials met inclusion criteria (testing drugs for some new *DSM* disorders). Sixty-one percent of the *DSM* Task Force members and 27% of Work Group members reported FCOI to the trial drug manufacturers. In 5 of the 13 trials (38%), PIs reported ties other than research funding to the drug manufacturer. In three of the trials (23%), a PI had financial ties to the drug manufacturer and was also a *DSM* panel member who had decision making authority over the revision process.

Conclusions: These findings suggest that increased transparency (e.g., registration on ClinicalTrials.gov) and mandatory disclosure policies (e.g., APA's disclosure policy for *DSM-5* panel members) alone may not be robust enough strategies to prevent the appearance of bias in both the *DSM* revision process as well as clinical decisions about appropriate interventions for *DSM* disorders.

Previous research documented the financial ties between the panel members for the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)* and the drug companies that manufacture the medications used to treat the disorders identified in this manual [1]. To its credit, the American Psychiatric Association (APA) instituted a conflict of interest policy requiring all panel members on the *DSM-5* to file financial disclosure statements. This policy resulted in some changes in work group composition; compared to *DSM-IV* some *DSM-5* work groups had fewer individuals with industry ties. Elsewhere we reported [2] that this new APA requirement rendered the *DSM's* disclosure policy more congruent with most leading medical journals and federal policies on financial conflicts of interest (FCOI). *DSM* panel members were required to list any FCOI for three years prior to their appointment on the *DSM*, and they could not accept more than USD 10,000 from industry (e.g., for consultancies) per year or hold more than USD 50,000 in stock in a pharmaceutical company during their tenure on the *DSM* [2].

Although APA's increased transparency was an important step forward in restoring public trust, the revision process for (and recent publication of) the *DSM-5* ignited debates about the taxonomy of mental illness and the widening of diagnostic boundaries. The fact that the pharmaceutical industry had a major financial stake in the outcome of these debates raised additional concerns. Thus, the issue of trustworthiness in the revision process is a critical one. In 2010, the APA issued an official policy document, approved by the Board of Trustees, in which the APA leadership stated that:

We affirm our support of the Institute of Medicine report [*Conflict of Interest in Medical Research, Education, and Practice*]. Members involved in clinical practice, education, research, and administration must be diligent and aware in identifying, minimizing, and

appropriately managing secondary (personal) interests (financial, contractual, career-centered) that may inhibit, distract, or unduly influence their judgment or behavior in a manner that detracts from or subordinates the primary interest of patients and may be perceived by some as undermining public trust. [3]

Indeed, the perception of trustworthiness in relation to FCOI is critical in the medical field especially in terms of maintaining confidence in professional judgment. Harvard philosopher Dennis Thompson's work in this area has been highly influential (see e.g., the 1993 decision made by *NEJM* to develop an FCOI policy), and he emphasizes the fact that the conflict is not an indictment of wrongdoing but rather points to a generic risk: "The point is to minimize or eliminate circumstances that would cause reasonable persons to suspect that professional judgment has been improperly influenced, whether or not it has" [4]. Congruent with both the APA's and Thompson's concern that FCOI may undermine public trust, we investigated how FCOI function in these new diagnostic categories during this period of transparency.

The *DSM-5*, which was published in May 2013 [5], introduced new or revised diagnoses such as Binge Eating Disorder, Autism Spectrum Disorder, Disruptive Mood Dysregulation Disorder in children, Mild Neurocognitive Disorder, and Premenstrual Dysphoric Disorder. In addition to the newly included diagnoses, one of the most controversial revisions in the *DSM-5* is the elimination of the bereavement exclusion from the diagnostic criteria for a Major Depressive Episode. With this change, individuals who are actively grieving a loss may be diagnosed with Major Depressive Disorder (if they present with symptoms of depression two weeks after the loss). Some clinicians maintain that this change is a positive one in that now individuals who are actively grieving a loss may receive the diagnosis and treatment that they need. Others have

argued that people who are going through the normal process of grieving would now be diagnosed with depression.

