

Practicing research ethics: Private-sector physicians & pharmaceutical clinical trials[☆]

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Abstract

This paper focuses on constructions of research ethics by primary care physicians in the USA as they engage in contract research for the pharmaceutical industry. Drawing first on historical studies of physicians as investigators and then on 12 months of qualitative fieldwork in the Southwestern US, this paper analyzes the shifting, contextualized ethics that shape physicians' relationships with patients/subjects and pharmaceutical companies. Just as physicians followed professional codes of ethics prior to the codification of acceptable research conduct in the 1980s, physicians today continue to develop tacit systems of research ethics. This paper argues that private-sector physicians primarily conceptualize their ethical conduct in relation to the pharmaceutical companies hiring them, *not* to human subjects they enroll in clinical trials. This is not to say that these physicians do not follow the formal U.S. regulation to protect human subjects, but rather that their financial relationships with the pharmaceutical industry have a greater influence on their identities as researchers and on their constructions of their ethical responsibilities.

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Introduction

The practice of medicine is imbued with ethical concerns. These concerns influence relationships between physicians and their patients, guiding choices about treatment and care. While the routine work associated with standard medical care may not often require concerted ethical deliberation, new arrangements with the pharmaceutical industry introduce new ethical complexities. Specifically, physicians are

increasingly conducting clinical trials as contract researchers for the pharmaceutical industry. Whereas academic physicians have long been researchers as well as practitioners, now *private-sector physicians* operating private practices and/or for-profit research centers make up more than 70% of all pharmaceutical investigators in the United States (Steinbrook, 2005).

In spite of the bulk of pharmaceutical clinical trials occurring in the private sector, scholarly attention has focused primarily on academic physicians with little analysis of their non-academic counterparts in local communities around the U.S. (e.g., Hoeyer, Dahlager, & Lynoe, 2005; Miller, Rosenstein, & DeRenzo, 1998). While the conflict between research and care has been well examined in the bioethics literature, there has been little sociological inquiry into the

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ways in which contemporary physicians actively construct their own codes of ethics as clinical researchers (Halpern, 2004). In fact, there are currently more empirical studies on research staff, such as nurse coordinators, and their construction of ethics than on physicians (Davis, Hull, Grady, Wilfond, & Henderson, 2002; Fisher, 2006a; Mueller, 1997).

This paper focuses on private-sector physicians' constructions of research ethics as they engage in contract research for the pharmaceutical industry. Drawing first on historical studies of physicians as investigators and then on current qualitative research, this paper analyzes the shifting, contextualized ethics that shape physicians' relationships with patients/subjects and pharmaceutical companies. Just as physicians followed professional codes of ethics prior to the codification of acceptable research conduct in the 1980s, physicians today continue to develop tacit systems of research ethics. This paper argues that private-sector physicians primarily conceptualize their ethical conduct in relation to the pharmaceutical companies hiring them, *not* to human subjects they enroll in clinical trials. This is not to say that these physicians do not follow the formal U.S. regulation to protect human subjects, but rather that their financial relationships with the pharmaceutical industry have a greater influence on their identities as researchers and on their perceptions of their ethical responsibilities.

Background: physicians as investigators

Physicians have long served as investigators on research projects involving human subjects, whether for the development of new products and therapies or for the assessment of existing treatments. Much scholarship has examined the history of human subjects research in the U.S., focusing particularly on research malfeasance or unethical treatment of subjects. For example, the case of the Tuskegee syphilis study — in which rural African American men were denied effective treatment for their illness over the course of a 40-year study to document the natural history of the disease — may be the most well-known case of ethically problematic conduct within the U.S. medical community and government agencies (e.g., Jones, 1981; Reverby, 2000). Other cases of human subjects abuses have also received significant scholarly examination, such as medical and military research conducted on prisoners (Hornblum, 1998).

What have received much less analysis are the non-sensational examples of human subjects research in which there is no direct evidence or suggestion of

unethical conduct. In part, the dearth of scholarly attention to the mundane instances of research on human subjects stems from the long-held assumption that prior to regulation enacted in the early 1980s, there simply were no ethical norms or standards governing researchers' interactions with human subjects (e.g., Faden & Beauchamp, 1986; Jones, 1981). This has proven not to be the case. For example, historians of medicine have shown the extent to which there were existing codes of ethics since at least the end of the 19th century that physicians and other researchers were expected to follow in their interactions with human and animal subjects (e.g., Lederer, 1995).

