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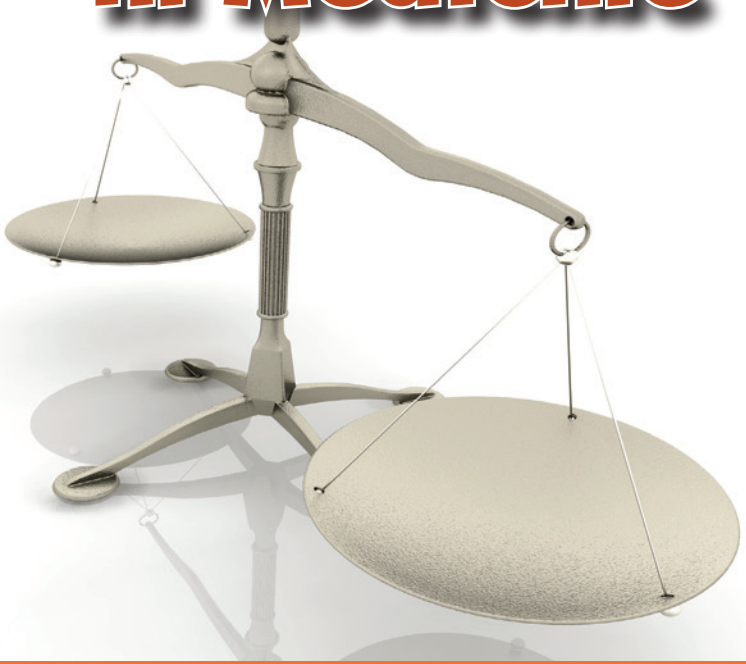
The Ethics of Pharmaceutical Industry Influence in Medicine



THE ETHICS OF PHARMACEUTICAL INDUSTRY INFLUENCE IN MEDICINE

By

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Julian De Freitas is a research associate in the Psychology department at Yale University. As an affiliate of a number of labs and research groups at both Yale and Harvard, Julian takes an interdisciplinary approach to studying how the mind works — blending the methods of cognitive, social and evolutionary psychologies and of experimental philosophy. Julian's work is mainly focused on how humans pay attention to information in space and time, and on the psychological biases that shape their judgments. In addition to his work in the core cognitive sciences, Julian has published articles in psychiatric ethics and bioethics, examining issues surrounding ethical decision making and undue influence. Julian has also written popularly for publications such as *Scientific American Mind* and *Nature*. He is currently co-writing a book with Omar Haque on the science and ethics of defining death.

Abilash A. Gopal, M.D., practices psychiatry in San Francisco, where he focuses on psychodynamic psychotherapy and psychopharmacology. His main areas of scholarship include psychiatric and medical decision making, ethics, and the law; informed consent and risk management; substance abuse; and forensic neuropsychiatric evaluation of disability and diminished capacity. Dr. Gopal completed his undergraduate education at Princeton University, medical school at Tufts University, residency at University of California, San Francisco (where he was Chief Resident), and fellowship at University of California, San Francisco, Program in Psychiatry and the Law. He has also trained at Harvard Medical School, where he completed an apprenticeship in forensic psychiatry and was selected for the Doris Duke Clinical Research Fellowship. He has won numerous awards throughout his career,

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Omar Sultan Haque, M.D., M.T.S. is a psychologist and physician, and is an Instructor and Postdoctoral Fellow in the Department of Psychology at Harvard University and in the Program in Psychiatry and the Law at Harvard Medical School. He is a co-Director of the UNESCO Chair in Bioethics, American Unit. His research investigates questions at the intersection of psychology, medicine, ethics and religion. He graduated from Brown University with a Sc.B. in Neuroscience and an A.B. in Religious Studies (with honors). He graduated from Harvard Divinity School with an M.T.S. in Islamic Studies, and from Harvard Medical School with an M.D. (with honors) with scholarly concentrations in Neurology and Medical Ethics, where he was a member of the Oliver Wendell Holmes Society. At Harvard and Brown, he has taught in the Departments of Biology, Neuroscience, Psychology, Political Science, and Religion, and has received a number of teaching awards. Dr. Haque's work has been supported by many national and international awards, grants and fellowships, and presented at dozens of universities and scholarly meetings.

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Samuel Wolfman, J.D., Ph.D. of the International Center for Health, Law and Ethics at the Haifa University in Israel, is a Law Professor at the Law School of the Zefat Academic College and teaches also in the Law Faculty at Haifa University. Dr. Wolfman's academic teaching and research focus on Bioethics, Medical Law and Psychiatry, and he has published numerous papers on these topics in the medical and legal literature. Dr. Wolfman also served as the head of the Israeli UNESCO unit for Bioethics and teaches Bioethics courses and seminars in universities in Israel, United States and other countries. Dr. Wolfman is a member of the editorial board of *Medicine and Law*, a journal of the World Association for Medical Law, and is a fellow of the American College of Legal Medicine. Dr. Wolfman served in senior executive positions in the Israeli and international pharmaceutical industry for many years (until 2002), where he was in charge of regulatory and medical issues, as well as of overseeing the conduct of clinical trials.

Preamble

Harold J. Bursztajn, M.D.

Our aim in this casebook is not to write categorical prescriptions for the diagnosis and treatment of ethical problems that have arisen out of the interaction of pharmaceutical influences on clinical practice with human vulnerabilities when making decisions under conditions of uncertainty (Bursztajn et al., 1981/1990). Rather, it is to provide a series of case descriptions and analyses, a series of Wittgenstein's context-dependent "family resemblances," that make up a memorable family photograph of a spectrum of clinical and ethical dilemmas and methods of analysis. We are mindful that an action that may be meaningfully ethical in one time or context may be unethical in another time or context.

We hope readers across all levels of professional experience and ethical sophistication will be reminded of some of these vignettes in the course of their everyday practice, when it comes time to ask first, "Is there an ethical question here?"; next, "How can we talk about it?"; and finally, "What is to be done or not done?" We hope these questions can be asked without doing more harm than good. Self-righteous or overly certain ethical discourse imposed on complex fact patterns can as often lead to harm as ethical tone-deafness or obliviousness (Bursztajn, 1986). In some instances different fact patterns or different ethical models may yield different answers; in other instances the answers may be the same. Navigating between the Scylla of relativism and the Charybdis of absolutism, these cases and their analyses can be thought of as notes for the ongoing development of an ethical professional practice in an age of pharmaceutical influence on clinical decision making under conditions of uncertainty.

Introduction

Medicine is an industry-dominated climate, with physicians and patients relying on pharmaceutical companies to provide the medications needed to adequately address patient health concerns. However, because pharmaceutical companies stand to profit from the drugs they sell, they have an incentive to influence consumers to buy the drugs they manufacture. These efforts introduce a conflict of interest: between the objective of pharmaceutical companies to maximize profits and the need of patients to receive the most safe, effective, and individualized medications at any given time. Thompson (1993) defines conflicts of interest as follows:

> …a set of conditions in which professional judgment concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain) (573).

Regardless of the distorting incentives for corporate profit, the primary ethical interest within medicine should be the maximization of the health and wellbeing of patients. Whenever this aim is put into jeopardy, it is the first priority of the health care profession to undo the circumstances and conflicts of interest that endanger this primary ethical imperative of health care.

In the context of pharmaceutical marketing, "consumers" include patients as well as their prescribing physicians, since in order for a prescription to be sold, it must be deemed medically necessary by a doctor, as well as consented to in an informed manner by a patient. Pharmaceutical companies, therefore, seek to influence both physicians and patients through "provider-directed" and "direct-to-consumer" approaches, respectively. The majority of these marketing efforts are provider-directed, although both marketing types have been found to be effective at boosting drug sales (Donohue et al.,

2007). Pharmaceutical marketing strategies may take on a variety of approaches, direct and indirect (for example, at the institution-level vs. at the individual-level), and over recent years a precise understanding of how conflicts of interest exist across different approaches has slowly developed.

Although a comprehensive list is impossible, any of the following financial associations with pharmaceutical companies — most of which are relevant primarily to physicians — may entail conflicts of interest: receiving pharmaceutical-sponsored gifts, honoraria, meals, grants, contracts, drug samples, promotional material, travel, or lodging, research funding, or funding toward continuing medical education; being a principal in a startup company, a member of a scientific advisory board or speakers' bureau of a drug company, an expert witness for a company in litigation, a company patent or copyright holder, a collaborator in an industry-funded study, or a consultant; representing or speaking on behalf of a pharmaceutical company at a conference; meeting directly with pharmaceutical representatives; and holding equity in a drug company (Cosgrove et al., 2009).

More recently, pharmaceutical companies have also extended their marketing efforts to online technologies and applications, with pharmaceutical ad spending projected to increase from $1.03 billion in 2010 to $1.86 billion by 2015 (Iskowitz, 2012). The growth of online information services and patient forums can be seen as an encouraging development. These resources facilitate an unprecedented support community for millions of patients and provide invaluable health information to otherwise isolated communities. Physicians also find them useful (e.g., Frye, 2011; Parekh et al., 2009). At the same time, concerns continue to surround the many new ways in which the Internet has permitted pharmaceutical companies to bypass traditional doctor-patient relationships and market products directly to consumers (Nisbet, 2011). The Internet as a medium introduces its own host of intricacies, operating over a different time frame from other communication media, and within a different psychological and social architecture. In particular,

there are a number of unique and ever-emerging Internet domains in which pharmaceutical companies can now market their products, including but not limited to: search engines, drug company websites, e-mail lists, blogs, wikis, health information services, social networking sites, and mobile health software.

Yet, to influence the consumer is an integral objective of advertising, so when might this influence be characterized as unethical or "undue"? A number of definitions of "undue influence" exist in the literature, typically differing across academic disciplines and among jurisdictions (APA, 2008; Quinn et al., 2010; Shulman et al., 2007). "Undue influence" can be understood as a party's intentional, inappropriate, and self-serving use of knowledge or power to subvert another party's autonomy of informed decision making. Although this definition may be construed as that of advertising itself, the important distinction lies in the word "inappropriate," which in a medical context entails harm to health. Even conventional marketing techniques may become inappropriate within a medical context, because of the possibility of harm to patient health through specific marketing practices. In principle, this behavior is regulated by drug administrations, which typically work to ensure that drug marketing not be false or misleading, as well as that it always include drug risks presented in a balanced manner (USDHHS et al., 2009). Yet some pharmaceutical manufacturers have repeatedly admitted to failing to meet such requirements, and on several occasions have pled guilty to illegal marketing (Almashat et al., 2010).

Therefore, although there may often be benefits associated with the kinds of pharmaceutical efforts described above — such as improving a physician's ability to identify and treat complicated illnesses — many of these efforts may also produce negative effects, particularly when they unduly influence consumers (Wazana, 2000). Inaccuracies, imbalances, failures to meet accepted scientific standards, and other misleading presentations may all lead to poor patient outcomes, including increased health care costs when patients are

persuaded to buy new drugs over cheaper alternatives (including non-pharmaceutical treatments), and death or injury when patients are persuaded to buy drug treatments when there exist safer alternatives, or when these advertised drugs are not fully approved. Bias may also erode public trust in medical care, leading to a diminished response to clinicians and treatment. Wazana (2000) summarizes some of these and other negative outcomes of biased marketing:

> … an impact on knowledge (inability to identify wrong claims about medication), attitude (positive attitude toward pharmaceutical representatives; awareness, preference, and rapid prescription of a new drug), and behavior (making formulary requests for medications that rarely held important advantages over existing ones; nonrational prescribing behavior; increasing prescription rate; prescribing fewer generic but more expensive, newer medications at no demonstrated advantage).

Therefore, the objectivity of company marketing efforts cannot be taken for granted. When patient health is at stake, it is important that users be presented first and foremost with sources completely free of bias or *the potential for bias*.

Whenever pharmaceutical companies mislead users or withhold from them relevant safety or efficacy information, this influence may be counted as misinformation or mismarketing. Pharmaceutical company misinformation lies not only in misleading information strategies, however, but also in the vulnerabilities and decision biases of people who rely on this information — especially in stereotypically vulnerable patient groups, such as older patients and those suffering from serious mental illnesses. Vulnerable consumers — whether patients in need or time-strapped clinicians — are more likely to be misled. There is also a need, therefore, for a more nuanced understanding of the interaction between marketing practices and preexisting human vulnerabilities to this mismarketing.

A number of steps have been taken toward addressing some of the problems mentioned here, although much work still lies ahead. These kinds of approaches will need to clearly separate the primary mission of health care and academia from the mission of industry marketing (Insel, 2010). That said, there are also many good reasons to encourage academic and research collaborations with the pharmaceutical industry — foremost among them, the prospect of developing more effective treatments that can bring about increased patient welfare. The best ethical solutions, then, should include creative ways of facilitating as many of these collaborations as possible, while also implementing the necessary safeguards to keep primary and secondary interests separate. However, until society's regulation measures catch up with online pharmaceutical marketing (if they ever can), education may be the key. By nurturing physician and patient awareness of conflicts of interest, human vulnerabilities to misinformation, and the potential means of undue influence in pharmaceutical marketing, the benefits of access to crucial health information and care may be maximized, while the clinical risks of misleading promotion are reduced.