Indeed, pharmaceutical companies were already operating clinical trials of drugs that could be used to treat new *DSM-5* disorders before the publication of the manual in May 2013. Certainly, these companies have a fiduciary responsibility to serve their shareholders' interests by working to increase their shareholder value. Although questions of potential bias may be raised with any treatment modality, if the heavy emphasis on the use of psychotropic medications to treat new *DSM-5* disorders is linked to the financial interests of APA panel members and researchers who test the safety and efficacy of drugs, then the objectivity of scientific findings will be questioned. The purpose behind federal and professional conflict of interest rules is to reduce the probability of bias entering into the decision-making process (see e.g., [6]).

In fact, concerns about preventing bias and producing high quality science led the Institute of Medicine (IOM) to recommend that only independent experts (i.e., individuals without commercial ties) be involved in clinical guideline decision-making [7]. Questions about the potential for bias when making judgments about the validity of new *DSM* disorders, and about what interventions should be developed to treat these conditions, are rendered even more salient when drugs being investigated as treatments for them are under patents that have expired or will soon expire. Without patent protection, companies lose considerable profit to generics, providing a strong incentive to find new indications that will effectively grant extended patent protection to a drug. In light of this incentive, it is critical that researchers charged with the responsibility of making decisions about psychiatric diagnosis and treatment do not have FCOIs that could increase the probability or appearance of bias in clinical decision-making. Over-

diagnosis in the mental health field can have significant adverse public health consequences because it leads to unnecessary drug treatment [8]. This is the first study that investigates FCOIs with ongoing clinical trials, showing the three-part relationship among *DSM* panel members, PIs of clinical trials for new *DSM-5* diagnoses, and drug companies.

Methods

We examined the FCOI of *DSM* panel members responsible for decisions about the inclusion of five new *DSM* disorders and one major revision (elimination of the bereavement exclusion for Major Depressive Disorder) and the pharmaceutical companies conducting clinical trials for drugs to treat these new disorders. We also examined the FCOI of PIs for the clinical trials of treatments for these newly included disorders, whereby FCOI is defined in this study as financial associations with the manufacturers of trial medications. Congruent with previous research [1,2,9-11], financial associations are defined in our study as consultancies, honoraria, speakers bureau membership, expert testimony, research funding, and stock holdings.

The disorders investigated were: Bereavement-Related Depression, Binge Eating Disorder, Disruptive Mood Dysregulation Disorder, Autism Spectrum Disorder, Mild Neurocognitive Disorder, and Premenstrual Dysphoric Disorder. These disorders were selected because of the questions raised regarding their validity [12-15], concerns that these diagnoses lack specificity and will result in unnecessary diagnostic inflation [16], and documented problems with reliability [14,17].

We searched ClinicalTrials.gov for the six disorders of interest. Because previous research has found that industry-affiliated clinical trials are more vulnerable to bias than government-funded ones [11], we excluded trials that were exclusively funded by one of the National Institutes of Health. It is possible that receiving NIH or NIMH funding also presents a

conflict of interest (financial and/or intellectual), although probably a much subtler one. There are ties between NIH funded investigators and grant reviewers and possibly *DSM* panel members. However, these ties are not the focus of our study. Industry sponsorship of the trials was identified by the sponsors and collaborators listed on the trial page. Manufacturers of the drugs and patent status information were identified using the U.S. Food and Drug Administration's (FDA) Orange Book (<http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm>).