The recent work of Sydney Halpern (2004) and Nancy Campbell (2007) adds sociological detail to these claims. Halpern (2004) illustrates the existence of ethical norms through case studies of vaccine experimentation in the first half of the 20th century. By delving into the “indigenous moralities” structuring investigators' scientific and ethical decision-making, she shows a relational ethics at work as investigators assess the path of lesser harm for human subjects and patients. Likewise, Campbell's (2007) study on prison experiments conducted in the 1950s through 1970s on addictive drugs explores the ways in which researchers respected and valued their subjects' expertise both as recreational and experimental drug users. These scholars argue that in spite of sensational examples to the contrary, the research community did conduct human subjects research in ethically responsible ways in the period leading up to the 1980s. Moreover, their work point to the importance of examining the actual practices of researchers as they balance their responsibilities to their subjects/patients with their commitment to science.

As the scandals surrounding human subject abuse like Tuskegee and prison experiments erupted in the 1970s, social scientists initiated empirical projects to assess medical researchers' relationships with human subjects and their constructions of ethics (e.g., Barber, 1980; Barber, Lally, Makarushka, & Sullivan, 1973; Fox, 1976; Gray, 1975). Most notably, Bernard Barber et al. (1973) completed an empirical study on the gap between the ethical principles that researchers said they espoused and their actual practices. Mobilizing the concept of social control to explain researchers' behavior, they discussed the reasons researchers avoid or adopt unethical practices in their research. For example, they noted that peer review of the ethics and scientific conduct of research (in the earliest instantiation of what are contemporary institutional review boards — IRBs) is an important form of social control,

but that in order to be effective, peer review needs to continue beyond *initial* review throughout the course of the research. During the same period, Bradford Gray (1975) examined patients' decisions to participate in medical research. This work evinced a profound tension between the human subject volunteer as patient and as subject and indicated how crucial social context is to informed consent. For example, Gray's most important finding was that 41% of the volunteers did not know they had been involved in medical research until their interview with Gray, and all of these volunteers had signed (but many had not read) the consent form they were given on admission to the hospital.

More recently, the ethics of everyday medical practice as well as the role of physicians as investigators have begun to receive renewed scholarly attention from social scientists (Bosk, 1995; DeVries, 2004; Zussman, 1992, 1997). By directing inquiry into the structural conditions impacting upon ethical decision-making, the approach of scholars in the social sciences attends to multiple ways in which ethics are understood and enacted by various research communities (e.g., Epstein, 1996; Evans, 2002; Fisher, 2006b). For example, changes in science and medicine, such as the increasing prevalence of research on the clinical application of genetics, shape physicians' as well as patients'/subjects' perceptions of ethical uses of biological information (Hedgecoe, 2004; Konrad, 2005).

In spite of this social science interest in physicians and ethics, there has been little empirical examination of the involvement of private-sector physicians in pharmaceutical clinical trials (Bodenheimer, 2000). Scholarship in this topical area has been generated mainly in the field of bioethics, and most of that research does not differentiate between clinical trials conducted in academic medical centers and the private sector. In addition, bioethics tends to privilege discussion about how ethics *should* be constituted in the clinic rather than what are the current practices and constraints placed upon investigators (Klein & Fleischman, 2002; Miller & Shorr, 2002). Moreover, there is little discussion about the extent to which private-sector physicians are represented in pharmaceutical research, the reasons why they become contract researchers, and how these reasons shape physicians' orientation toward research ethics (Lader et al., 2004).

The pharmaceutical clinical trials industry provides a rich field to discuss the ethics of human subjects research. Bioethics has focused predominantly on consent issues (Appelbaum, Lidz, & Meisel, 1987; Caplan, 1998), and social scientists have added significantly to scholarship on challenges and limitations to informed

consent as well as strategies for optimizing the process (Corrigan, 2003; Featherstone & Donovan, 2002; Morris & Balmer, 2006). Focusing solely on informed consent, however, often leads to a fairly weak notion of "ethics" (Zussman, 1997). For example, discussions of ethics should account for the types of patients enrolled as subjects and the extent to which pharmaceutical research is exploitative of disenfranchised groups within the U.S. and around the world (Petryna, 2007). Elsewhere, I examine the influence of the political and economic context of pharmaceutical clinical trials on ethical practices in the clinic (Fisher, *in press*). The purpose of this paper, however, is more descriptive than normative; rather than analyzing the extent to which physicians are conducting clinical trials ethically (a very complex issue because of the organization of clinical trials work), it instead examines one aspect of ethics: how physicians define what their ethical roles and responsibilities are to the pharmaceutical industry employing them and to the human subjects whom they enroll in studies.