It is with this educating and ethical vision in mind that we have compiled this casebook. In it you will find a series of vignettes, ethical questions, and discussions that together touch on recurring issues surrounding pharmaceutical industry influence on medicine today. The characters in these vignettes range from high-ranking drug administrators to physicians and their patients. For each vignette, we highlight an important ethical question and then provide motivated answers in both the affirmative and negative. In some cases, the best solution to a scenario is relatively clear, but in most cases the issue is more complex. Our intent is not to provide definitive answers that unequivocally solve each ethical issue, but, rather, to inspire the reader to think about them in a nuanced and thoughtful manner, giving each issue careful, weighted consideration. Our hope is that these discussions will prove fruitful for confronting similar dilemmas in real-life scenarios across the developed and developing world. Some

of the vignettes have been derived from real-world cases: for these we have added a citation after the case in question. Other vignettes are composites of issues the authors have dealt with or observed in their practices. Most of the vignettes are short and concise, and so we hope readers will find them easy (and maybe even fun) to grapple with. In all vignettes we have strived to keep the language as clear and jargon-free as possible. We hope that the casebook may serve a number of audiences and purposes, say, as a helpful textbook for embarking medical students or as a quick reference for busy physicians in parts of the world that may not have ready access to the newest books.

We (Omar Sultan Haque and Julian De Freitas) would like to thank and acknowledge our co-authors for their invaluable contributions to the respective cases in this casebook: Itay Shuv-Ami, 1-6; Robindra Paul, 7-11 and 13-14; Samuel Wolfman, 12 and 15-21; Abilash Gopal, 22-29; Steven Lehr & Mahzarin Banaji, 32; Carl Elliott, 31; and Lisa Cosgrove, 30 and 33. We gratefully acknowledge the important contribution Brian Falls has made through his work on the definition of undue influence (De Freitas et al., in press; Falls et al., 2012). Finally, we would like to thank Harold Bursztajn and Archie Brodsky for their contributions to various aspects of the entire book, and we also extend a warm thanks to the research assistants, Jason Huffman and Jeremy Salinger, for their meticulous and thoughtful contributions.

Omar Sultan Haque and Julian De Freitas
Cambridge, MA, USA
August 15, 2012

Case 1: Misleading practices by a pharmaceutical company

(pharmaceutical marketing; conflicts of interest; off-label drug marketing)

A recent court ruling has found a pharmaceutical company guilty of marketing an anti-epileptic drug for inappropriate indications. The drug had originally been approved by the national drug administration for the treatment of epilepsy, but it has gone on to become one of the highest-selling drugs in the world because the drug has also been heavily marketed toward the treatment of psychiatric disorders.

Ethical Question

Should companies market a medication for the treatment of a disorder when the medication has not received formal approval from the relevant national regulatory body?

Possible Answers

- Yes, as long as empirical evidence exists that supports the drug's use toward the treatment of a given disorder, it is the company's right to make this information known — whether or not national regulatory bodies have formally weighed in on the evidence.

- No, the absence of a formal indication may suggest that there is inadequate evidence that the drug is effective and that it does not have a problematic safety profile. A formal indication by the regulatory body serves as a testimony that a third party, with the patient's best interests in mind, has examined the drug and found it to be sufficiently effective and safe.

Discussion

On the one hand, the company has the right — even the duty — towards its shareholders to maximize profits and to expand the potential market

for its drugs. Moreover, some medications that are developed to treat a certain disorder are sometimes found to be beneficial in the treatment of completely different disorders. If a company finds that an existing medication can aid in the treatment of a disorder or disease for which it is not primarily indicated, it is useful and necessary for physicians and patients to be informed about this. On the other hand, when a drug company markets a drug for a certain indication, it is implied that the drug was found to be both effective and safe for the treatment of that indication. The lack of approval by a regulatory body raises serious questions regarding the adequacy of these claims, since expanding the formal indications of the medication is certainly in the economic interest of the drug company.

Off-label marketing can be more justified if the medication has received a formal indication in another country, if there is robust accumulated evidence in favor of its usage for that indication, or if the indication is a difficult-to-treat entity with unsatisfactory present treatment options. In evaluating the total level of evidence, one must consider the quality and quantity of supporting evidence, refuting evidence, safety profiles, and possible risks. In the absence of formal indication, the requirements for full transparency and disclosure of conflicting data become especially important. Unfortunately, off-label marketing is ubiquitous, and often based on poor evidence. This practice may be found to a greater degree in non-formal settings, such as in sales pitches during a meeting between a drug representative and a physician. Physicians must carefully consider their decisions regarding the off-label usage of drugs and must not simply rely on marketing claims, but rather become as familiar as possible with evidence for and against such usage.

References

(Braillon, 2012)

Case 2: Providing drug-risk information in pharmaceutical advertisements

(pharmaceutical marketing; communication of drug risk information; misleading portrayal)

A pharmaceutical company has just received approval to market its new drug. The company is thinking of launching an extensive advertisement campaign spanning many different media, including television and online social media forums. The drug has several side effects, some of them very serious, and the national drug administration has warned the company to include this information in all of its advertisements. At the same time, the company does not want to discourage patients from buying the drug. The company starts thinking of effective ways to include the necessary drug risk warnings in its advertisements without drawing too much attention to this information. The company's marketing department thinks that this strategy will improve the company's marketing success while simultaneously satisfying what it believes are overly strict drug regulation rules.

Ethical Question

Is it ethically appropriate for pharmaceutical companies to use advertising techniques that divert attention from adverse effects and other possible dangers of drugs?

Possible Answers

- Yes, because it is the duty of the federal regulator to find a legal balance between the company's interest to increase sales and the public's interest to be protected from unnecessary harm. As long as the company's conduct complies with present laws and regulations, its conduct should be considered ethical.

- No, as any attempt to knowingly compromise the audience's full and clear understanding of important safety information is purposefully misleading, and therefore should be considered unethical.

Discussion

Being a commercial entity, the primary goal of a drug company is to generate income, and it has a responsibility towards its shareholders to do so. It could be in the company's best economic interest to minimize the effects of any publicized information that might hurt sales. Since there already exists an external regulatory body in order to protect the public, the private company may claim that, as long as its practices are not illegal, a proper balance is struck between the economic good of the company and the safety of the potential consumers. By this view, if any lack of balance still exists, then it is the duty of the regulator — not the company — to intervene.

However, if a company purposefully takes action to make a drug warning less effective, understood, or memorable, then the company is not truly communicating the *essence* of the message — as is required by the regulatory body. There is no doubt that there is an ethical duty to warn customers, both doctors and patients (in instances in which direct-to-consumer marketing is legal), of potential risks. Therefore, to mask the warnings' intelligibility is not only deceptive in nature, but also unethical, since it puts patients at unnecessary risk solely so that private companies can profit.

Some of the psychological methods that companies may employ to mask a drug warning's intelligibility include: stating side effects in a rapid voice-over, displaying overly optimistic photos or videos while side effects are being stated, and making exaggerated promises about the drug's effectiveness. As targets of drug advertisements and marketing tactics, physicians and patients must be aware of such practices.

Case 3: Downplaying drug risk information in televised pharmaceutical marketing

(misleading pharmaceutical marketing; direct-to-consumer advertising; drug risk warnings)

A large pharmaceutical company has recently released an advertisement promoting an anti-depressant drug. When people in the advertisement take the drug, they immediately turn from gloomy to happy. Even as the side effects are listed in rapid voice-over, the picture on the screen continues to show a happy, recovered patient, who has already benefited from the drug. The advertisers assume that these scenes of happy patients will draw attention away from the drug risk information, ensuring that viewers only remember the positive aspects of the drug, without also remembering the quickly stated risks of taking the drug.

Ethical Question

Is it ethical to advertise directly to lay people who do not have the medical knowledge and tools to differentiate between a balanced and unbalanced advertisement?

Possible Answers

- Yes, advertising can serve as a means by which the company promotes health by informing the public about the risks of diseases, as well as about the benefits of available medications and their side effects. The company also has a right to advertise its products — a right derived from the basic freedom of speech.

No, since the physician's clinical judgment is necessary in order to determine the appropriate intervention for the patient's condition. Advertising to consumers serves as an indirect method to pressure

physicians into prescribing certain medications, since patients end up requesting those medications that they have seen advertised. This behavior can compromise patient health, as well as jeopardize the doctor-patient relationship.

Discussion

The topic of direct-to-consumer advertising (DTCA) is hotly debated. DTCA is prohibited by law in the vast majority of countries, and permitted in a regulated manner in a few countries. Drug companies claim that DTCA carries advantages for the public. For instance, DTCA is meant to promote public awareness and education about diseases, disorders, and available medical treatments. Companies argue that public education is especially important, given that many patients are under-diagnosed and under-treated. The economic value of DTCA is clear, since it may lead to a significant increase in sales of prescription drugs. As for-profit entities, companies have a duty towards their shareholders to do as much as possible to increase income. Moreover, the right to advertise can be conceptualized as an extension of the basic freedom of speech, and therefore, one that must be protected and honored.

On the other hand, DTCA can compromise the relationship between doctors and patients and can potentially compromise a patient's health. Advertisements of prescription drugs are designed primarily to sell, not to educate. Because the average consumer does not form a balanced opinion about a drug's appropriate use before acting — since the average consumer does not read academic articles and other more objective data — he/she may rely on the advertisement. This is a highly biased and erroneous source of information. Most advertisements focus on creating an emotional response and an expectation of "instant benefit" from the drug being advertised. This can lead patients to pressure their physicians into prescribing the advertised medication, even if this medication may be less appropriate than other interventions. If the physician insists that he will not prescribe the requested medication, then this may lead to a number of

negative consequences, including: the patient leaving the physician to seek the advertised drug from another physician instead; refusal by the patient to take any alternative treatment; the creation of a nocebo effect (negative psychological expectations about a given treatment leading to detrimental effects on health) in the event that the patient eventually agrees to a different intervention from the one he/she requested. DTCA also creates an atmosphere in which quick drug fixes are seen as preferable to non-drug interventions (such as lifestyle changes), thereby contributing to the creation of a lazier community that is less willing to confront certain problems such as obesity and depression at the root. The belief that there is a drug solution to every problem may temporarily treat symptoms without truly addressing causes.

Case 4: Inclusion of drug interaction risks in a medication package insert

(drug interactions; prescription practices; drug risks; conflicts of interest)

An elderly female patient began vomiting and experiencing muscle cramps a couple of days after starting her medication for arthritis pain. She thinks that her medication might be responsible for her symptoms, although she is not completely sure, as her new doctor reassured her that the medication was standard treatment.

During a consultation with her doctor, she nervously tells him about her current symptoms and concerns regarding the medication. The doctor is surprised by the news. Although the medication is still relatively new on the market, none of his other patients have complained of bad symptoms. He remembers, though, that the elderly woman's prescription also included some other basic painkillers. The doctor now wonders whether the new medication cannot be taken in combination with painkillers. When he looks up the risks of the medication in the package insert, however, he finds no warnings about how it may interact with other medications.

Ethical Question

Is it ethically acceptable for a pharmaceutical company to exclude less obvious drug risk information such as drug interaction risks, even if these risks are relatively rare?

Possible Answers

- Yes. Pharmaceutical companies are only ethically obliged to include the main risks associated with taking the drug. They should not be obliged to include information about drug-drug interactions (DDIs),

especially if these interactions are rare; rather, it is the responsibility of the physician to know this information and to communicate it to the patient.

- No. Pharmaceutical companies are ethically obliged to include DDI risks, since these have the potential to affect patient health. Physicians cannot be expected to know every risk associated with a drug.

Discussion

DDIs are a real health threat, especially in complicated cases or in elderly patients, as these patients are likely to take more prescription drugs than the norm. DDIs may adversely affect or harm the patient, and so information about DDIs must be made easily available in the package insert. Since new drugs are constantly being released, it is unrealistic to expect physicians to know this information off the top of their heads. Rather, it is the responsibility of the pharmaceutical company to include these risks. In most cases, this responsibility will extend to the inclusion of relatively rare DDIs.

Even non-prescription drugs may carry DDIs, and so in these instances it is especially important that patients taking the drug are able to easily find information about potential DDIs. Furthermore, it is the company's responsibility to include this information not only on the package insert, but also wherever else information about the drug is provided — such as on websites, brochures, or television ads.