There are two main groups who serve on the *DSM* and are charged with decision-making authority: Task Force members and Work Groups. Task Force members provide oversight for the entire manual, and members of a *DSM* Work Group are a team of individuals who review a specific diagnostic category (e.g., Eating Disorders). Following previous research, we use “panel members” to refer collectively to both Work Group and Task Force members included in the study. Posted disclosure statements from the *DSM-5* website for the included members of the *DSM* panel were reviewed to identify: 1) financial ties to pharmaceutical companies, and 2) any *DSM* panel member who was also a PI for one of the clinical trials. Members of the *DSM-5* Work Groups that were responsible for the five new disorders and one major revision included in the search (e.g., Eating Disorders Work Group for Binge Eating Disorder) were screened for FCOI using their posted disclosure statements on the *DSM-5* website (www.dsm5.org), accessed between March 15, 2013 and March 25, 2013. Because of their importance in clinical decision-making, all *DSM-5* Task Force members were also screened for FCOI. Task Force members, who include Work Group chairs, played a critical role in the revision process by shaping the panel through nomination of other Work Group members, contribution to the draft criteria, and review of the final revisions to the draft before its final approval.

Additionally, we conducted internet searches to determine if PIs of the clinical trials had financial associations to manufacturers of trial drugs. Internet searches were conducted for sources published three years prior to the start of the clinical trial, a time period congruent with published research on FCOIs and consistent with the APA's own FCOI policy. Searches included ProPublica, peer reviewed articles, conferences, participation in continuing medical education events (i.e., courses and/or seminars for health professionals), and self-reporting of any industry ties following interviews with the media. Internet searches were also conducted for speakers bureau participation of *DSM* panel members because speakers bureau membership was not an identified FCOI category in the *DSM-5* disclosures. Speakers bureau participation was included in our analysis only when there was unambiguous information.

Results

Thirteen clinical trials met inclusion criteria. These clinical trials were designed to investigate 10 patented drugs and one investigational new drug. Nine of these trials were testing "blockbuster" drugs with patents that had expired or would expire in the next two years. Table 1 provides a summary of trial drugs, their patent status, and their 2012 revenue (obtained from the drug manufacturers' 2012 annual reports). The trial drug manufacturer was one of the sponsors or collaborators for eight of the thirteen trials (62%).

Financial ties between *DSM* panels and drug manufacturers. Of the 55 Work Group members, 15 (27%) reported at least one FCOI to a trial drug manufacturer, while 19 of 31 (61%) of the Task Force members similarly reported at least one FCOI to a trial drug manufacturer.

In 3 of the 13 trials (23%), a *DSM* panel member reported speakers bureau participation (i.e., Company X sponsored a clinical trial for a new indication and a panel member responsible for decisions about inclusion of the new disorder served on the speakers bureau of Company X).

There were three instances in which *DSM* panel members were also PIs (i.e., an individual was both a *DSM* panel member responsible for making decisions about including a new disorder and a PI for a trial for a drug to treat the new disorder); each of these three panel members reported an FCOI to the trial drug manufacturer. (See Table 2 for a summary of *DSM* panel member FCOI data by trial.)

Financial ties between PIs of clinical trials and trial drug manufacturers. In five (38%) out of 13 trials, at least one of the trial PIs reported an FCOI other than research grant funding to the trial drug manufacturer (i.e., in addition to the pharmaceutical company sponsoring the trial, the PI reported an additional FCOI to the company).

Because some of these 13 clinical trials had more than one PI, and one individual was a PI on multiple trials, there were a total of 41 PIs. Twelve out of the 41 (29%) PIs reported research funding from the trial drug manufacturer and 8 (20%) had ties other than grant funding to the trial drug manufacturer, including three PIs that reported participating on the speakers bureau for the company. (See Table 3 for a summary of the PI FCOI data by trial.)

Discussion

In all but one trial, FCOIs were found between *DSM-5* panel members and the pharmaceutical companies that manufactured the drugs that were being tested for the new *DSM* disorders. The financial associations of panel members included research grants, consultation, honoraria, speakers bureau participation, and/or stock. Seven out of the 10 patented drugs included in the trials either are currently or have been blockbusters for their manufacturers. (A blockbuster drug

is defined as a drug that earns over USD 1 billion in revenue in one year; see e.g., [18]). Our data show that there are financial ties between some *DSM* panel members and pharmaceutical companies that have a vested interest in finding a new indication for their drugs. A new indication allows the drug manufacturer to obtain an additional three years of exclusivity for that drug. Pharmaceutical companies have used “exclusivity” as an informal mechanism to effectively extend patent protection for that time period [19]. However, it should be emphasized that trials examining off-label indications conducted after a patent has expired are not necessarily meant to obtain a secondary indication.