Methods

The research on the clinical trials industry informing this paper is based on 12 months of fieldwork in the Southwestern United States from October 2003 to September 2004. Specifically, it involved participant observation and 63 semi-structured interviews at more than 20 private-sector sites conducting pharmaceutical drug studies. The purpose of this fieldwork was to examine relationships between physician investigators, research staff, patients/subjects, and pharmaceutical company representatives within the clinical setting as mediated by clinical trials and the pharmaceutical industry more generally. Interview questions directed at physicians solicited their perceptions of research ethics and of their responsibilities to human subjects, pharmaceutical companies, and to science. Other interview questions explored the organization of pharmaceutical clinical trials, including the companies and employees engaged in contract research.

Sites conducting pharmaceutical clinical trials in two major cities in the Southwest that were listed on an industry clearinghouse web site were approached to participate in interviews and/or participant observation. At least one individual at 75% of sites in one city and 50% of sites in the other agreed to an interview. Although no incentives were offered to promote participation, most sites, particularly research staff such as coordinators, were happy to schedule an interview. Scheduling time with physicians was more difficult,

and the most effective way to conduct interviews with them was to interview their staff first and then, at that scheduled appointment, request time with the physician. There was no discernable difference between sites that agreed and refused to participate based on types of studies conducted, size of the clinical trial operation, or experience of the site (using information listed on the clearinghouse web site). The majority of sites conducted studies to test the efficacy of new products that were targeting illnesses and diseases that already have safe and effective treatments on the market (e.g., allergies, asthma, high cholesterol, insomnia). Only one site consistently tested products for life-threatening conditions, such as AIDS or cancer.

Out of 63 interviews with investigators, research staff and administrators, pharmaceutical industry representatives, and human subjects, 10 were conducted with physicians hired as principal investigators and 2 others with a physician and a PhD researcher employed in administrative roles (11 MDs and 1 PhD; 11 men and 1 woman; 11 white and 1 Hispanic). Interviews lasted an average of 40 min with a range of 10–90 min. Participant observation in clinics included primarily interactions between investigators and subjects, as well as between coordinators and subjects. Specific demographic information about the physician investigators quoted in this paper can be found in the [Appendix](#).

Clinical trials as an emerging medical specialty

Physicians practicing medicine in the private sector — as part of community hospitals, private practices, and clinics — are reporting ever increasing economic and legal constraints impacting upon health-care services. Trends in managed care have decreased the revenue physicians can expect from seeing patients (Tu & Ginsburg, 2006). Dramatic increases in malpractice insurance premiums dip into physicians' diminishing incomes, and the litigious environment of the U.S. makes malpractice suits seem like a daily — rather than a distant — possibility (Sage, 2004). Add to these conditions the overhead costs of running an office, paying salaries, and processing billing, and many physicians are finding that not only is medicine no longer lucrative but it is a business that their training ill-prepared them to run efficiently and effectively.

As a result, physicians are seeking new channels within the context of their practices to augment their incomes (Pham, Devers, May, & Berenson, 2004). These emerging revenue streams range from selling patients/clients “nutraceuticals,” such as vitamins

and herbal supplements, to offering cosmetic procedures, such as facial peels and Botox[®] injections. In addition, many physicians are looking to the pharmaceutical industry for revenue. Association with the pharmaceutical industry offers many possibilities for physicians to profit. From mundane perks offered by drug reps to cash rewards for prescribing and/or promoting certain products, physicians have ties with pharmaceutical companies that vary from loose affiliations to payrolled consultation positions (Kassirer, 2005). Yet, in addition to marketing drugs and devices, physicians' involvement with the pharmaceutical industry is now frequently extended to the research and development of these products. By becoming contract researchers for the pharmaceutical industry, physicians mobilize their patient populations as potential resources for clinical trials.