References

(ConsumerProtectionLawFirms.com, 2012)

Case 5: Influence of pharmaceutical marketing on a physician's prescribing behavior

(pharmaceutical marketing; off-label prescriptions; incentivizing in drug marketing)

During Dr. A's final year of medical school, he does a rotation at a primary medical doctor's (PMD) suburban practice. One of the patients there is a 40-year-old man with no history of psychological problems. However, Dr. A discovers that the patient has been taking a powerful antipsychotic for the last couple of months. Dr. A proceeds to question the patient about his psychiatric symptoms, and learns that the patient does not have any symptoms in the major categories of psychiatric disease (i.e., mania, psychosis, depression, and anxiety). The patient complains only of some mood trouble, explaining that sometimes he feels like he is "not himself" and can become more irritable with his wife. Dr. A is surprised by what he learns, and asks the PMD why he had decided to put the patient on an anti-psychotic drug. The PMD explains that, back when pharmaceutical representatives were promoting the drug a lot, he figured it would be a useful drug to help ease the patient's irritability. Hearing this, Dr. A is even more confident that the patient should not be taking the drug. He is also concerned about the influence that pharmaceutical marketing had on the PMD's prescription.

Ethical Question

Should drug companies have promotional encounters with physicians?

Possible Answers

- Yes. They help to educate busy physicians about medical drugs.

- No. They create bias in physicians about medications, influencing

their clinical judgments, when really physicians should only be considering patient needs.

Discussion

Regular meetings between drug company representatives and physicians in clinics and hospitals have become a common, everyday practice in many places. These meetings occur in many forms — such as short gatherings during the workday or lunch, or organized lectures for a department/team. During such meetings, information regarding drugs is distributed to physicians, and drug samples are often dispensed. Many times, these meetings will involve handouts of refreshments or of minor gifts such as pens, clocks and calendars displaying the company logo. This common practice is ethically problematic. On the one hand, drug representatives are usually very knowledgeable about the medications they promote: They can answer many questions, search for articles and evidence requested, and inform physicians about recent important information regarding a certain medication.

On the other hand, while seemingly neutral information exchange occurs, the primary purpose of these representatives is to effectively market their drugs and increase the likelihood that physicians will prescribe them. One result of this approach is that the information provided by the representative will tend to be biased in favor of promoting the medication, overemphasizing positive effects, and minimizing negative effects. Psychological techniques are often employed to do this, such as repeated exposure to the company logo, or creation of a sense of indebtedness in the physician's mind after a representative has searched for valuable information on his or her behalf or has provided a free lunch. These techniques can create an undue bias in the physician's mind towards the medication. This bias can even extend to other drugs within the same class of medications — or, more generally, to a preference for drug treatments over other interventions. Since these representatives also provide free drug samples, it becomes even easier for a patient to be started on a

medication. Perhaps most important is that much of the effects of these industry-physician interactions operate at an unconscious level. When asked about their own biases, physicians drastically underestimate the extent to which pharmaceutical marketing has influenced their own prescribing behaviors (Wazana, 2000). In general, the influence of pharmaceutical marketing in clinical settings strains the clinical neutrality that is essential for physicians to effectively tailor medical treatments to individual patients. Therefore, physicians should take care to: seriously consider the extent and consequences of their cooperation with any drug representative; overestimate rather than underestimate the effect that subtle social influences may have on their clinical judgments; and make efforts to obtain information regarding drugs from independent and varied sources.

Case 6: Early influences on physician prescribing habits

(hierarchy in medical professions; drug conferences; conflicts of interest; public perceptions of the health care professions)

A doctor in California has been a member of a university psychiatry department for over 20 years. He has published many journal articles related to the use of pharmaceutical medications. A major pharmaceutical company pays the doctor speaking fees to promote the use of one of its medications, which the doctor has previously researched. Residents from the psychiatry residency program attend some of the speaking engagements because they get to spend time with colleagues, receive a free meal amidst their busy schedules, learn about a new medication, and see prestigious doctors speak. The information they learn at the event emphasizes the positive aspects of the medication. During the course of the event, the interns make contact with the pharmaceutical representatives, who then arrange a follow-up meeting to further discuss the medications. At the follow-up meeting, the representatives emphasize various positive aspects of the medication, and some of the residents indicate that they will try to use the medication because of these reported positive aspects. Over the next few years, the residents prescribe the medication and maintain contact with the pharmaceutical representatives. The information the pharmaceutical representatives present to the residents is tailored toward the residents' interests. Over the course of years, it has become apparent that the residents prescribe and promote the medication produced by the pharmaceutical company over other treatment alternatives.

Ethical Question

Should physicians give company-sponsored educational lectures to other health care workers?

Possible Answers

- Yes. As long as the speaker says what he believes is true.

- No. The physician places himself in a situation that creates a conflict of interest between the patient's interests and those of the company which is paying him. This conflict of interest can potentially compromise patient care — even the mere appearance of this conflict may severely hurt public trust in the medical profession.

Discussion

Picture a situation in which your investment consultant receives payment from a trust fund that he or she suggests would be a good investment for you, based on the needs you have described. This is considered highly unethical in financial circles, and is usually illegal. Despite the illegality of such practices in financial circles, parallel practices exist on a daily basis in the field of medicine. This has major ethical consequences. First, consider the issue of trust. The practice of medicine in society depends upon public trust as a prerequisite for its organized existence. Implicit in the medical encounter is that the physician's main concern is the patient's best interest. Marketing strategies in which drug companies pay prominent physicians to endorse a certain brand of drug — either explicitly during the lecture, or psychologically by means of associating themselves with a given brand name — capitalizes on the presupposition that the physician is impartial. This practice results in a weakening of the public trust in physicians and the health care professions more generally. Moreover, as we see in the above case, such practices can create a bias in physicians towards certain medications. By creating an unjustified preference for a certain drug, this bias may steer physicians away from freely considering other treatment choices that are tailored to the individual patient. Even if all companies are engaged in such promotional practices, a bias could still be created in favor of the newer classes of drugs over the older ones, as well as in favor of medications in general over other forms of intervention (such as lifestyle changes).

It is worth noting, though, that, modern health care systems are underfunded, with insufficient resources outside of private industries to support necessary research and educational activities. Currently, without pharmaceutical industry funding, many of these activities would be severely diminished. The optimal framework, then, might be one in which industry can contribute to financing research and education, while also severing the direct link between a specific company and a specific physician or institution. In the absence of such a framework, it is the physician's duty to be as aware as possible of the influence of such practices; to minimize undue influence on residents, interns and students; and to ensure that his or her actions do not contribute to a weakening of public trust in medicine.

Case 7: Pharmaceutical access to physician prescription records

(drug data; marketing techniques; confidentiality; conflicts of interest)

Dr. C has been prescribing a new drug quite frequently. One day he receives a phone call from a pharmaceutical rep, thanking him for prescribing the drug and inviting him to a dinner sponsored by the company. Dr. C, who did not even know that the pharmaceutical company had access to his prescription records, is outraged by this intrusion into the way he practices medicine.

Ethical Question

Is it ethical for the pharmaceutical industry to have access to physician prescription information?

Possible Answers

- Yes. By having access to physician prescription data, pharmaceutical companies can tailor their interactions to physicians' needs, so that physicians are notified only about those medications they are likely to find useful. This approach helps both the physician and the pharmaceutical company: the physician does not have to deal with irrelevant marketing calls, and the pharmaceutical company has a higher chance of selling its drugs.

- No. Pharmaceutical companies often use this information to provide perks and biased information to physicians, so as to influence their prescription habits. This activity is unethical, since physicians' medical decisions should be based on the best interests of patients, not on incentives.

Discussion

A doctor's prescription record is a powerful tool in a pharmaceutical representative's hands. Although such records can serve as important data sources in medical research, they are also frequently used by pharmaceutical companies to inform drug marketing strategies and to tailor drug marketing to individual physicians.

Although such interactions might, in principle, be permissible if all that pharmaceutical reps did was provide objective information about drugs, this is not the reality. A pharmaceutical representative may use prescription information to encourage the physician to write more prescriptions for the company's drug, and fewer for a competitor's drug. Often these representatives are even paid bonuses for increasing company sales. Many physician-pharma interactions also feature incentives, such as pharma-provided gifts or meals. Doctors who receive these benefits may form positive associations with the company, and/or feel obliged to return these favors, potentially biasing their prescription behaviors.

Doctors should be allowed to decide whether or not they want the pharmaceutical industry to have access to their prescription data. Wherever possible, doctors should also strive to obtain drug information from more objective sources than pharmaceutical representatives, who (given their conflict of interest) are more likely to be a biased source of information. Particularly when incentives are involved, physician-pharma interactions become ethically problematic.

References

(Saul, 2006)

Case 8: Misleading claims by a pharmaceutical company in order to obtain funding

(pharmaceutical marketing; conflicts of interest; funding by health care programs)

A large drug company has been found guilty of misrepresenting the negative side effects of one of its drugs. The company had taken measures to make it seem as though the drug was less likely to cause diabetes than it actually was. The company had done this in order to obtain funds from a health care program. Details from the investigation reveal that the company had sent letters to thousands of doctors across the country, recommending the drug and saying that it was more effective than any other of its kind. The company had also made thousands of similar marketing calls.

Ethical Question

Should health care programs fund pharmaceutical companies, given that these companies may breach ethical codes in an attempt to maximize profitability?

Possible Answers

- Yes. health care programs have standards that they must adhere to when providing pharmaceutical companies with funding. These standards help to promote the development of medications that further the goals and objectives of the program, rather than that of the pharmaceutical company. Stopping this funding may lead to fewer medication options for health care participants, and continued suffering from their illnesses. Furthermore, pharmaceutical companies want to continue to obtain funding from health care programs, and

having a reputation for misrepresentation can lead to less funding for their endeavors. Therefore, these companies have an interest in promoting positive health for patients, and ensuring that they do not harm their reputation or the patients who purchase their products.

- No. health care programs know that pharmaceutical companies have financial motives, which may lead to biased advertising of medications. There have been many instances of pharmaceutical misrepresentation leading to adverse outcomes in patients. By receiving funding from health care programs, the pharmaceutical company not only gains financial support, but also benefits from the reputation of the health care program that is funding it. In order to maintain their relationship with — and funding from — health care programs, pharmaceutical companies may continue to present an overly positive portrayal of their medications.

Discussion

Health care programs play an important role in funding the development of pharmaceutical medications. Ideally, pharmaceutical companies use the money they receive to develop medications and market them responsibly. This can be a virtuous cycle, since patients who benefit from these medications are more likely to support further funding by health care programs, which, in turn, leads to further innovation from these pharmaceutical companies. The health care program gains a positive reputation, the pharmaceutical company is able to profit, and the patient population is healthier.

However, problems can occur when medications are improperly marketed. This occurs when the pharmaceutical company's motive to profit leads it to market its medications in a biased manner. Biased presentations may prevent patients and doctors from adequately evaluating or understanding the drug's side effects, potential long-term adverse effects, or the availability of other useful treatment alternatives. At the extreme, patients may even die.

Therefore, it is important for health care programs to monitor how the medications they fund are marketed, and for pharmaceutical companies to strive towards an accurate portrayal of their medications. Finally, it is important for doctors and patients to continually be informed about the benefits, risks, and alternatives to any treatment — including whether the best alternative is no treatment at all.

References

(Kleinpeter, 2012)

Case 9: Misleading marketing by a pharmaceutical company

(differential diagnosis; misdiagnosis; direct-to-consumer advertising)

Dr. D is concerned about a recent advertisement he has seen for an antidepressant. In the advertisement, a voice-over informs the viewer that "sometimes patients think they only have PMS" (Premenstrual Syndrome), "when in fact they may be suffering from PMDD" (Premenstrual Dysphoric Disorder). However, Dr. D notices that nothing in the images or text differentiates these two disorders. He suspects that the company is trying to broaden its market by suggesting that even patients with PMS are candidates for the new drug.

Ethical Question

Should the company market the drug to a wider audience, given the risk that patients who only have PMS may start to believe they have PMDD and ask for unnecessary treatment?

Possible Answers

- Yes. Patients should know details about different medical conditions — even conditions that can be mistaken for one another — so that they can make informed choices about treatment. Ideally, both the patient and the physician should have knowledge about a condition and a differential diagnosis, in order to best determine which treatment or range of treatments will be ideal for the individual patient.

- No. Pharmaceutical companies risk blurring the lines between different pathologies if they suggest that patients with one condition may, in fact, have another condition. Especially in vulnerable populations, for whom one treatment or a variety of treatments

has failed, there is a risk that patients will believe they have been misdiagnosed, leading them to seek treatment that may harm them.

Discussion

Different conditions may have differential diagnoses with similar and overlapping symptomatologies. In an effort to adequately address their ailments, patients may often try different remedies. Doctors attempt to accurately diagnose patients in order to provide them with accurate treatment. However, part of a doctor's diagnosis is influenced by the symptoms that the patient reports.

There are times when patients may learn about different ailments, and then self-diagnose. The danger occurs when patients falsely believe they have a condition that they do not in fact have, and then attempt to convince the doctor to prescribe them potentially inappropriate treatments. It is possible that, in these instances, patients may experience relief from their symptoms, and yet the underlying condition may not be optimally treated. At worst, patients can suffer from significant side or adverse effects from the treatment and — in addition to their underlying pathology — from an illness caused by medical treatment. They may even risk death.

