“The Hidden Manipulation: The Influence of Pharmaceutical Companies on Physicians and Researchers”

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The Hidden Manipulation: The Influence of Pharmaceutical Companies on Physicians and Researchers

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Abstract

Pharmaceutical companies spend a significant amount of money on physician advertising and industry sponsored research. Involvement from pharmaceutical companies in these areas can divert the focus away from patient safety and causes changes in prescribing behavior and can cause the "funding effect." Therefore, it can be concluded that industry involvement in research and physician marketing does negatively impact patient safety, and the relationship between physicians, researchers and the industry should not be eliminated, but more strictly regulated. When physicians are visited by pharmaceutical sales representatives (PSR), their prescribing habits are negatively affected. PSRs also do not provide accurate information to physicians about medications, and therefore physician advertising should be more strictly regulated to protect patients. Possible solutions such as providing federally funded PSRs and licensing PSRs to improve the quality of information they provide should be implemented not to eliminate, but to control physician advertising. Industry presence in research causes bias in designing and publishing research studies. The funding effect causes industry funded research to report greater benefits and safety of the medications being studied. Bias in research and lack of laws regulating disclosures of conflicts of interests also raise questions about the authenticity of studies published in medical journals. Since research cannot continue without the funding from pharmaceutical companies, they should continue to fund research, but strict ethical regulations should be followed.

Introduction

Pharmaceutical companies have a large influence on the world of health care as they spend a significant amount of money on advertising. The most common form of advertising is direct to consumer advertising, which directly influences patients. While direct to consumer

advertising is a very overt effort to influence the medical community, the pharmaceutical industry also has an understated presence through physician advertising and industry sponsored research. Physician advertising and industry sponsored research often go overlooked because they do not directly affect the general public but since both practices tend to become aggressive, their effects can reach patients. The goal of advertising directed toward physicians is to educate the physicians about new medications and to increase profits. Pharmaceutical companies sponsor research to get their medications approved for sale. Physicians and researchers are focused primary on patient safety and the effectiveness of treatments while pharmaceutical companies are focused on increasing profits. When the pharmaceutical industry becomes involved with physicians and researchers, physicians and researchers often feel the need to support the interests of the industry either by prescribing more of a certain medication or by publishing positive research results. Focusing on the goals of the pharmaceutical companies can divert attention away from patient safety. Therefore, there have been debates about the ethics of physician advertising and industry sponsored research. These conflicting goals can sometimes lead to problems, but the presence of the pharmaceutical industry is sometimes necessary. Thus, the question of whether pharmaceutical industry money should be used in research and physician advertising is raised.

Industry sponsored clinical research is necessary because industry involvement grants access to resources that are otherwise unavailable. Involvement from a pharmaceutical company also presents patient benefits because it can keep the costs of medications low once they have been approved for sale, therefore reducing the burden patients face with high healthcare costs. Physician directed marketing presents patient benefits because it keeps the physicians educated on the newest medications, which can allow them to provide effective care, therefore improving

treatment outcomes. However, the risks of pharmaceutical advertising and industry funded research include harming patient safety and losing trust in physicians. Any involvement from a pharmaceutical company creates a "conflict of interest," which is "a set of circumstances that creates a risk that professional judgement or actions regarding a primary interest will be unduly influenced by a secondary interest" (Gagliardi et. al.). In this case, the secondary interest would be those of the pharmaceutical company. Conflicts of interests can cause bias, and skew clinical trial results, causing what is called "the funding effect," which refers to how "study outcomes could be statistically correlated with funding sources, largely in drug safety and efficacy" (Krimsky 1). This means that industry funded clinical research typically tends to report greater benefits and safety of the drug being tested. Thus, industry involvement in research and physician marketing does negatively impact patient safety, and the relationship between physicians, researchers and the industry should not be eliminated, but more strictly regulated.