The fact that in 3 out of 13 (23%) of the trials the PIs were also *DSM* panel members raises questions about the potential of such multi-vested interests for implicit bias when making decisions about inclusion of new *DSM* disorders and their respective treatments. These questions are pressing in light of the fact that there are no biological markers for the majority of psychiatric disorders; the use of subjective discretion to widen diagnostic boundaries becomes more likely when there are no biological tests to ground clinical decision-making.

For example, Binge Eating Disorder may be diagnosed in individuals who do not have Anorexia or Bulimia Nervosa and who have the following three “symptoms” one time per week for 3 months: 1) eating more rapidly than normal, 2) eating until uncomfortably full, 3) and eating large amounts of food when not physically hungry [5]. Mild Neurocognitive Disorder may be diagnosed based on “concerns of the individual, a knowledgeable informant, or the clinician that there has been a modest decline in cognitive function.” These cognitive deficits “did not interfere with capacity for independence in everyday activities” and the decline may be based on a “clinical evaluation” (i.e., formal testing is suggested but not required for the diagnosis) [5]. Certainly some individuals consistently overeat and some individuals struggle with age-related

cognitive decline. However, both researchers and clinicians have expressed concerns about “diagnostic inflation” [16] when non-specific diagnoses such as Binge Eating Disorder and Mild Neurocognitive Disorder are identified as specific mental disorders. In fact, a former president of the APA writing about the revisions to *DSM-5* noted that:

The flexible boundaries of many psychiatric diagnostic categories, in the absence of definitive diagnostic tests, may encourage expansive definitions of affected populations and create opportunities for industry to promote treatments for people who would not previously been seen as having a disorder. [20]

Indeed, our study shows that increased transparency (e.g., registration on ClinicalTrials.gov) and mandatory disclosure policies (such as APA’s disclosure policy for *DSM-5* panel members) may not be robust enough to prevent the appearance, if not the reality, of bias in both the *DSM* revision process as well as clinical decisions about appropriate interventions for *DSM* disorders. In fact, a 2012 comparison between *DSM-IV* and *DSM-5* panel members showed that despite increased transparency, commercial ties remained strong. Although some work groups had decreased the number of individuals with industry ties, overall, 69% of the *DSM-5* task force members reported financial ties to industry, representing a 21% increase in the proportion of *DSM-IV* task force members with such ties. Also, three-fourths of the work groups continued to have a majority of members with ties to drug firms, and it is noteworthy that, as with the *DSM-IV*, the most conflicted panels are those for which pharmacological treatment is the first-line intervention [2].

In light of the decrease in government funding of clinical trials over the past two decades, it is not surprising that 29% of the PIs of trials in this study reported research funding from a trial drug manufacturer. However, 20% of all of the PIs in our sample had financial ties other

than research funding with the trial drug manufacturer, and three were on speakers bureaus for the manufacturers of the drugs they are investigating. Many policy makers, medical journal editors, and bioethicists have raised concerns that the line between marketing and research has become blurred [21,22] when researchers have ongoing, close, and lucrative ties with industry such as speakers bureau participation.

Our findings suggest that there may be a risk of industry influence on the *DSM* revision process. Additionally, our findings of FCOI of PIs running the clinical trials suggest that there also may be a risk of industry influence on the clinical decision-making process for identifying interventions to treat these new “disorders.” Of particular note is the fact that in three of the clinical trials, PIs reported that they participated on company speakers bureaus. Such participation may have a biasing effect. Transparency of FCOI and of clinical trial data are important first steps in strengthening public and professional trust in evidence-based medicine. However, the improvements facilitated by transparency are insufficient. Disclosure alone is not a satisfactory response to prevent bias in the revision process for psychiatric diagnostic guidelines or for maintaining integrity of psychotropic drug research.