The convergence of physicians' interest in or need to find alternative sources of income with the pharmaceutical industry's interest in cutting costs and speeding up research and development creates a lucrative arrangement for both parties (Rainville, 2002). Physicians continue to practice medicine but incorporate the enrollment of patients as human subjects and get paid by pharmaceutical companies instead of by insurance providers or government agencies for their time and services. From the perspective of the pharmaceutical industry, private-sector physicians offer them a ready pool of patients that can be recruited into their studies more rapidly and more efficiently than can academic physicians who rarely have non-research patient populations in reserve (Fisher, 2007). This contract research arrangement is so beneficial to private-sector physicians and the pharmaceutical industry that 13% of all practicing physicians are currently conducting at least one pharmaceutical study and 33% have conducted studies for the pharmaceutical industry at some point during their careers (HarrisInteractive, 2004). These changes have catalyzed a veritable industry to support both the pharmaceutical companies and the private-sector sites conducting clinical trials (Mirowski & Van Horn, 2005). For example, a primary goal of contract research organizations (CROs) is to aid pharmaceutical companies in selecting appropriate clinical sites that have large patient populations appropriate for specific clinical trials.

In spite of the rapid increase in the number of private-sector physicians signing on to conduct pharmaceutical studies, there is little movement to provide investigator training for physicians. This is not because conducting pharmaceutical studies is straightforward or transparent. In fact, many physicians working in

the industry describe the knowledge that is necessary to be effective investigators as comprising a new medical specialty. For example, a physician with decades of experience conducting trials explained,

Medical training is certainly important because there's, of course, a lot of medicine in [clinical trials], but that [training] is not enough. It's not sufficient. Clinical trials is a specialty unto itself, both the business of clinical trials as well as the ethics of clinical trials, dealing with IRBs, dealing with pharmaceutical companies, dealing with a whole bunch of things, as well as how to manage a large center... so there are certainly a lot of things lacking in a medical education that didn't prepare me for that. (Physician Investigator A)

The emphasis within the framing of clinical trials as a specialty — as this physician and others articulate it — consists of three parts: the business, logistics, and ethics of conducting studies. In this way, it is not a specialty like most others requiring additional professional training. In other words, the expertise is not medical, per se, and the additional knowledge needed to run studies has little to do with biological systems or etiologies of diseases.

When it comes to the medical end of trials, many physicians assert that there is no difference between practicing medicine and conducting research. Some even take this a step farther to argue that clinical trials are easier to do than is standard medical care. For example, a fairly new investigator said, “You're over-qualified as an MD for clinical trials” (Physician Investigator B). In large measure, this is because there is no need for scientific or pharmacological expertise associated with contract research. Unlike investigator-initiated studies conducted by academic physicians and funded by government agencies like the National Institutes of Health, pharmaceutical clinical trials are offered to physicians as prepackaged studies in which they choose to participate or not. Pharmaceutical company employees design these drug studies, and physicians rarely have the opportunity to comment on or influence the various components of the trial. Explaining the role of contract researchers, a highly successful physician running a profitable clinical trials site said,

We really don't have a lot of leeway in the scientific department. I mean, if somebody says we have this really great drug that works for blood pressure, I have no idea how this damn thing works!... I have no idea about science!... I'm not a scientist... We [physicians in the private sector] bring a *techne* — it's

an old Greek work — as opposed to a science. Pharmaceutical companies can hire the scientists, but at some point the end has to be executed... So I think at this point what we offer is an execution. (Physician Investigator C)

In a sense, physicians who engage in contract research do not need to understand the principles of research or clinical trial design; they simply need to be able to follow a study protocol that is given to them by the pharmaceutical company for which they are working. As the physician quoted emphasizes, contract researchers have practical clinical skills (*techne*) that are mobilized to complete studies for pharmaceutical companies.

Because clinical trial work takes a different kind of expertise, there is little focus on providing physicians with any specific training or guidance. Specifically, pharmaceutical companies rarely, if ever, provide ethics training for investigators. In fact, the only training in ethics that most physicians receive for clinical trials work is limited to the medical school curriculum, which focuses largely on ethical issues in patient care not research. Moreover, because regulatory oversight is provided by commercial (read: for-profit) institutional review boards rather than those associated with universities or large hospitals (Lemmens & Freedman, 2000), ethics training is often absent from requirements for protocol approval, and most IRBs limit their monitoring of ethical oversight to documentation of informed consent. There is no formal education for physicians in recognizing or resolving conflicts of interest they might experience between care for human subjects and financial arrangements with the pharmaceutical industry.