Ideally, it is important for pharmaceutical companies to clearly state what condition their medication treats. Although off-label uses of treatments by physicians may be legal, off-label marketing by pharmaceutical companies may sometimes be illegal. When there is a risk that diagnoses will be confused, educating patients and providers about the source of this confusion can lead to informed patients and providers, appropriate treatment of underlying conditions, and decreased risk of unnecessary or harmful treatment.

References

(Stockbridge, 2000)

Case 10: Pharmaceutical marketing on a drug software application

(Internet pharmaceutical marketing; conflicts of interest; drug software applications)

A new company offers a Smartphone application that allows doctors to look up drug dosages, drug interactions, and insurance coverage while they are seeing their patients. However, this application also features many drug advertisements, which doctors must bypass before they can access the information they want. The application also remembers the search history of the doctors, so that the advertisements doctors see are always related to their interests. Some doctors are concerned about the possibility that the company will disclose their browsing histories.

Many doctors also think that the company promotes drugs that are more expensive and less effective, even though the company claims that it advertises only the most effective drugs. The company believes that medical practitioners will tolerate the advertisements in exchange for useful medical information.

Although some doctors believe that they are not influenced by the advertisements, the company has run studies showing that pharmaceutical companies profit for every advertisement featured on the application; the company is refusing to disclose this research, however, saying that it was funded by drug companies and is confidential. An independent study revealed that doctors exposed to the advertisements prescribe more expensive drugs of lower quality, and do so more often. Because 70% of the company's funding comes from the pharmaceutical industry, some medical practitioners are worried that the content of these advertisements may be biased.

That said, the company says it knows its success depends on doctors believing that the content is credible.

Ethical Question

Is it ethical for pharmaceutical companies to advertise their products on Smartphone medical applications?

Possible Answers

- Yes. Many doctors are aware that advertisements can influence their prescribing, yet they are still able to mitigate this influence by actively learning about alternatives, so as to present their patients with unbiased information. Applications like the one described in the case allow for faster access to accurate information, which can help the patient. Not using the application would lead to decreased knowledge about the advertised treatments and a greater inconvenience to obtain the information.

- No. Advertisements only provide partial information about treatment options. Being overly influenced by these advertisements can lead to: 1) the prescription of medications that may be too expensive for the patient, 2) the prescription of medications that may not have been on the market long enough for all potential adverse effects surrounding them to be determined, and 3) a decrease in the prescription of treatment alternatives, especially of those that have been on the market longer.

Discussion

Technology continues to evolve and many doctors now obtain information from a variety of platforms, such as from smartphones and tablets. Drug applications on these platforms are often accompanied by advertisements. Although many applications are free, the cost incurred by providers and patients is the influence that advertisements can have on prescribing behavior. Physicians should be aware that many of the medications prescribed may be expensive and may not have been on the market long enough for all their adverse effects to

be determined, since some of these effects may not have yet emerged during clinical trials. Even for advertised medications that have been on the market long enough for their safety risks to be fully determined, doctors must be aware of the possibility that they have been influenced to prescribe these advertised medications, without having made adequate cost/benefit analyses of available alternatives.

Doctors should consider reviewing available alternatives to different treatments on the market, so that they will be able to present patients with a variety of alternatives that can suit the patient's particular needs and circumstances.

Case 11: Commercial ties between a pharmaceutical company and a physician

(Internet pharmaceutical marketing; conflicts of interest; responsibility of medical staff; medical networking settings)

A few months ago, a doctor received an e-mail invitation to join an international medical networking site. Besides facilitating connections with other doctors around the world, the website claimed that it allowed transparent communication between doctors and pharmaceutical companies. In the beginning, the doctor was hesitant to communicate directly with any of these companies, but soon started interacting with one of them after filling out a survey about a drug it manufactured. The doctor then started receiving occasional updates from the company and found some of this information useful. After two months, some of these updates started including promotional material for the drugs. The doctor is afraid that this pharmaceutical marketing might influence his prescription decisions. Yet he is reluctant to discontinue the drug updates, which otherwise include useful information.

Ethical Question

Is it ethical for pharmaceutical companies to network with doctors on medical networking sites, given that these marketers have a vested interest in profiting from what doctors prescribe?

Possible Answers

- Yes. These settings provide valuable communication among medical professionals and allow for the exchange of ideas on various medical topics. If pharmaceutical participation in these settings is limited, then there is a risk that doctors will miss out on valuable information that would help their patients.

- No. These settings may give doctors the impression that both their colleagues and the organization sponsoring the networking setting support the treatments that are being advertised within the setting. This may lead the doctors to prescribe treatments for reasons other than drug efficacy rates, and possibly without proper consideration of the drug's side and other adverse effects. In general, these kinds of forums are supposed to be places where ideas are freely exchanged, and so any risk of doctors being influenced by pharmaceutical companies should be minimal or nonexistent.

Discussion

In current times, doctors network mostly over the Internet, through various organizations, at places of work, and at meetings. Any one of these venues may be frequented by sponsors or participants who have a vested interest in what doctors prescribe. Marketers who financially sponsor a networking forum may have an influence on how, where, and when they have access to the people attending these forums. A doctor may be exposed to a number of marketing pitches that are either formal or informal in nature.

It is important for doctors to be notified which marketing entities will be participating in a given forum and how these entities will interact with attendees — for instance, whether attendees have the option to limit contact with these entities, or to not interact with them at all.

References

(D'Arcy & Moynihan, 2009)

Case 12: Pharmaceutical company's marketing influence on a doctor's medical practices

(conflicts of interest; hierarchy in medical professions; incentives)

Dr. E is an anesthesiologist who has started assisting with surgeries at a local hospital. During the anesthesia, the anesthesiologist must administer what are called "pharmacological agents" to the patient. In this hospital, the surgeons decide what pharmacological agent the anesthesiologist should administer in order to reach the desired effect. After working at the hospital for a month, Dr. E realizes that the doctors always request Drug B, even though there is a cheaper generic (same drug, cheaper brand name) available. After further investigation, he finds out that Drug B is made by Company B, while the generic is made by a different company. Dr E. asks the surgeon why he always chooses to use Drug B. The surgeon answers: "because it is better," without further explanation. Dr. E finds out that the surgeons are also occasionally invited to meetings at Company B, where products are presented and free food is offered. However, Company B is not the only company that engages in these kinds of practices, and it is unclear whether the surgeons are receiving anything else besides the free meals from Company B. No one in the hospital has raised the matter for discussion, and there has been no hospital hearing about it.

Ethical Question

Should the company refrain from inviting doctors to promotional meetings, and from serving free food?

Possible Answers

- Yes. The marketing activity of inviting doctors to free meals is unethical, as it biases doctors' judgment. Needless to say, if doctors

also receive other benefits from the company (besides the free meals) then this is definitely a major breach of ethics, as it may add to the doctor's bias. Although there is supposedly no difference between the original and the generic drug, the doctors may have had no real data on which to justify their preference for the original drug. Doctors should be very conscious of the reasoning behind their use of different medications — "because it is better" is not a sufficient answer to the colleague's enquiry.

- No. It is assumed that both the doctors and the pharmaceutical company are honest and careful to avoid undue influence, making it unlikely that the good meal would skew the doctor's prescription decisions. On the other hand, it is reasonable to believe that the company will present its data in a favorable light, making it important that the doctor also gain first hand access to the data. The company should also use these meetings as an opportunity to ask doctors for feedback about the quality of its drugs and drug information provided, so as to ultimately improve this quality.

Discussion

Human beings cannot be totally detached from their environment and interactions with other people. Therefore, even when a doctor believes that he is completely neutral and objective, it is unlikely that he can escape feeling thankful to people who have provided him with pleasure and enjoyment. Therefore, there is a real possibility that such incentives will bias the doctor's prescription behavior. Although it is unlikely that a physician will prescribe a drug that is not appropriate for a patient, there is a higher potential for bias when a physician is choosing between different drugs that have similar effects. If the only difference between drug alternatives is the price, a doctor may forget about the hospital budget, or about how exhausting these limited funds may result in decreased resources for other patients. A feeling of moral indebtedness to a company that has provided the doctor with pleasure may lead the doctor to prescribe the more expensive drug.

It is not clear whether the surgeon who said he preferred Drug B "because it is better" really believes this, or whether he was just trying to quell Dr. E's curiosity about his choices (or even his potential bias). There is a possibility that the surgeon, who had been previously exposed to company B's free meals and other pleasures, may have simply convinced himself that the drug manufactured by company B is really better than those made by other companies.

The surgeon's decision to prefer the more expensive drug B over the less expensive generic also has repercussions for the public, who may consequently have fewer resources available to them from the diminished hospital resources.

Case 13: Ethical obligations of an industrial doctor

(conflicts of interest; ethics of medical staff; formularies)

Dr. J has recently been employed as an industrial doctor at a pharmaceutical company, making him responsible for the treatment of health issues in the workplace. A number of times, Dr. J has felt conflicted when trying to decide whether to prescribe the drug he believes is really best, versus a similar drug that is manufactured by the company. He feels added pressure when making these decisions, because the company makes its own manufactured drugs cheaper to its employees. Sometimes, when he prescribes a drug known to have a company equivalent, he receives concerned questions from company employees regarding the efficacy or safety of the company-manufactured drugs. Despite being concerned about these questions, he still does not feel comfortable prescribing some of the company-manufactured drugs, which he knows carry more side effects.

Ethical Question

Should Dr. J mainly prescribe medications that his employer has a financial interest in, and that are also cheaper to employees, but carry more potential side effects? Or, should he prescribe potentially better medications manufactured by other companies, but then risk hurting the company's reputation to its employees?

Possible Answers

- Yes. The doctor should prescribe the company's medications. The medications provided by the company are cheaper and will help to conserve financial resources. Furthermore, even though the company's drugs carry more side effects, they are good drugs with which to begin treatment — more expensive alternatives can be considered at a later stage, if needed.

- No. The doctor should not mainly prescribe the company's medications. The company's medications are known to have additional side effects, compared to alternatives. Even though the company-manufactured drugs are cheaper, the chance that these drugs' additional side effects may adversely affect patients is too great a risk to justify using these drugs.

Discussion

It is not uncommon for some organizations to have only certain medications on formulary. Such medications are usually cheaper and require fewer additional levels of approval. Doctors in such organizations may sometimes have no access to expensive alternatives.

What should doctors do to obtain the best treatment for a given patient? Depending on how we define "best", the best treatment may not necessarily be the most efficacious, but rather, a relatively effective drug that is also affordable to the patient over the long term. A problem is introduced when none of the medications from the formulary are optimal for a given patient. Furthermore, industrial doctors may feel additional pressure to prescribe company drugs, in order to ensure company employees' confidence in the drugs the company is manufacturing. At the same time, if the formulary only/mostly includes company drugs, patients might doubt whether they are truly receiving the best treatment (as opposed to whatever treatment is most cost-effective for the company). These patients may lose confidence in the company's health care system as a whole, potentially leading to nocebo effects when they take the company medications, or leading them to seek treatment elsewhere.

Doctors still need to educate patients about treatment alternatives not immediately available to them or preferred by the company. Although the company has a desire to treat its patients while also saving money, any individual patient may not necessarily put the same weight on these company values. For instance, a given patient may prefer a more expensive alternative to a company equivalent. When obtaining the

treatment they most desire, patients should have the option to utilize other services or benefits not provided by the company. Given that doctors may sometimes need to make prescriptions that are not in the best financial interests of the company, it is important that there also be measures in place to safeguard doctors' job security in such instances. Although such prescription decisions may potentially decrease employee confidence in the company's drugs, the patient's health must be the first priority.

Case 14: Pharmaceutical subsidizing of clinical trials

(violation of equipoise; research incentives; conflicts of interest)

A researcher works at a company that conducts clinical trials on new drugs before the drugs are permitted to enter the market. Although the researcher has only been working at the company for a month, he finds the work both meaningful and enjoyable. He meets with a pharmaceutical representative from a very well known company, who explains that the company wants him to conduct clinical trials on their newest drug. The representative informs him that, in addition to financial compensation for his research, they are offering him additional compensation contingent upon the success of his research.

Ethical Question

Should a research company offer benefits for a researcher's work that is based upon the success of the research, if doing so might lead the researcher to report excessively positive results from the research?

Possible Answers

- Yes. Providing additional benefits/compensation is necessary, because doing so increases the company's chances of acquiring and retaining dedicated, talented researchers, who discover treatments that benefit both the company and the patients.

- No. The research results can potentially be biased. There is a risk that, by the time the medication reaches the market, adverse outcomes that could have been detected at earlier stages in the development and clinical trial process will lead to patient harm.

Discussion

Researchers strive for objectivity in their results through the scientific process. However, other factors may influence how researchers report

their results, such as a motivation to publish positive results in favor of research that did not actually yield any useful results. The academic and financial rewards are greater for researchers who make more substantial discoveries and publish more articles.