The present study has several limitations. Our study did not include all of the revised or new *DSM-5* diagnoses and thus our findings for the six new or modified disorders should not be overgeneralized. The sample size is small and caution should be exercised when interpreting the data. Also, our metric for assessing independence in clinical decision-making (*DSM* panel members’ and PIs’ financial associations with industry) is an indirect measure and thus no conclusion can be drawn about actual bias in decision-making. Moreover, the complexity of the debate over FCOI and the potential for bias is compounded by the fact that trials that are commercially funded often report negative findings. For example, researchers found that half of

the studies on the efficacy of antidepressants failed to show an advantage over placebo (and over older tricyclic antidepressants) even though many of these were industry funded studies [23]. Despite these limitations, our examination of financial ties among *DSM* panel members, PIs of drug trials, and trial drug manufacturers suggest that the public, clinicians, and policy makers should be concerned about the way in which new diagnoses in the *DSM-5* may provide an opportunity for pharmaceutical companies to effectively extend their patents on blockbuster drugs. For example, Eli Lilly is listed on ClinicalTrials.gov as a collaborator for a clinical trial to test the efficacy of one of Lilly's antidepressants (Cymbalta) for "bereavement-related depression," and Eli Lilly is listed as a sponsor for a clinical trial testing Cymbalta for "Binge Eating Disorder." The patent for Cymbalta expires in December 2013. Five of the 12 members of the Mood Disorders Work Group and three of the 12 members of the Binge Eating Disorder Work Group have ties to Eli Lilly. If the FDA approves Cymbalta for these new indications, Lilly will benefit by obtaining another three years of market exclusivity for this drug. It has been one of Lilly's recent blockbuster drugs: In just the fourth quarter of 2012, Lilly reported revenue of \$1.42 billion from Cymbalta alone (24% of total revenue for that quarter) [24].

There are also three clinical trials for "Binge Eating Disorder," testing an antidepressant, a "mood stabilizer," and a psychostimulant as potential treatments for this new condition. (The three trial drugs, Cymbalta, Lamictal, and Nuvigil, made US\$5 billion, US\$937 million, and US\$347 million in revenue in 2012, respectively.) The FDA requires at least two trials to obtain authorization to market a drug for a new indication. Although more trials are needed before the FDA would grant authorization, it is important to note that the pharmaceutical companies that manufacture these three drugs would clearly benefit financially if they received such authorization.

A call for drug trials that are not sponsored by for-profit entities. Our FCOI findings show the tripartite inter-relationship among *DSM* panel members, PIs of clinical trials for new *DSM-5* diagnoses, and drug companies. These findings suggest that FCOI may function subtly, but powerfully, to shift the direction of the research, focusing on interventions that are the most commercially attractive but that do not necessarily represent the best science. Indeed, as was recently noted, when NIH decreased funding of clinical trials for new drugs, “turning new drug development over to industry, many clinically important clinical trials... were simply not done” [25; see also 26]. Hence, there must be systemic valuing and support of disinterested experts and their scientific contributions [27], and there is a clear need for drug trials that are not sponsored by and managed by industry. In our opinion, PIs should be prohibited from participating on a speakers bureau for a company whose drug they are testing. Speakers bureau participation is usually prohibited elsewhere (e.g., for faculty in medical schools), as it is widely recognized to constitute a significant FCOI [2]. Pharmaceutical companies refer to individuals who serve on speakers bureaus as “key opinion leaders” (KOLs) because they are seen as essential to the marketing of drugs.

Finally, as a policy objective, it is critical that the APA recognize that transparency alone is an insufficient response for mitigating implicit bias in diagnostic and treatment decision-making. Specifically, and in keeping with IOM's most recent standards, we recommend that *DSM* panel members be free of FCOI. In the future, *DSM* panel members should also be prohibited from serving as PIs of trials for any disorder being considered for inclusion in the *DSM*.