Establishing ethical practices

How do physicians determine what count as ethical practices with pharmaceutical research? How do they determine what their responsibilities are to human subjects? And what role do their financial interests play in shaping their conduct? These are questions that have raised debate within the bioethics community and have also begun to circulate in the clinical trials industry. It is interesting to note that even without any training in research ethics, private-sector physicians report that they are keenly aware that their ethics are under scrutiny, especially with regard to potential financial conflicts of interest in recruiting human subjects. Although they have not received formal training in ethics, these physicians develop strong opinions about what is

ethical — even some that counter mainstream ideas in bioethics — through their relationships with patients/subjects, the pharmaceutical industry, the media, and the regulatory apparatus of the U.S. government. This section will explore the process and result of private-sector physicians developing codes of ethics in locally contingent and reflexive ways.

Physicians conducting pharmaceutical clinical trials often develop what seem like contradictory modes of explaining ethical practices. On one hand, they report that the ethics of individual studies or research protocols are handed down to them from the pharmaceutical companies, and therefore, physicians themselves have little control over defining what is ethical. On the other hand, they report that it is the physicians who establish the ethical “tone” of the investigative site by communicating to their research staff what are acceptable and unacceptable practices. These two positions tend not to clash for physicians because they are constructing their research ethics to a large degree in relation to the pharmaceutical companies that hire them, not to the human subjects they enroll in studies. To understand how and why physicians resolve this contradiction, it is necessary to explore each position in more detail.

Because physicians who participate in contract research are given clearly defined study protocols to follow, they insist that the responsibility for ethics rests in the domain of the pharmaceutical companies that are outsourcing the research. This attitude stems from several constraints on contract researchers. First, they do not construct their identities as scientists or as having expertise in pharmacology or toxicology. Second, they do not have input into the study design so their responsibility lies in following the protocols given to them. Third, physicians cannot begin conducting studies until IRBs have reviewed the protocols to examine and resolve any ethical concerns that might be associated with studies. Finally, the majority of studies conducted in the private sector are double-blind protocols, meaning that neither the physicians nor the subjects are aware whether they are receiving the investigational drug or the comparison product (i.e., an inert placebo or a product already available on the market). Because of these reasons, physicians often feel that third parties are responsible for determining the ethics of the clinical trials they are conducting.

To make this position more concrete, a physician explained how the responsibility for ethics belongs to the pharmaceutical companies, even if their conduct is not as ethical as he would like. Since the late 1980s, the U.S. Food & Drug Administration (FDA) has amended its rules on what animal testing is

required and the length of studies measuring the toxicity of products before human testing of those products can begin (Cauteren et al., 2000). As a result, many of the products in clinical trials are being administered to human subjects before the long-term toxicity studies using animal data are complete. The physician commenting on this shared his frustration with the change:

Now they start the human studies before they get the results of the long-term tox studies. So now we just had a big study, actually we had *nine* studies going on because we had been doing a lot of work for this one company. When all of a sudden, they had [results from] long-term tox studies that showed the drug was bad; it caused tumors in mice. So as soon as they found out, they stopped development. But of course, *we* were well on the way, and we had a *huge* number of patients involved. (Physician Investigator A)

To this physician, contract researchers cannot be blamed for potentially endangering subjects in this way when the responsibility comes down not only to the pharmaceutical companies developing the products but also to the U.S. government setting rules for those companies to follow. Through this lens, his conduct was ethical because he followed the protocols as given to him by the pharmaceutical company sponsoring the studies.

The point at which physicians do make a determination about the ethics of studies in regard to patient care occurs when they are considering whether or not they want to accept specific contracts for pharmaceutical research. Rather than interpreting their decision-making in terms of an ethical evaluation, however, physicians often refer to the process in terms of the safety of studies for patients. For example, a physician said,

My concern as an investigator is, is it safe for the patient? If it's not safe or if I don't like the fact that they're going to put an actively psychotic schizophrenic patient on a placebo, then I'm just not going to do, or a seizure patient on an inadequate dose of the medication. Sorry, I've got plenty of other business down here without having to lose sleep at night. (Physician Investigator C)

Although this physician did not refer to his deliberation in terms of ethics per se, his decision to avoid clinical trials that may be unsafe for his patients can nonetheless be seen as an ethical position. That clinical studies are deemed scientifically valid and approved by IRBs is not necessarily sufficient for physicians to take on any protocols offered to them.