Industry Relationships with Physicians

Industry companies primarily interact with physicians through pharmaceutical sales representatives (PSR). In 1990, debates began after the 1990 Committee on Labor and Human Resources report was published about the nature of physician-industry relationships. In 2007, the Sunshine Act became a part of the Patient Protection and Affordable Care Act, and it continues to be updated. This law "requires companies to begin recording any physician payments, including stock options, research grants, knick-knacks, consulting fees, and travel to medical conferences that are worth more than ten dollars" (Lewin and Arend). In 2009, the Pharmaceutical Research and Manufacturers of America (PhRMA) announced "new voluntary pharmaceutical industry guidelines on marketing to physicians" (Grande).

The marketing techniques used by PSRs are referred to as detailing. Detailing involves visiting physicians' offices to provide gifts such as promotional material, free drug samples, meal vouchers, and free education about new medications. According to industry companies, the "promotional activities aim to provide health care professionals with scientific and educational information" (Brax et. al.) and in that sense, detailing is necessary because it grants physicians with free access to knowledge about new medications. One reason why concerns regarding physician marketing have risen is because of how much money is spent on detailing: "in 2012 alone, pharmaceutical industry spent $89.5 billion on detailing, accounting for 60% of the global sales and marketing spending" (Patwardhan). Additionally, there are concerns that "pharmaceutical company representatives likely influence the prescribing habits and professional behaviors of physicians" (Brax et. al.). The actions of researchers and physicians affect patient safety. Since industry involvement can change the actions of physicians and researchers, the relationship pharmaceutical companies have with these parties must be examined.

There is overwhelming evidence that physician industry interactions have a direct effect on prescribing habits. This is because many of the marketing strategies are corrupt and unethical. In 2009, a survey found that 85% of physicians had contact with a PSR and these physicians stated that PSRs were their primary source of information regarding the newest medications (Mintzes et. al.). This places PSRs and pharmaceutical companies in a unique spot because the quality of information the PSR provides can control the clinical decisions of physicians and by extent, patient safety. In an ideal world, PSRs would realize the importance of providing high quality, accurate information. However, when PSRs and physician interactions were closely studied, the "results suggest a serious lack of information on harmful effects of promoted medicines. Information on health benefits was provided twice as often as information on harm,

with not a single harmful effect mentioned in over half of the [studied] promotions" (Mintzes et. al. 1380). This is a problem because one of the responsibilities of physicians is to make sure that the treatment does not harm the patient. The treatment is more likely to harm the patient if the physician is not fully educated about the harmful effects of a medication. Ignoring the risks patients face, "the US FDA's website explains that efficacy information with no risk information violates US regulations" (Mitzes et. al.). Therefore, providing biased information is not only incompetent and immoral, it is also illegal.

Additionally, the very nature of detailing is inherently faulty, and can change the behavior of physicians. If physician marketing is meant to educate doctors on the appropriate uses of new medications, then there is no reason to provide gifts to physicians. Detailing is synonymous to bribery. PSRs present physicians with free drug samples and free meals hoping that the physician prescribes that certain medication more frequently. Providing gifts can cause physicians not to act in the best interest of the patients, but in favor of the pharmaceutical company. As Brax et. al. shows, analysis of several studies "found a consistent association between interactions promoting a medication, and inappropriately increased prescribing rates, lower prescribing quality, and/or increased prescription costs" (Brax et. al.). The key word is "inappropriately." This means that even though the patient might not have required the medication, it was prescribed to them anyway. In addition to unnecessarily receiving the medication, the patient now must deal with increased treatment costs. This happens because promotion "may create false claims and expectations about the ability of drugs to meet [treatment] needs" (Mulinari). The physician will believe that the new medication is necessary to treat the patient even when there is a cheaper, safer, and equally effective alternative. And since physicians cannot always objectively evaluate their behavior, many believe that "gifts and

samples have no impact on their practice" (Connors 258). This is troubling because it means that physicians see no problem in accepting these gifts and they do not realize the negative effects of accepting gifts. In fact, "many feel they are entitled to gifts and samples, considering it a sign of status" (Connors 258). In the end, the marketing and its effects take the focus away from the patient. Physicians are placed in a tricky spot because they must act in the patient's best interest and the gifts make them want to act to favor the industry. Many times, these conflict.