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Competing Interests

The authors have no competing interests to declare.

Abbreviations

FCOI = financial conflict of interest

Figure 1. Results from searching ClinicalTrials.gov.

Table 1. Summary of included trial drugs, patent expiration dates, and 2012 revenue.

| | Trial Indication | Trial Drug | Trial Sponsors and Collaborators | Trial Drug Company | Compound Patent Expiration Date | Global Revenue in 2012 (in millions) |
|----|---------------------------------|---------------------------------------|--|---------------------------|--|---|
| 1 | Bereavement-related depression | duloxetine hydrochloride (Cymbalta) | Eli Lilly | Eli Lilly | December, 2013 | \$4,990 |
| 2 | Complicated grief | citalopram hydrobromide (Celexa) | Jefferson Clinic, P.C. New York State Psychiatric Institute | Forest | Expired | Unavailable [†] |
| 3 | Binge Eating Disorder | armodafinil (Nuvigil) | National Institute of Mental Health Cephalon Lindner Center for HOPE University of Cincinnati | Cephalon | June, 2024 | \$347 |
| 4 | Binge Eating Disorder | duloxetine hydrochloride (Cymbalta) | Eli Lilly | Eli Lilly | December, 2013 | \$4,990 |
| 5 | Binge Eating Disorder | lamotrigine (Lamictal) | University of Cincinnati GlaxoSmithKline | Glaxo-SmithKline | Expired | \$937 |
| 6 | Binge Eating Disorder | lisdexamfetamine dimesylate (Vyvanse) | Lindner Center for HOPE University of Cincinnati Shire | Shire | June, 2023 | \$1,030 |
| 7 | Autism Spectrum Disorder | arbaclofen (STX209) | Seaside | Seaside | Unpatented | N/A |
| 8 | Autism Spectrum Disorder | methylphenidate (Daytrana) | University of Oklahoma | Noven | September, 2018 | Unavailable [‡] |
| 9 | Severe mood dysregulation | lisdexamfetamine dimesylate (Vyvanse) | Shire | Shire | June, 2023 | \$1,030 |
| 10 | Severe mood dysregulation | risperidone (Risperdal) | University of California Los Angeles National Institute of Mental Health Federal University of Rio Grande do Sul | Janssen | Expired | \$1,425 |
| 11 | Premenstrual Dysphoric Disorder | paroxetine hydrochloride (Paxil) | Hamilton Health Science Corporation | Glaxo-SmithKline | Expired | \$571 |

| | | | | | | |
|----|---------------------------|-------------------------------------|--|---------|---------|--------------------------|
| 12 | Mild cognitive impairment | donepezil hydrochloride (Aricept) | North China Pharmaceutical Group Corporation | Eisai | Expired | \$1,480 |
| 13 | Mild cognitive impairment | galantamine hydrobromide (Razadyne) | Johnson & Johnson | Janssen | Expired | Unavailable [§] |

[†] Revenue for individual drug not found. US\$3,694 million reflects total revenue for all Forest Pharmaceuticals central nervous system drugs.

[‡] Revenue for individual drug not found. US\$71 million reflects 2009 revenue data from Shire Pharmaceuticals, which held licensing rights until between 2003 August, 2010. Total 2012 sales of all products for Noven Pharmaceutical's parent company, Hisamitsu Pharmaceutical Co., were US\$1,707 million.

[§] Revenue for individual drug not found. US\$2,874 million reflects total revenue for all Johnson & Johnson neuroscience drugs except for Concerta, Invega, and Invega Sustena.