The problem occurs when the incentive or pressure to find favorable results distorts the scientific process that the researcher employs. At worst, data may be fabricated or withheld. By the time the drug reaches the market, it may inaccurately appear to provide more benefits or carry fewer side effects than it truly does. Such a portrayal may lead to harmed patient health, and even patient death.

Researchers should be aware of any — even seemingly harmless — incentives to provide positive results. In doing so, researchers should then work to minimize the effect of these motivators on the fidelity of their scientific discoveries and communication of results.

References

(Pfizer, n.d.)

Case 15: Requisite publication of clinical trial results by a pharmaceutical company

(clinical trials; meta-analyses; conflicts of interest; online publication of research)

A meta-analysis has finally been conducted on an anti-diabetic drug that has already been on the market for three years. This is the first study of this drug that combines data from all previous clinical trials carried out on it, and the first to give a full explanation of the heart-related and other risks associated with taking the drug. Such a meta-analysis might have been completed sooner, but the pharmaceutical company that manufacturers the drug had published only two of the major clinical trials that ultimately formed part of the meta-analysis. Only four months ago, however, the company finally released the results from the other trials, after receiving a warning from the drug administration for suppressing this clinical research. The company posted the research on a poorly constructed website, which is very difficult to follow. Furthermore, the company did not publicize the website and never attempted to conduct its own meta-analysis of the clinical trials. In retrospect, this behavior is concerning, given that the new meta-analysis shows serious implications for use of the drug in elderly populations and reveals that previous studies have not sufficiently investigated the effects of the drug on pregnant women. A legal investigation of the company is currently taking place, revealing other alarming information — such as the fact that many company researchers had been concerned about the drug risks all along, but yet had been silenced by the company.

Ethical Question

Do company researchers have an ethical responsibility to publicize their concerns about a drug's risks?

Possible Answers

- Yes. The researchers who were involved in the development of the drug had a moral obligation to society and potential users of the drug to publish their concerns, since they were the people who developed the drug.

- No. The researchers form only one component of the company, and their role is limited only to the scientific development of the drug. Responsibility for issues concerning usage of the drug by the end user is solely the responsibility of the management and the marketing people. Once the researchers revealed their concerns to the management, they fulfilled all responsibilities expected of them.

Discussion

Even the highest esteemed scientist needs to earn a living, and perhaps provide for the basic needs of his or her family. Therefore, scientists will be hesitant to voice concerns, if doing so may put their jobs in jeopardy. It is important that companies have systems in place that allow workers to publicize concerns without also putting their own financial livelihoods at risk. Awareness of these concerns may allow the drug in question to undergo a more thorough investigation, which may reveal any problems with the drug that would otherwise go undetected.

The drug may need to be taken off the market completely, its drug information revised, or its indications restricted, among other possible consequences. Given that these actions will likely cost the company money, the company may have a financial incentive to avoid any of these consequences. However, there is no justification for putting patients' health at risk, which is exactly what the company would be doing by ignoring or discouraging these concerns. Furthermore, the potential reputational and legal costs that the company could suffer, in the event that its attempts to hide information about the drug's risks were discovered, could be far worse.

Case 16: Malpractice during a vaccine trial

(clinical trials; informed consent; kickbacks; collaboration between pharmaceutical companies)

The court found two pharmaceutical companies — Company J and Company B — guilty of malpractice during a vaccine trial. Both companies have been fined very large sums of money. The vaccine was intended to treat severe diarrhea, and the clinical trial was conducted in a number of rural villages where this health problem prevails. Company J, the larger of the two companies, was responsible for both manufacturing the drug and formulating the clinical trial guidelines. Company B was responsible for the implementation of the clinical trials, as well as for recruiting participants to the trials. Families of participants have raised a number of accusations against the companies, but there remains much uncertainty surrounding the case, especially since both companies have denied all accusations. To complicate matters, since Company J was not based in the country where the trial was conducted, there seems to have been a communication gap between the two companies during the trial.

Some trial participants complained that they were not allowed to read the lengthy consent documentation, because (they were told) there simply was not enough time, given that many other participants also wanted the vaccine. While Company B completely denies this accusation, Company J claims that it does not know whether or not it is true, and is still investigating the case. Some participants also claimed that the consent material contained a number of scientific and technical terms that they did not understand. Furthermore, worried families of participants had reportedly attempted to contact doctors during the trial, but the doctors had been completely unresponsive. Unions claim that doctors were paid for every participant they could recruit toward

the study. However, both companies say that there is no evidence to support these accusations, claiming that such behavior, which is completely against trial guidelines, would never have gone unnoticed. The guidelines themselves have recently been submitted to the court, as they were not previously available to the public. The companies have accused unions of spreading terror among the families of participants, and of encouraging families to spin erroneous accusations in the hope of making money off the pharmaceutical industry.

Ethical Question

Was Company J breaching ethical codes through its lack of involvement in the clinical trial and its failure to ensure that Company B fully disclosed trial information to participants?

Possible Answers

- Yes. Company J was the dominant of the two companies, as it was the manufacturer of the vaccine and designer of the trial protocol.

- No. Company J made sure that a local pharmaceutical company, Company B, was in charge of the actual conduct of the trial. This responsibility includes providing full disclosure to trial participants.

Discussion

From a strict, legal point of view, Company J may have a good argument for assuming that Company B should have taken all the necessary measures. However, as the manufacturer of the vaccine and designer of the clinical trial, it had at least the moral and ethical obligation not to leave loose ends regarding whether these measures were in fact being implemented. Rather, it should have ensured that Company B was indeed adhering to the strictest rules of trial protocol, which include full disclosure of the data to participants in the trial.

References

(Rada, 2012)

Case 17: Conflicts of interest in a seeding trial

(conflicts of interest; seeding trials; drug administrators; review boards)

The primary purpose of a "seeding trial" is not so much to conduct research on a drug as it is to familiarize doctors with the drug. A pharmaceutical company will identify a number of doctors, then ask them to provide subjects to participate in the clinical trials. Doctors are paid for every subject they can recruit for these trials and are given feedback on the trials' results. In a recent investigation, a pharmaceutical company was accused of running its seeding trials very poorly: the investigators were inexperienced and untrained, 60 patients were harmed by the drug, and 10 patients died. Despite these negative outcomes, the trials have attracted little attention and nothing has been done about them. In fact, it appears that the company may have only been pretending to run scientific trials, using the "seeding trials" as a cover story in its attempts to market its drugs to doctors. The national drug administration permits seeding trials, because the drugs used in them are those already approved by the administration. The only other obstacle in the way of conducting a seeding trial is an experiment review board, which determines whether or not the study is ethically sound. These boards seldom have the required expertise, however, to differentiate between the studies that are for genuine research and those that are simply for marketing purposes. Furthermore, these review boards are often for-profit themselves. As such, they are often pressured into being less strict, since review boards with reputations for being strict can simply be avoided by pharmaceutical companies, who can go to more lenient boards instead.

Ethical Question

Should doctors receive payment for recruiting subjects for seeding trials of already approved drugs, given that these trials are directly intended to

"familiarize" doctors with how to use the drugs, and may also indirectly increase a company's sales?

Possible Answers:

- Yes. Seeding trials enable doctors to familiarize themselves with the use of the drug and to monitor efficacy and safety issues surrounding the drug. It is only fair that doctors be paid for their efforts in finding subjects, and for filling out forms, questionnaires and case reports for participants. After all, a busy doctor's time is valuable, and the doctor's help may significantly contribute toward the drug's ultimate marketing success.

- No. Doctors should not be paid for recruiting patients for seeding trials, since the combination of medical and financial incentives (for both the doctor and drug company) may not work to the benefit of patients, but rather, may serve as a means of masking payment to doctors for using a company drug.

Discussion

Human beings cannot totally detach themselves from financial temptations. Paying doctors to recruit patients for seeding trials involving products for which most of the data has already been revealed may tempt doctors to recruit patients who are not quite suited to a given drug. In such instances, patients are deprived of more suitable treatment, putting their health in jeopardy.

Another consideration is that paying doctors to recruit subjects for clinical trials involving a particular drug product may still be perceived as a bribe by patients and colleagues, regardless of whether the doctor actually treats it as such. This perception may breed a lack of trust in the doctor and in the institution or health care profession in general. Patients in these situations may choose to avoid treatment altogether or to seek their own alternatives, which — given their lack of expertise in making informed medical decisions — could potentially put their health at risk.

Case 18: The use of placebo as an alternative to drug medication

(placebo effect; clinical environment; therapeutic discretion; pharmaceutical research incentives)

The placebo effect (the phenomenon of a patient's medical improvement after taking an inert substance) has been both a blessing and a curse in medicine. On the one hand, it illustrates the power of the human body to heal itself, and on the other, it suggests that some of our own treatments are only a small improvement upon a sugar pill. And although drug studies repeatedly reveal that placebo pills may be useful in treating a multitude of illnesses (including depression and hypertension), pharmaceutical companies are understandably reluctant to invest in randomized controlled trials to study the placebo effect, because they have very little financial incentive to do so. The pharmaceutical bias against the placebo effect is particularly concerning given that it is becoming increasingly difficult for experimental drugs to prove their superiority to sugar pills in trials carried out by the drug administration.

The growing field of placebo research, however, has affirmed the body's power to heal itself, including its ability to reduce pain and inflammation, lower the production of cortisol (released in response to stress), and even lower blood pressure and tremors. This speaks to the potential for doctors to use placebos as a much cheaper and equally effective way to treat disease, but heretofore the placebo effect has been based on deception: in studies, patients are told that these pills are the real thing, not just sugar. Hence the ethical dilemma, since doctors would rather not lie to their patients.

A recent study may change this trend. Researchers at Harvard University tracked the health of 80 volunteers with irritable bowel syndrome (IBS) for three weeks, while half of them took placebos

and the other half did not. In a previous study, the same group of researchers had demonstrated that placebo treatment could be highly effective for alleviating the symptoms of IBS. This time, however, the trial was "open" instead of "blinded," such that patients were also informed that the body could heal itself with the help of placebo.

Results showed that the combination of a placebo, the lesson of the "placebo effect," and a supportive clinical environment was an effective way to treat IBS. People in the placebo study improved on standard scales of symptom severity and overall quality of life. In fact, the volunteers in the placebo group experienced improvement comparable to patients taking a drug treatment (the current standard of care for IBS).

Ethical Question

Should researchers expose patients to the potential hazards of an experimental drug when pharmaceutical trials have revealed the possibility that patients could be helped with just a placebo pill?

Possible Answers

- Yes. Even though some of the patients who participate in clinical trials and who are treated with experimental drugs could be helped with just a placebo, the benefit of a new drug — if proven effective in clinical trials — could still serve very wide population groups suffering from that particular disease. Therefore it is crucial that the study be conducted in a way that enables researchers to come to a definite conclusion regarding the efficacy and safety of the new drug. Such a conclusion can be determined with a high degree of confidence only when two treated groups are compared — the active drug group and the placebo group. Therefore, it is important that companies leading clinical trials ensure that one group of participants be treated with an active drug, while the other group be treated with a placebo.

- No. Placebos are clearly a safer, cheaper alternative, and although using them entails a kind of deception of the patient, and also means

less profit for companies, these drawbacks are validated by the efficacy of the treatment.

Discussion

There is consensual agreement that treatment with placebo may be efficacious in various illness conditions, and the IBS case described is only one example of such positive placebo effects. Therefore, if the doctor believes that the patient can be helped merely by placebo, he should not deprive the patient of such an option. When it comes to clinical trials, in which it is important to maintain the blindness of the study (in order prevent bias when the patients or the doctors know which patient received the active drug), it is important to explain to the patient the purposes and methodology of the study and the importance of the "blindness" of the study. If the patient gives full informed consent to the possibility of being treated with the active drug — even though there may be a possibility for him/her to be helped by a mere placebo — then the ethics could be much more favorable.

References

(Kaptchuk et al., 2008)
(Kaptchuk et al., 2010)

Case 19: Approval of a new drug by a drug administration

(drug administration; clinical trials; 'quality of life' drugs)

The national drug administration has decided not to approve a new drug that claims to restore a depressed female sex drive, as the pharmaceutical company that manufactures the drug did not conduct a proper case study, and the benefits of the drug were minimal. Additionally, the drug had many side effects, including dizziness, nausea and fatigue. The drug administration explains that, although clinical trials were run on the drug, there were too many patients excluded under "medical criteria," and so it is not clear whether the results of the study apply to all women or not. The drug administration is worried that the drug might interact too easily with other medications in a manner that might harm patients.

Ethical Question

Should a drug administration approve a drug that is aimed "merely" at improving the quality of life, and not necessarily at saving life?

Possible Answers

- Yes. It is unethical for the drug administration not to approve a "life quality" drug without first considering the available clinical trial data for the drug or, if necessary, giving the company another chance to readdress the data — even if this means repeating the clinical trials.