Unethical marketing practices and its harmful effects have become a public health concern as the safety of an increasing number of patients is being threatened. Therefore, physician-industry interactions must be regulated. Following marketing regulations makes sense because "it helps build trust in the industry and its products, as well as among regulators, prescribers, payers, and consumers of medicines" (Mulinari 5). In addition to the Sunshine Act, which requires reporting physician gifts above a certain dollar value, other regulations can be implemented. One solution is to publicly fund academic detailing programs. This way, the government can control the quality and accuracy of information that is provided to physicians. However, "it seems unlikely that any state could scale up to a level that would rival the pharmaceutical industry" (Grande 81). It is not economically possible for the government to provide as many PSRs as pharmaceutical companies do. Another solution is to license pharmaceutical sales representatives. If sales representatives are licensed, they can be required to follow a code of ethics that have been enacted by a state legislative board. This way, sales representatives cannot engage in "deceptive or misleading marketing" (Grande 81). Licensing sales representatives does not come without drawbacks: "licensure implicitly defines pharmaceutical sales as a professional activity when motives underlying such activities seem at odds with the traditional definition of professions" (Grande 81). Traditionally, patient safety and

ethics is top priority to medical professionals. Sales representatives place increased medication sales at the top of their priority list. Balancing both these priorities will be problematic and might defeat the purpose of licensing sales representatives. Additionally, by branding the PSRs as licensed professionals, physicians might place too much trust in them rather than using their own judgement and knowledge to treat the patient. This creates the possibility that PSRs might misuse their influence and continue to withhold the negative information about the medications they are promoting. Since neither of these solutions are guaranteed, fool-proof fixes, physician advertising cannot be eliminated. Instead, some combination of these solutions must be implemented, and the Sunshine Act should continue to be enforced in order to contain the threat posed to patients.

Industry Funded Research

In addition to physician-industry interactions causing problems, industry involvement in research is also raising concerns. Much of the research conducted today is sponsored by industry. This can include providing funding for the resources necessary to complete the study as well as paying the medical professionals and administrative staff that run the clinical trials (Tereskerz et. al.). Drug development and clinical trials are very expensive. Total costs for putting a single drug through human clinical trials to get FDA approval can cost as much as $2500 million (in 2013 dollars) and due to inflation, the current costs only continue to rise (Dimasi, Grabowski, and Hansen). Many trials conducted today occur through academic centers, but these centers do not have enough money to run the study by themselves (Chen et. al.). As a result, industry funding in research is necessary for innovation. When a clinical trial is funded by a pharmaceutical company and the researchers and authors receive payments from the company, it is referred to as a “conflict of interest.” Research results are published in medical journals, which are the primary

method through which knowledge is spread in the medical community. When publishing the results of the study, the authors have a moral obligation to disclose any and all conflicts of interest. However, there are no universal rules for requiring disclosures. Instead each medical journal has its own specific rules which are often not enforced. Thus, many conflicts of interest go undisclosed. Charles Ornstein, a senior editor at ProPublica researched this issue and interviewed Dr. Mehraneh Jafari, who is a professor at the UC Irvine School of Medicine Dr. Jafari and her colleagues found that "of the 100 doctors who received the most compensation from device makers in 2015, conflicts were disclosed in only 37 percent of the articles published in the next year" (Ornstein and Thomas). This raises concerns in the medical community because "scholars discovered many layers of industry bias in the selection, design, publication, and dissemination of clinical studies" (Mulinari). When a pharmaceutical company sponsors research, the company can design the study in a way that increases the likelihood that the medication being tested will be proved to be safe and effective. The pharmaceutical company can also withhold valuable research information by preventing negative results from being published or prevent publication completely. Additionally. "researchers' ties to the health and drug industries increase the odds they will, consciously or not, skew the results to favor the companies with whom they do business" (Ornstein and Thomas). This is a widespread problem today because a large portion of medical research is sponsored by industry, and it raises the question of the accuracy of published study results.