Table 2. Summary of FCOI among the included *DSM* panel members by trial.

| Trial | New DSM-5 Diagnosis | Trial Drug Manufacturer | Work Group | Work Group FCOI to Any Pharmaceutical Company | Work Group FCOI to Trial Drug Manufacturer | Task Force FCOI to Any Company | Task Force FCOI to Trial Drug Manufacturer |
|--------------|--|--------------------------------|--------------------------------|--|---|---------------------------------------|---|
| 1 | Major Depressive Episode, bereavement exclusion eliminated | Eli Lilly | Mood Disorders | 8/12 | 5/12 | 20/31 | 15/31 |
| 2 | Major Depressive Episode, bereavement exclusion eliminated | Forest | Mood Disorders | 8/12 | 1/12 | 20/31 | 5/31 |
| 3 | Binge Eating Disorder | Cephalon | Eating Disorders | 6/12 | 0/12 | 20/31 | 2/31 |
| 4 | Binge Eating Disorder | Eli Lilly | Eating Disorders | 6/12 | 3/12 | 20/31 | 15/31 |
| 5 | Binge Eating Disorder | Glaxo-SmithKline | Eating Disorders | 6/12 | 3/12 | 20/31 | 5/31 |
| 6 | Binge Eating Disorder | Shire | Eating Disorders | 6/12 | 1/12 | 20/31 | 1/31 |
| 7 | Autism Spectrum Disorder | Seaside | Neuro-developmental Disorders | 5/13 | 2/13 | 20/31 | 1/31 |
| 8 | Autism Spectrum Disorder | Noven | Neuro-developmental Disorders | 5/13 | 0/13 | 20/31 | 0/31 |
| 9 | Disruptive Mood Dysregulation Disorder | Shire | Child and Adolescent Disorders | 0/10 | 0/10 | 20/31 | 1/31 |
| 10 | Disruptive Mood Dysregulation Disorder | Janssen | Child and Adolescent Disorders | 0/10 | 0/10 | 20/31 | 5/31 |
| 11 | Premenstrual Dysphoric Disorder | Glaxo-SmithKline | Mood Disorders | 8/12 | 2/12 | 20/31 | 5/31 |
| 12 | Mild Neurocognitive Disorder | Eisai | Neurocognitive Disorders | 7/8 | 2/8 | 20/31 | 1/31 |
| 13 | Mild neurocognitive Disorder | Janssen | Neurocognitive Disorders | 7/8 | 3/8 | 20/31 | 5/31 |

Table 3. Summary of FCOI data among trial PIs by trial.

| Trial | New DSM-5 Diagnosis | Trial Drug Manufacturer | PI FCOI to Any Pharmaceutical Company | PI Research Funding to Trial Drug Manufacturer | PI All Other FCOI to Trial Drug Manufacturer |
|--------------|--|--------------------------------|--|---|---|
| 1 | Major Depressive Episode, bereavement exclusion eliminated | Eli Lilly | 0/1 | 0/1 | 0/1 |
| 2 | Major Depressive Episode, bereavement exclusion eliminated | Forest | 5/5 | 3/5 | 2/5 |
| 3 | Binge Eating Disorder | Cephalon | 1/2 | 0/2 | 0/2 |
| 4 | Binge Eating Disorder | Eli Lilly | 1/1 | 1/1 | 0/1 |
| 5 | Binge Eating Disorder | GlaxoSmithKline | 1/1 | 0/1 | 0/1 |
| 6 | Binge Eating Disorder | Shire | 17/21 | 4/21 | 3/21 |
| 7 | Autism Spectrum Disorder | Seaside | 5/8 | 3/8 | 1/8 |
| 8 | Autism Spectrum Disorder | Noven | 0/1 | 0/1 | 0/1 |
| 9 | Disruptive Mood Dysregulation Disorder | Shire | 1/1 | 1/1 | 1/1 |
| 10 | Disruptive Mood Dysregulation Disorder | Janssen | 1/1 | 0/1 | 1/1 |
| 11 | Premenstrual Dysphoric Disorder | GlaxoSmithKline | 0/0 | 0/0 | 0/0 |
| 12 | Mild Neurocognitive Disorder | Eisai | 0/1 | 0/1 | 0/1 |
| 13 | Mild Neurocognitive Disorder | Janssen | 0/0 | 0/0 | 0/0 |