- No. The drug administration has the mandate and the obligation to ensure that any drug submitted for approval meets all efficacy and safety criteria according to medical standards. The less severe the medical condition for which the new drug is indicated, the stricter the requirements should be for the clinical trial data that the company submits to the drug administration.

Discussion

The drug administration operates according to strict regulations, which aim to ensure that only safe and efficacious medications are marketed. Although there are rare cases involving lifesaving drugs in which it may be unethical not to approve drugs that have potential lifesaving effects — even if these drugs carry heavy side effects — in most cases it is fully the duty of the administration to approve or not approve drugs. This approval will be influenced by whether or not, based on their evaluation criteria, the administration is satisfied with the investigational data. As long as these criteria are met, it should be possible for a "quality of life" drug to eventually reach the market.

Case 20: Conflict of responsibility between a pharmaceutical company and a drug administration

(limits of responsibility; boundaries of informed consent; drug risk information; rare drug risks)

Dr. L administers a drug intravenously, or by the "drip," to a patient, and a day later the patient develops gangrene in her arm and has to have it amputated. In the local court, Dr. L claims that the pharmaceutical company that manufactures the drug failed to provide an adequate warning about the significant risks of administering the drug via the intravenous method. The local court agrees, and awards the patient damages. However, the pharmaceutical company appeals the case, arguing that because the drug had been pre-approved by the drug administration, the company cannot be accused of failing to provide drug warnings. Furthermore, the company argues that the odds of such an infection occurring are 20 such instances in about 200 million injections. The case is taken to the national court, where the ruling is made in the company's favor.

Ethical Question

Should a pharmaceutical company warn doctors or patients of rare side effects that the company is aware of, if the federal drug administration has not required that the company include such warnings?

Possible Answers

- Yes. The company has an ethical obligation to reveal all potential, even rare, side effects to its potential drug users and especially to prescribing physicians. By not doing so, the pharmaceutical company

breaches the autonomy of both the patient and the doctor, who should be able to decide for themselves whether or not they are willing to take the risk of using the drug.

- No. The company is not expected to list all rare potential adverse drug reactions, since doing so may frighten patients and doctors, and deprive patients of a potentially highly effective treatment for their ailments.

Discussion

This case points towards a definite ethical question, since the law (the appeal courts) ruled that from a legal point of view there were no breaches of the company's tort obligations.

However, as an ethical company dealing with products that may determine the fate of real people, the pharmaceutical company should operate not only according to good business conduct and legal criteria, but also according to ethical considerations. The pharmaceutical company should bear a moral and ethical obligation to protect the safety of its potential customers, the patients. Hence it should take all necessary and appropriate measures to safeguard the health of patients, regardless of the negative influence this may have on company profits. When listing possible side effects, companies should also highlight the most likely risks, so that patients do not merely experience information overload, either in marketing materials or in print. That said, this might not preclude the ethical obligation to include information about rare potential adverse drug reactions.

Case 21: Granting a clinical trial waiver to a pharmaceutical company

(clinical trial waivers; conflicts of interest; extension of drug patents)

A large pharmaceutical company has received a waiver from the national drug administration for assessing the effectiveness and safety of a drug for Bipolar Disorder and Schizophrenia in children. The company currently sells the very same drug as a treatment for Bipolar and Schizophrenia in adults. Only six months ago, the company received funding to assess the effectiveness and safety of the same drug for autism. Some wonder whether the fact that the company had been granted prior approval for studying the effects of the drug in child populations made it easier for it to obtain the most recent waiver. Some also question whether the new intended uses of the drug are simply a way of extending the drug's existing patent for the treatment of Bipolar Disorder and Schizophrenia in adults, which is soon set to expire. The drug administration's decision to waive the drug trials may have also been influenced by the fact that the researchers hold stock in competing companies. Although this in itself may have been potential cause for investigation, the drug administration said that, because the stocks were not worth a very large sum of money, they did not think these holdings were enough to constitute a conflict of interest.

Ethical Question

Should a pharmaceutical company try to influence the drug administration to approve additional indications for its drugs by using the techniques described in this case?

Possible Answers

- Yes. The company did not breach any ethical codes. On the contrary: it channeled all its activities to the further development of new indications, in full coordination with the drug administration.

- No. The company used shortcuts for approval of clinical trials of one indication in children by conducting a clinical trial of another indication (autism) in children. This approach may unnecessarily introduce side effects of the new indication for children.

Discussion

The regulatory responsibility for approval of the use of pharmaceutical drugs is within the domain of the drug administration. However, the manufacturing company that developed the drug, which may have much more data on the drug, should not manipulate the drug administration. A pharmaceutical company that claims that all its actions have been approved by the drug administration, so that the company is not breaching regulatory regulations, may still be breaching ethical principles. The ethical obligations of pharmaceutical companies are aimed primarily towards the users of their drugs, not necessarily towards the drug administration.

References

(Gibb, 2007)

Case 22: Changing the diagnostic threshold of a psychological disorder

(diagnostic thresholds; pharmaceutical marketing; balancing benefits; conflicts of interest; over-prescription of medications)

Historically, bipolar disorder was thought of as a single category of psychiatric disease. However, in 1994 Bipolar II was added to the national classification of mental disorders. Unlike Bipolar I, in which the patient experiences periods of depression and mania (a state of abnormally elevated or irritable mood, arousal, and/or energy levels), patients with Bipolar II experience periods of depression and hypomania (milder symptoms of mania). Bipolar II can often be confused with unipolar depression, as both illnesses involve long periods of depression. However, it is useful to be able to identify patients with Bipolar II, as they must be treated with different medications from those with unipolar depression. In particular, antidepressants that would be effective at treating unipolar depression may be ineffective at treating the same symptoms in someone with Bipolar II; moreover, they may even increase such patients' risk for developing a manic episode.

Despite the practical benefits of this new classification, however, there have also been some associated consequences in the form of an overall increase in the diagnosis and treatment of bipolar disorder. On the one hand, this may be due to better diagnoses of newly classified patients. On the other hand, the explosive growth of bipolar diagnoses may be attributed to aggressive drug-company marketing of new drugs aimed at increasing public and physician inclination to regard irritability and even relatively minor mood elevations as indicators of bipolar disorder. The cost to patients of taking these medications is high: the

medications can cause significant weight gain and increased risk of diabetes, heart disease, and elevated cholesterol.

Thus, although the harm of prescribing incorrect medications to patients with bipolar has now been largely avoided, the harm of potentially over-prescribing medications with serious side effects to other populations has been created. Many doctors think that the problem has been compounded by misleading drug studies carried out by drug manufacturers, as well as by direct company-to-consumer and company-to-physician marketing.

Ethical Question

Should doctors use information provided by pharmaceutical companies — including research studies carried out by drug manufacturers — to influence their diagnostic categories and prescribing habits?

Possible Answers

- Yes. The research pharmaceutical companies conduct can be used to illuminate doctors' understanding of mental illness. Not using this information when it is available would be irresponsible.

- No. It is unethical for doctors to make decisions based on information provided to them by drug manufacturers.

Discussion

Certain factors may make accepting information from pharmaceutical companies appealing to doctors and patients. For example, the information companies provide may be more accessible than that from other sources, especially due to direct-to-consumer advertising and events hosted by pharmaceutical companies to which doctors are invited. Also, doctors may be paid for their endorsement, or for using drugs manufactured by pharmaceutical companies.

However, there is a possibility that the company may be biased in the information it promulgates. For example, there have been reports of 'ghostwriting' of scientific articles by pharmaceutical companies,

in which researchers are paid by pharmaceutical companies to report specific results, and in some cases data contradicting a drug's supposed efficacy have been suppressed or even altered. Thus, doctors have to be aware that there may be inherent conflicts of interest in a pharmaceutical company's conduct of research, as well as in its marketing of information about the drugs it manufactures. Keeping these considerations in mind, as well as the medical duty to choose the treatment that best suits a patient's needs, doctors have a responsibility to examine any drug information they receive for evidence of bias before allowing this information to influence their clinical decisions. It would be unethical for doctors to accept information from a pharmaceutical company without first scrutinizing it carefully.

Case 23: Lobbying by pharmaceutical companies

(pharmaceutical lobbying; ethical and moral commitment of pharmaceutical companies to drug consumers; drug costs; patient welfare)

Patient E is a senior citizen who spends a set amount of money every month on anti-depressants. Recently, he has been very concerned about how expensive the drugs have become and his lack of medical aid to cover these costs. In desperation, he starts surfing the Internet for a cheaper alternative and finally finds one. The next day, Patient E goes to the nearest pharmacy to buy the drug he found, but is dismayed to learn that he is not allowed to do so. The pharmacist informs him that the medication is a foreign-made prescription drug, and that there are laws preventing the import of prescription drugs.

Frustrated by the news, Patient E returns home and does some online research on this law. He discovers that although the government had previously been considering the legal import of prescription drugs, the decision was most likely prevented by the interference of pharmaceutical companies: The companies had paid millions to government officials to influence their collective decision regarding this law. Patient E learns that the companies did this to avoid having to compete with foreign drug prices. He is also surprised at how much company earnings have increased after the passing of the law, and is angry that so much money is going to pharmaceutical companies when taxpayers like him suffer exorbitant prices.

Ethical Question

Should pharmaceutical companies lobby with the government in this manner?

Possible Answers

- Yes. Pharmaceutical companies have the right to lobby for political and policy decisions that favor the marketing and selling of their drugs.

- No. It is unethical for pharmaceutical companies to spend money to influence government decisions, as this behavior may result in policies that end up harming patients.

Discussion

Pharmaceutical companies have an interest in maintaining profits, so it is not so surprising that they would use various techniques, such as lobbying and marketing, to promote sales. In this particular case, however, they are trying to achieve an unfair advantage by maintaining a monopoly on the sale of a certain drug. This kind of activity comes at a cost to individual citizens, who suffer the economic burden of expensive drugs: some patients may be forced to pay for cheaper, but less effective, medications; others may not be able to afford even the cheapest of these overpriced drugs.

Furthermore, it does not seem to be the case that the pharmaceutical industry is trying to protect its intellectual property rights over the drug it has developed; rather, it is trying to remove the competition from another, equally effective, but cheaper, drug. This behavior is unethical, as it involves an unfair financial advantage at the cost of patient welfare.

References

(Ismail, 2005)
(Zimmerman, n.d.)

Case 24: The court's involvement in a pharmaceutical case

(conflicts of interest; ghostwriting; legal penalty; admission of guilt)

An investigation was launched on a well-known pharmaceutical company for its marketing of an anti-inflammatory drug that was used by millions of people. Reports revealed that the company was marketing the drug even after discovering that it increased the risk of heart problems. The company was also charged with trying to minimize the drug's risks, publishing conclusions that were incompatible with the evidence it obtained, and even setting up its own online "academic journal" in which to publish the results. The local court found the company guilty of many of the charges. When the case was taken to the national court, however, the company managed to settle it for a very large sum of money without having to plead guilty to any of the charges.

Ethical Question

Should the court allow the company to settle the case by paying a large sum of money, without returning a verdict on whether or not the company is guilty of the charges in the first place?

Possible Answers

- Yes. The court's decision was ethically correct, as justice was served through the company's payment of the large sum of money.

- No. Since the court's resolution of the case did not also require an admission of guilt from the company, the court's punishment was unethical and insufficient.

Discussion

Pharmaceutical companies have large sums of money at their disposal to aid in their defense. This money allows them to influence the extent of punishment that is exacted by courts. However, a proclamation of guilt carries enormous weight in the minds of the public and even to the pharmaceutical companies themselves. This can be achieved either by a verdict of "guilty" or, in the case of a settlement, an admission of wrongdoing by the guilty party. Both of these outcomes have the advantage of signaling culpability, which can influence consumers to be more wary of the claims of a pharmaceutical company. Moreover, a pharmaceutical company's admission of wrongdoing in such a case creates an atmosphere of accountability that can influence other companies to be more strict and ethical in their research and marketing practices. Thus, findings or admission of guilt can lead to changes in consumer and pharmaceutical behavior that together increase the wellbeing of consumers.

Case 25: The court's flexibility in a pharmaceutical case

(conflicts of interest; company stock; categorical vs. contextual decisions; interests of shareholders)

A pharmaceutical company is being investigated because the nasal spray it manufactures has been found to cause a loss of the sense of smell: a condition called anosmia. Investigations reveal that the company had received scattered reports about this problem for three years prior to the opening of this case. However, the company did not disclose these reports and at the beginning of the year said that it was ready to continue company growth, despite the fact that the nasal spray accounted for 70% of its sales. Soon the news about the nasal spray's side effects became public, and the company stock price dropped significantly. Finally, the national drug administration warned the public not to use the product.