Researching and developing a new medication is a costly process. Therefore, as federal funding has been declining in the past ten years, industry funding is becoming pervasive in medical research (Tieney, Meslin, and Kroenke). This has raised many concerns in recent years regarding the integrity of the results of industry funded research and whether or not industry

funding is helping push research towards effective innovation. To begin, one major fault of industry funded research is that there are no clear, uniform regulations dealing with reporting conflicts of interest: “The reporting system still appears to have many of the same flaws that the Institute of Medicine identified nearly a decade ago when it recommended fundamental changes in how conflicts of interest are reported” (Ornstein and Thomas 1). This lack of regulation has the potential to alter the quality and accuracy of the results that are published. Since the industry involvement does not always have to be reported, the industry can control things such as preventing the publication of the results for free in medical journals and it can also prevent publication of negative results (Hottenrott and Thorwarth). Additionally, several researchers at top United States research universities took a survey in which they rated how important industry funding is to them. The survey found that the researchers to whom industry support is more important “are significantly more likely to report receiving requests to withhold research results, delay publication, present results in ways that favor the sponsor’s product, or keep the project and results secret” (Tereskerz et. al. 7). False research publications can have a significant effect on patient safety because medical journals are the primary method through which knowledge is conveyed in the medical community. Hospitals and physicians rely on medical journals to determine the effectiveness and safety of medications. Therefore, it is important that the results published in medical journals is accurate. Preventing publication of negative results and skewing results can harm patients. Physicians can unknowingly prescribe a harmful medication to a patient because of faulty research results. Additionally, if false research results are submitted to the FDA, a potentially harmful medication could end up being approved for use.

Lastly, when a study is published by a pharmaceutical company, it takes the researchers’ focus away from their initial goal of advancing medical knowledge. While the researcher is

focused on medical innovation and patient safety, “the goal of research funding by for-profit companies is maximizing income to their shareholders” (Tierney, Meslin, and Kroenke 228). As researchers receive grants and personal payments from industry companies, there is a worry that “commercial interests may induce scientists to select research projects on the basis of their perceived value in the private sector and not solely on the basis of scientific progress” (Hottenrott and Thorwarth 535). Indeed, this study concluded that there is evidence that industry funding can reduce the number of meaningful studies a researcher or academic center will publish. This means that the focus of research has shifted away from advancing medical knowledge and towards economic profit, which again is detrimental to the medical community.

Despite these downfalls to industry funding, it is necessary if medical science is to move forward. Most importantly, industry involvement is necessary because of the funding. Without the money supplied by pharmaceutical companies, medical research and clinical trials would not be possible. Therefore, a carefully structured relationship between researchers and the industry must be achieved. Additionally, the goals of researchers and industry sometimes align and working together to achieve those goals can lead to successful outcomes. For example, “clinicians and pharmaceutical companies have obvious interests in drug adherence and in developing and validation methods for assessing and improving adherence” (Tierney, Meslin, and Kroenke 229). Drug adherence is of importance to clinicians because when a patient adheres to a drug regimen, the chances of a successful treatment increase. Adherence is of importance to the pharmaceutical industry because if a patient continues to take the medication, the profits for the company will increase. No one party can achieve adherence without the help of the other.

Alternative Explanations for the Funding Effect

Bias leading to the funding effect is the main reason why scholars are apprehensive of increased industry funding. While Tierney and his colleagues point out that the goals of industry and clinicians can align, they also acknowledge that "industry funded research has a risk of bias and misconduct that can mislead readers, consequently causing pain, suffering, and sometimes death" (229). To understand why this happens, a concept known as the funding effect, or funding bias, must be examined. This term describes how "industry funding leads to more optimistic outcomes or interpretations of outcomes than public funding" (Gartlehner et. al. 122). A common conclusion that is drawn about this occurrence is that the positive findings are a result of bias: The researchers received money from the pharmaceutical company, so they are more likely to report findings that support the financial interests of the pharmaceutical company.