In the court case, the company argued that it should not be expected to disclose a number of small, scattered reports that do not show any statistical relevance; it stated, "Every pharmaceutical company receives daily complaints about supposed side effects." Despite these arguments, the judge decided that the company should have published these reports, as they included information that would have influenced "any reasonable" shareholder's stock-buying decisions.

The court also clarified that it was not implying that companies should publish every single negative report on their drugs, but that they should take into account the "source, content, and context of the reports." In this particular case, the court explained, the reports had come from a number of medical professionals and showed that eleven patients had suffered adverse effects. These results were concerning enough that the company should have made them public and investigated

them further. Court officials stated, "The reports suggested that the drug caused a loss in the sense of smell, exactly the kind of information that shareholders would want to know." In an interview, the judge was asked exactly how we could ever know when to take scattered reports seriously. The judge simply repeated a variant of her previous statement: "The test is what a reasonable person would react to, given all the evidence."

Ethical Question

Should a pharmaceutical company adhere to a categorical (rather than contextual) rule in deciding to publish reports on side effects?

Possible Answers

- Yes. If reports regarding a drug's side effects do not reach statistical significance, a pharmaceutical company is under no ethical obligation to disclose them.

- No. It is unethical for a pharmaceutical company to decide whether to disclose reports on a drug's side effects based solely on whether these reports reach statistical significance.

Discussion

Since categorical rules often fail to account for the complexity of life, courts sometimes use a contextual inquiry to settle questions of wrongdoing. This practice is supported by well-accepted empirical methods of establishing causation other than statistical significance or expert consensus (Bursztajn et al., 1981/1990; Hill, 1965; Mill, 1843/2002). One such method is the challenge/dechallenge or challenge/dechallenge/rechallenge case report. This empirical method involves tracking whether or not an adverse event occurs when a person initially takes a medication (challenge), when the medication is discontinued (dechallenge), and when the medication is resumed (rechallenge). The strength of causation increases when the adverse effect ceases or subsides on dechallenge, and increases even more when the adverse effect returns on rechallenge.

The "reasonable person" standard is often applied to matters regarding the disclosure of side effects by doctors and pharmaceutical companies. This standard is useful for cases in which a drug may cause rare side effects and in which reports of these side effects may not reach statistical significance, but in which, nevertheless, there is emerging expert consensus that such side effects can be attributed to the drug in question. Thus, a pharmaceutical company or doctor is expected to disclose such side effects that a "reasonable person" may want to know about. When information regarding harmful drug side effects is made available to the public, consumers and other stakeholders can make more informed decisions, and additional harm can be prevented.

Case 26: Omitting a conflict of interest disclosure in government-funded research

(conflicts of interest; health administration; pharmaceutical law)

The highest administrative court has just forced the national health administration to withdraw two of its guidelines because of potential bias and undeclared conflicts of interest among the authors. The guidelines of the health administration conflicted with the national law on conflicts of interest. Investigators say that the guidelines may have been indirectly responsible for a recent incident in which an appetite suppressant was marketed as an anti-diabetic drug, leading to the deaths of 800 people. The health administration defended itself by saying that it had not violated any conflicts of interest, since it was allowed to have members with some conflicts of interest in areas that required very specific technical expertise. Furthermore, it said that it was a financially independent institution that developed its guidelines using rigorous scientific principles.

Ethical Question

Should the national health administration allow members of its committee who are responsible for creating practice guidelines to have conflicts of interest?

Possible Answers

- Yes. It is ethical to allow members of a committee responsible for drafting practice guidelines to have conflicts of interest, given that these members are required to have very specialized expertise.

- No. It is unethical to allow members of a committee responsible for drafting practice guidelines to have conflicts of interest.

Discussion

Practice guidelines promulgated by national health administrations have enormous influence over clinical decision making. The intent of such guidelines is to ensure that patients receive optimal treatment and that potential harms be minimized. Thus, it is imperative that those individuals selected to such committees be scrutinized for the possibility of undue influence. Conflicts of interest can corrode the commitee's mission to create guidelines that optimize the treatment of patients and minimize harms. Individuals with a stake in the use of certain drugs may be biased to create guidelines that promote use of these drugs without regard for the potential drug risks posed to patient health.

Case 27: Pharmaceutical-controlled foundation

(pharmaceutical-controlled foundations; shell games; conflicts of interest)

Recently GH has been seeing a lot of advertisements by a non-profit, philanthropic advocacy group that says its mission is to protect the senior citizens of the country. This group has interested him because he is a senior citizen and has been struggling with financial problems. He thinks that a group like this might be able to address some of his financial concerns. However, despite his interest in the group, he has been a little confused by some of its advertisement campaigns: although the group claims that it is nonpartisan, many of its political campaigns have been in support of one particular party. The group also spreads advertisements that have nothing to do with senior citizens, such as a recent campaign to allow nuclear waste disposal in an old mining town. Surprised that the group can afford such an extensive advertisement campaign, GH decides to find out more about the group online.

After researching the group, GH is surprised to learn that it has never filed any tax returns. Furthermore, most of the group's financial contributions have come from one big pharmaceutical company. GH also finds out more about the political candidate whom the group is supporting, and learns that she is the only candidate promoting a prescription drug plan that is supported by the same pharmaceutical company sponsoring the group. After learning all of this, GH feels insecure about listening to this group. He is concerned that the pharmaceutical company may be using the group as a front for its aims.

Ethical Question

Are the advocacy group's practices — operated by a pharmaceutical company to promote the financial interests of that company — ethical?

Possible Answers

- Yes. It is ethical for the pharmaceutical company to operate such an advocacy group in order to conceal its sources of funding.

- No. It is unethical for the pharmaceutical company to operate such an advocacy group in order to conceal its sources of funding.

Discussion

Like other groups in the marketplace, pharmaceutical companies seek to maximize their profits. In this case, it seems that a pharmaceutical company is advancing a particular politician's agenda (which may have potential feedback effects for the company's profits) through the guise of an advocacy group. There is also a lack of transparency in the pharmaceutical company's practices, since the company has concealed its affiliations with the advocacy group, as well as what seem to be its affiliations with the politician in question.

It is important that any financial conflicts of interest among the company, advocacy group, and politician be made public. Otherwise the result is akin to false advertising, in that consumers are misled to believe that the advocacy group in question intends to protect the interests of the people, rather than to advance the agenda of a particular politician or company. Such practices are unethical because they avoid transparency and mislead consumers.

References

(Dr. Rath Health Foundation, n.d.)

Case 28: Pharmaceutical-funded medical journal

(pharmaceutical-funded medical journals; conflicts of interest; shell games)

Dr. L has recently started prescribing a new antibiotic after reading an article about it in a well-known medical journal. The article seemed to have only good things to say about the antibiotic. For example, the article described the drug as fast-acting and having only minimal side effects. One day, Dr. L is talking with a colleague and mentions the journal article. His colleague tells him that she had done some research on the journal and discovered that it is heavily funded by two major pharmaceutical companies. Later that night, Dr. L decides to do some research of his own and discovers that more than fifty percent of the journal's board members have connections to pharmaceutical companies. Despite his best attempts, however, he cannot find any statements disclosing the amount of funding that the journal receives from these companies. He is frustrated because he knows that journals are required by law to disclose this information. Dr. L discovers that many of the members also hold stock in the two pharmaceutical companies in question. In light of all this information, Dr. L is worried that the journal has promoted the antibiotic only in the interest of the pharmaceutical companies, and not because the drug is effective.

Ethical Question

Is it ethical for the medical journal to be secretly or indirectly funded by pharmaceutical companies?

Possible Answers

- Yes. The medical journal is under no ethical obligation to disclose its sources of funding. Its behavior is ethical.

- No. The medical journal is acting unethically, because it has not disclosed its sources of funding.

Discussion

Bias can affect all types of behavior. For example, primary investigators who are conducting research trials have an interest in seeing their results published, thereby potentially biasing them towards reporting only certain results. However, bias can also result from conflicts of interest in having professional, financial, or other relationships with third parties. In the case above, it appears that the medical journal has a financial interest in publishing favorable results about a certain drug, due to its relationship with the pharmaceutical company that markets that drug. This bias is more problematic than that of an individual investigator, due to the critical role that the journal's selection process plays in removing or minimizing any bias that may exist in articles submitted for publication. Doctors rely on journals to have addressed bias in the articles they publish. If journals themselves demonstrate bias in their publication practices, then their selection process has failed in this respect, with potentially negative consequences for patients' health.

It is also worth noting that a journal may account for the bias it perceives in a study by disclosing the conflicts of interest that the authors of that study may have. Again, however, if the journal itself has financial conflicts of interest and does not disclose this information, then the published information will likely not be suspected of bias, and could unduly influence doctors and patients.

References

(Cosgrove & Bursztajn, 2010)

Case 29: Ghostwriting of an academic paper

(pharmaceutical marketing; conflicts of interest; hierarchy in academic organizations; whistleblowers)

JE works for a small medical journal. On more than one occasion, she has been surprised that the journal publishes articles promoting Drug T, which has been shown in other studies to cause harmful side effects. JE raises her concerns about the latest Drug T article with her editor. The editor hears her concerns and says that he will investigate the case. However, when the next issue is published, JE sees that the Drug T article is still featured. After deeper investigation, JE learns that the article was actually written by a pharmaceutical affiliate, although neither this person's name nor his company affiliations are mentioned in the article. This practice is referred to as "ghostwriting."

Ethical Questions

Is it ethically problematic for pharmaceutical companies to ghostwrite academic articles?

Possible Answers

- Yes. Ghostwriting constitutes a breach of ethics.

- No. Ghostwriting does not constitute a breach of ethics.

Discussion

In principle, ghostwriting may not be problematic if, say, the ghostwriter is merely adding flair to an article, or correcting language errors. However, the problem with some instances of pharmaceutical ghostwriting is that often these ghostwriters are paid large sums of money to present information in a manner that is financially favorable for the paying company, i.e., by emphasizing the drug's benefits and

de-emphasizing its risks. Ghostwriters themselves may be convinced that they are merely helping busy researchers, or fulfilling a technical role that has no direct bearing on the actual research findings

In some problematic cases, ghostwriters will write most of the article, and then the pharmaceutical company will pay distinguished professors to sign their names as authors, in order to lend the article an air of distinguished credibility. Such articles may essentially be drug advertisements disguised as academic research. The problem is that doctors are, nevertheless, likely to believe that these articles are in fact scientifically reliable, and to make medical decisions based on them that may harm patient health. Furthermore, because discoveries of unethical ghostwriting are sometimes made public news, some doctors may become less willing to trust the academic articles they read, and this skepticism may cause them to avoid other articles that are in fact reliable.

In order to prevent such negative consequences, a number of controls need to be in place for medical journals, editors, ghostwriters, authors, and pharmaceutical companies. Perhaps foremost among them is a requirement that authors provide detailed information about all contributions (academic and financial) to an article, as well as all conflicts of interest they hold, regardless of how "small" or "indirect."

References

(Dr. Mercola, 2011)
(Logdberg, 2011)
(Singer, 2009)

Case 30: Pharmaceutically funded research universities

(shell games; drug patents; conflicts of interest; drug research funding; collaborations between pharma and academia)

The pharmaceutical industry has started collaborating with research universities to develop new antidepressant drugs. Three major companies have contracted with these universities to continue funding their departments if the drugs pass Phase I trials. In this event, the universities will share the patents with these pharmaceutical companies. The companies started this collaboration in an attempt to find creative ways to bring new medications to market. Part of the problem that has inspired the collaboration is that these companies frequently have to lay off in-house researchers whenever the companies are acquired or merged. Furthermore, many of the patents for the companies' top-selling antidepressant drugs will soon expire. When these pharmaceutical companies were doing very well, they never invested in universities; now that their financial situation is more desperate, however, it seems their strategy has changed.

Ethical Question

Does this collaboration create intellectual and/or financial conflicts of interest?

Possible Answers

- Yes. Academic-industry collaborations inevitably create conflicts of interest, because pharmaceutical companies have a responsibility to their shareholders to make money. Profit seeking may conflict with the truth-seeking goal of academic research.

- No. Collaboration with the pharmaceutical industry has created opportunities for innovation in the biomedical field and for the development of life-saving medications.

Discussion

Almost twenty years ago, Thompson (1993) gave a clear and often cited definition of conflicts of interest in medicine: "a conflict of interest is a set of conditions in which professional judgment concerning a primary interest (such as a patient's welfare or the validity of research) tends to be unduly influenced by a secondary interest (such as financial gain)." Thompson emphasizes that it is the generic risk incurred by financial conflicts of interest that undermines public trust. "[T]he 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"* (Thompson, 2009, p. 137, *italics added*).

This point is well-taken and directly related to the definition and focus of institutional (as opposed to individual) corruption. That is, a conflict is a "set of circumstances" that refers to a generic risk, and to identify a conflict is not an indictment of someone's character or an accusation of scientific misconduct. Indeed, it is often impossible to determine the motivations for a specific scientific or clinical decision. Additionally, cognitive dissonance and self-justification (e.g., "I know my research wouldn't be influenced by my industry relationships") can preclude accurate self-assessments. Thus, academic-industry collaborations create conflicts of interest, as well as the impression that a professional's judgment may be biased — whether or not it actually is.

Integrity and trust are at the heart of what it means to engage in biomedical research and evidence-based medicine. Any loss of trust and integrity undermines this ethical mandate. There is a need to develop mechanisms and policies that enhance public trust when the industry partners with the academy, (e.g., by creating "firewalls" between industry and academic researchers, such as by pooling industry funds and having a government agency distribute the pooled funds).

References

(Thompson, 1993)
(Thompson, 2009)

Case 31: Pharmaceutical funding of clinical trials at universities

(clinical trials; informed consent; conflicts of interest; scientific objectivity) - Carl Elliott

On April 11, 2003, R.W., a 22-year-old male, had a psychotic break. He was admitted to a university teaching hospital in the United States. R.W. was a recent graduate of the university. He believed that other people could read minds and cast spells, that he was being visited by aliens, and that he was part of a satanic cult that was calling on him to murder people, including his mother. R.W. was evaluated by a psychiatrist who was also the head of the schizophrenia program at the university, who thought that R.W. was psychotic, dangerous, and incompetent to make his own medical decisions. The psychiatrist recommended involuntary committal to a state institution. Several days later, a second clinician agreed.

In this state, patients who have been involuntarily committed are given another option called a "stay of commitment." A stay of commitment means that patients can avoid confinement as long as they agree to comply with the treatment recommendations of their psychiatrist. The treating psychiatrist recommended that R.W. be given a stay. The court agreed. But instead of simply treating R.W., the doctor asked him to enroll in a clinical trial. R.W. signed the consent form for the trial while his mother was not present. When his mother protested later, she was told that the decision whether or not to participate in the trial belonged to R.W., not her.

The clinical trial was aimed at schizophrenic patients experiencing their first psychotic break. Funded by a major pharmaceutical company, the study was a yearlong, multisite, randomized, double-blind

comparison of three different atypical antipsychotic drugs, and the university received approximately $15,000 for each subject recruited into the study.

The treating psychiatrist was also the Principal Investigator for the state site, and his department chair was the Co-Investigator. Both individuals had had significant personal financial relationships with the manufacturers of the atypical antipsychotics, including the company that funded the study.

R.W. was eventually discharged to a halfway house where, according to his mother, his condition worsened. His mother tried repeatedly to get him out of the study — phone calls, letters, visits to the Department of Psychiatry — but she could not get anyone to listen to her concerns. Finally, she left a voice message with the study coordinator, asking, "Do we have to wait until he kills himself or someone else before anyone does anything?" Three weeks later, R.W. stabbed himself to death in the shower with a box cutter. He left a note that said, "I went through this experience smiling." The university declined to investigate the suicide.

Ethical Question

Can a financial association between a Principal Investigator and a drug company breach ethical codes and inadvertently put a patient at risk of harm when a patient is enrolled in a clinical trial?

Possible Answers

- Yes. If a Principal Investigator (PI) has a financial stake in the clinical trial, he might act in ways that — while benefiting his financial ties with the company — put the patient's health at risk. In the first place, the PI should disclose his financial ties, so as to obtain the patient's informed consent. Furthermore, enrolling a patient in a clinical trial is not the same thing as providing treatment. A double-blind randomized controlled trial (RCT) is the 'gold standard' in medical research, because it allows the researcher to determine if the efficacy of the medication

being studied is truly due to the pharmacological properties of the drug, instead of as a result of other variables. Thus, there is trade-off in head-to-head comparisons like these: science is advanced because of the methodology employed (i.e., double-blind RCT), but enrolled patients and their physicians do not know what medication the patient is taking. If this information was not disclosed to R.W., an ethical breach occurred. Patients have the right to know the benefits, risks and alternatives to the medication they are taking or, if enrolling in a double-blind clinical trial such as this one, that this information will not be available to them. Patients who enroll as RCT participants have a right to know that, because the trial is randomized, they may receive treatment that is not of personal therapeutic benefit. If patients are not made aware of this fact, then they may not be adequately protected. Also, if a principal investigator has a financial stake in the clinical trial, he/she should disclose that information in order to obtain patients' informed consent. Additionally, study participants such as R.W. have a right to withdraw from a study at any point.

- No. Because this RCT was a head-to-head comparison. R.W. would have received standard of care treatment, as each of the arms of the study included treatment with atypical antipsychotics — the standard treatment for individuals presenting with schizophrenia and psychotic disorders. Therefore, even though the PI had a financial "stake" in the study, it did not compromise the care he provided to his patients, since the trial was double-blind and randomized.

Discussion

This case illustrates why there is growing concern that financial conflicts of interest (FCOI), in the form of industry-academic relationships, may put patients/trial participants at risk. In this case there are FCOI among various parties (e.g., the university and industry; the chair and the pharmaceutical company, the PI and the pharmaceutical company) and these conflicted relationships give rise to many ethical issues. The physician/researcher is obliged both to provide treatment that is in the best medical interests of the patient

and to obtain genuine informed consent. Even in the absence of financial conflicts of interest, these two obligations raise an ethical dilemma that is not easy to negotiate. This case reveals the many layers of conflict that often develop when universities engage with commercial entities: The PI's supervisor (the Chair of his department) is a co-investigator and funded by industry; the university has a pro-industry stance and also stands to benefit financially from its relationship to the specific pharmaceutical company.

Maintaining integrity in clinical research and practice requires both transparency of financial conflicts of interest (FCOI) and specific policies and procedures for how such conflicts should be disclosed and managed. The prevalence of academic-industry collaborations, the dramatic increase in industry-funded research, and the financial ties between prescribing providers, organized medicine, and the pharmaceutical industry have complicated (and in some ways compromised) the informed consent process. As a result of these collaborations, protecting the rights and welfare of research participants has become a critical public health issue (Grady et al., 2006; Krimsky, 2003).

The role of a psychiatrist as clinician is to be an advocate for his/her patient, while the role of an academic psychiatrist as researcher (PI of an RCT) is to be objective and ensure protocol is strictly followed in terms of the methodology. In this case that means that patients should not be 'switched' to a different medication. These conflicted roles may be detrimental to patients.

References

(Grady et al., 2006)
(Krimsky, 2003)
(Weinfurt et al., 2006)
(World Medical Association, 2000)

Case 32: Can radical transparency neutralize conflicts of interest in academic research?

(academic-industry collaborations; conflicts of interest; academic honesty; reputability of research)

Steven A. Lehr & Mahzarin R. Banaji

J is a scientist who specializes in studying the efficacy and safety of antipsychotic medications. In order to maintain integrity in her own research, J has tried to avoid financial conflicts and would characterize herself as "risk-averse" when it comes to choices that could undermine academic integrity, a matter on which she is considered an authority by her peers.

H is an unusual applicant for the Ph.D. program at J's university. H is the cofounder of a small pharmaceutical company called "Phoenix." In addition to manufacturing psychotropic medications, Phoenix offers people an integrated set of online tools to track the effects, both positive and negative, of their medications. As H has progressed in his career, he has decided that he'd like to attain a Ph.D. and pursue a career in academia. For the time being, H would continue to be an employee of Phoenix, which would fund his fellowship and provide datasets he could analyze for his thesis work, but he would give up most of his administrative roles. He finds J's lab to be the most appropriate for his work. H would like to complete his Ph.D. in J's lab, and J would like to take him as a student. However, J is concerned about H's involvement in the commercial sector, which H believes can form an important part of his academic identity.

Ethical Question

Can full transparency of H's position in the pharmaceutical company cure the ethically problematic situation of the involvement of potential economic interests in the academic research of H?

Possible Answers

- Yes. The position of H and his collaborators may be viewed in terms of a pragmatic calculus. H's choice to combine Phoenix with science is profitable to each side only to the degree that combining them creates benefits that outweigh the costs. Phoenix profits from the marketing of being validated by reputable research, and from the dissemination of data that document that the psychotropic medications it produces have a better risk/benefit ratio than that of its competitors. Academic collaborators (such as J) benefit from a new, cost-effective and extremely powerful data-source for scientific work, and from the lines of scientific thought arising from this dataset.

- No. Consider the process of conducting, interpreting and publishing a result. Results that happen to work out in a "beneficial" direction for Phoenix offer H salient economic benefits. Positive results will validate Phoenix's products, profiting a commercial venture in which H has a direct stake. But of course, in reality, academic results will not always be good for the company; in some cases, a "beneficial" result will prove just out of reach. The right wave of a statistical wand or the right turn of phrase in a paper, and a marginal result may become significant and publishable. Worse, sometimes interesting results will arise that go against the economic interests of Phoenix. It is unrealistic to assume that H will truly put the same degree of effort into analyzing and writing about such data. Nor will he be as likely to publish it in leading journals. It is doubtful that H will even be able to look at such data without being unconsciously biased in a direction that benefits his other interests.

Discussion

In science, objectivity is our most sacred value. Researchers strive for tests of ideas that are unbiased and can reveal the truth about whatever

reality they are attempting to understand. Yet many systematic influences undermine this quest for objectivity. A researcher's neutrality may waver in response to fame, money, social attachments, intellectual habits, or any number of other pressures.

A financial interest can actively corrupt research. As opposed to mere opportunity costs, conscious or unconscious bias in the experimental process can lead to incorrect information being actively utilized by H, J and other researchers. If data minimizing iatrogenic harms of medications are disseminated, H's involvement in Phoenix and academe could present a public health risk. Similarly, the race to profit from an experiment (whether financially or academically) can undermine the long-term integrity of Phoenix. Use of biased results can lead this pharmaceutical company to act directly against its ultimate mission to help people make medical decisions in a way that promotes health, happiness and longevity.

In these domains, the conflict can be seen as having a negative impact both morally and pragmatically. Bias in the experimental process can exercise a negative social impact, leading to less objective medical decision making and to errors in scientific inquiry. Further, even from a purely self-interested perspective, the conflict of interest can undermine the effectiveness and reputations of all the parties involved (H, J, and H's pharmaceutical company).

The calculus of the situation, while difficult to quantify, is conceptually simple: 1) The conflict of interest itself is broadly corruptive, and should be neutralized if possible; 2) To the extent that the conflict of interest is maintained in spite of attempts to neutralize it, it exerts an influence on both the moral (social) and pragmatic (selfish) calculus of the situation, which must be factored into value assessments. If in each domain, the benefits outweigh H's opportunity costs from spending time in the other domain, the "conflict" should not be viewed as corruptive. If these costs outweigh the benefits of an alliance between this pharmaceutical company and academia, than the alliance should not be created.

Case 33: Omitting a conflict of interest disclosure for a drug conference

(Internet pharmaceutical marketing; shell games; need for transparency)

A university is sending out an online advertisement for a conference it will be hosting on the negative side effects of antipsychotic drugs. The advertisement says that the conference will provide a scientific update of the most recent findings on promising antipsychotic drugs. This kind of conference, the advertisement claims, is particularly important given that many antipsychotics, although offering advantages, also carry many liabilities. Therefore, the university says it is particularly excited to be promoting drugs with very few or significant side effects. Although the advertisement lists all of the professors who will be presenting at the conference, it omits the industry's ties to these speakers. None of the conference funding is coming from pharmaceutical companies.

Ethical Question

Should the university omit speaker industry ties when the conference itself is not funded by pharmaceutical companies?

Possible Answers

- Yes. Because the conference is not sponsored directly by a pharmaceutical company, it is not necessary for individual speakers to report commercial ties.

- No. In keeping with disclosure policies recommended by the International Committee of Medical Journal Editors (ICMJE) and governmental bodies (e.g., the Institute of Medicine), transparency of all potential conflicts of interest is necessary to ensure public trust and honest science.

Discussion

The need for increased transparency has been well documented by ethicists, public policy makers, and researchers who study conflicts of interest in the biomedical field and government bodies. It is widely accepted that disclosure should not be limited to direct pharmaceutical funding of a randomized clinical trial or continuing medical education (CME) workshop. Rather, the International Committee of Medical Journal Editors (ICMJE) requires disclosure of all financial associations (e.g., honoraria and consultation), not only a disclosure of whether or not the research was industry-funded. Therefore, it is necessary to disclose the speakers' industry associations.

The speakers' ties may influence their discussion of the iatrogenic effects of antipsychotic drugs, among other subjects. The risk of bias is particularly great if the ties are long-standing and continuous (e.g., if any of the individuals own stock in pharmaceutical companies that manufacture antipsychotics). In light of the increasing evidence that newer antipsychotic drugs (those branded "atypical") have more severe side effects and are less efficacious than was initially believed, full transparency is especially important. Attendees of the conference may be more cautious about believing the statistics presented if they are aware of the conflicts of interest held by the speakers. Similarly, the speakers may feel added pressure to be objective in their presentations if they know that attendees are aware of conflicts of interest they hold, since attendees will be more skeptical of everything they say.

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