However, explanations other than bias exist, and solutions are available to ensure the success of industry – academic partnerships. This can assure scholars that industry funding is necessary to advance medical science. For example, "the higher frequency of good outcomes in industry supported trials may stem from a decision to fund the testing of drugs at a more advanced stage of development" (Krimsky 11). This means that before bringing a drug to clinical trials, the pharmaceutical company has already eliminated ineffective drugs. Therefore, the drugs that are tested in clinical trials have a higher chance of proving to be effective. Additionally, industry funded research compares the medication with a placebo and "comparison with placebo may produce more positive results than comparison with alternative active treatment" (Krimsky 11). A placebo is not designed to treat any medical condition so there will be no observable effect. Therefore, the medication being studied has a higher chance of proving to be effective. Circumstances exist which make the claim that the reason industry funded research unreasonably

favors the manufacturer false. Additionally, medical research cannot continue at the rate it does today without the money generated from industry funding. Therefore, carefully planned out relationships between industry and academic research institutions are necessary and should follow strict ethical codes. Tierney et. al. suggests some basic principles that should be enacted to ensure that academic – industry relationships are ethically credible. To deal with the publication issue, Tierney states, "Ensure the right of all researchers associated with the partnership to publish. Disseminate all research results at the conclusion of collaborative studies in a timely fashion" (232). To deal with the conflicting goals of researchers and industry, he states, "Structure the partnership to have the best chance of benefiting both partners and harming neither" (232). To deal with the problem of not disclosing conflicts of interest, he states, "Widely publicize the partnership agreement and collaborative opportunities to the public employees" (232). If such ethical guidelines are strictly followed, the benefits of industry funded research will remain without the negative effects stunting medical advancement and innovation.

Conclusion

The pharmaceutical industry also has an indirect effect on patients and society because it sponsors research and it markets to physicians. Physician marketing is just as aggressive as consumer advertising. Pharmaceutical sales representatives repeatedly visit physicians, offering them braded gifts, promotional material such as pamphlets, and free drug samples. Although physicians believe that they can shield their clinical decisions from the advertising, studies show that advertising leads to an increase in prescription rates and an increase in the average prescription cost. A solution to this problem is to employ federally paid sales representatives so that the government can control the information that is conveyed to physicians, but this solution is not economically viable. Another solution is to require sales representatives to be licensed, but

this might defeat the purpose of licensing PSRs. Since neither solution will eliminate the problem of affecting clinical practices, separating physicians from industry is not possible. Therefore, the best solution is to regulate the relationship between physicians and industry more strictly by employing some combination of these regulations.

When research is funded by industry, the lack of regulation regarding the disclosures of conflicts of interest mean that industry companies have control over the information that is published. As a result, many industry funded studies exhibit the funding effect, meaning they conclude in favor of the medication being studied and the results agree with the financial interests of the industry sponsor. However, alternative explanations exist for this bias. Overall, industry funded research and research sponsored by other means is very different and any comparison between the two will not be completely accurate. Industry funded research is usually of a higher quality and ineffective medications have already been weeded out before beginning clinical trials, both of which raise the likelihood that the study will conclude in favor of the medication being studied. Despite the downfalls to industry funded research, the money and resources that comes with industry involvement is necessary to advance medical science. Therefore, industry funding should continue but certain ethical guidelines need to be followed.

Containing these problems is necessary because the increasing influence the pharmaceutical industry has on patients, physicians, and researchers will harm everyone involved. The health of future generations will be in the control of the pharmaceutical industry, and its relentless pursuit of increasing profits will lead to serious problems. Regulations need to be implemented to shift the focus shift away from increasing profits and back to protecting patient safety and finding new, safer ways to treat patients.

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