This last point provides the hinge to how physicians begin to conceptualize what role they have in steering the ethics of their own research practices. As stated above, physician investigators often hold a contradictory position, saying both that the ethics of studies is determined outside of the clinic by the pharmaceutical companies or the FDA and that they themselves set the ethical tone within their investigative sites. Because physicians transfer responsibility to the pharmaceutical companies for the studies to be ethical, it then becomes physicians' responsibility — once they choose to conduct the research — to follow strictly the protocols they are given to produce accurate data about the products under investigation.

It occurs, however, that physicians and staff may have to make “ethical” choices about those rules. For example, a physician explained,

There's all sorts of ways people will justify blurring lines of distinction, which may or may not be clear actually. Throwing away a lab value is way over the line, right? Does it have to be fudged when you're doing a blood pressure study and this person is two points out of range on their fifth visit, and you've already put in a month of time on that person? I don't know. Does that betray the spirit of what you're trying to do? As opposed to 10 points out of line, then they're out. So I can see how individual people will sort of figure out where they're comfortable on that, but I think if the *doc* gives a clear message that we do things *right* in this organization, then the staff either shapes up or you're gone. (Physician Investigator C)

In other words, it is the responsibility of those conducting the studies to report the data honestly and accurately, even if physicians and research staff find that subjects who are enrolled in studies have laboratory or other test results that disqualify them from the study. Physicians find, however, that following the protocols is not always so clear-cut. They feel that there is often space for bending the rules, but it is establishing their own clinic guidelines for how much those rules can be bent that draws ethics into the decision-making.

Pharmaceutical companies generally can be flexible about their protocols. Physicians or research staff can contact the sponsoring company to report the situation and to ask for exemptions or waivers on a case-by-case basis. But, rather than clearing up an ethically questionable situation, physicians often feel that the minor cases should be left up to them — and their expertise — rather than to the pharmaceutical company; they think

that their clinical judgments should be allowed to trump the study protocols at least some of the time. In many cases, this attitude is a response to their concern that a waiver or exemption will not be granted after they have already reported the incident. This is compounded by physicians' frustration with what they perceive to be unreasonable protocols to begin with:

The criteria for the protocols are becoming ever more ridiculously difficult. As an example, I remember we were trying to recruit for a rheumatoid arthritis trial [using] someone's [results from a] SED rate test — an indication of inflammation on the blood test of how much disease activity may be... And you screen ten people, and 8 of them screen out because their SED rate test isn't elevated. Although they still have some swollen joints that meet the other criteria to get into the study, their screen fails... But what can you do? *Ethically*, you don't have any choice about it; they can't enroll. (Physician Investigator D)

It may appear that physicians are arguing that pharmaceutical companies' study protocols should be more flexible in order to benefit the patients they enroll (or would like to enroll) as human subjects. While this might be the case in a small number of studies that are testing products that may provide lifesaving treatments for illnesses such as cancer or AIDS, most studies being conducted by the pharmaceutical industry are for products that are far more mundane. Moreover, there is no guarantee that subjects enrolled in clinical trials are getting any treatment at all because the majority of studies are placebo-control trials, dictating that some percentage of human subjects will not receive any active treatment for their conditions (Temple & Ellenberg, 2000).

In fact, none of the physicians I interviewed claimed that the protocol exemptions that they would like to seek are in the best interest of subjects. Instead, they explained that the problem is financial. It is in their financial best interest to enroll a wider base of patients and be assured that subjects can remain in studies even when diagnostic tests required by study protocols indicate otherwise. One physician who quit his private practice to conduct studies full time analyzed the pressure he sees exerted on private practice physicians by the pharmaceutical industry, “If you ask me to find [subjects] faster than they come through [the practice], then I have to *create* them... I think once you take an aggressive timeline from the sponsor, and you *make* the physician fulfill it, you're asking for issues” (Physician Investigator F).

Thus, for many physicians, acting responsibly in the face of ambiguity in making decisions about subjects' enrollment constitutes ethics. Because their contracts are with pharmaceutical companies and their incomes depend on meeting the terms of those contracts, physicians' focus is frequently on their obligations to those companies rather than to the subjects they enroll. Yet, the line between behaving less than ethically and fraud with data reporting is not always clear. If the protocols are not going to be followed precisely, at what point do deviations become unethical or fraudulent? According to one physician,

Obviously, there's an ethical standard that the physicians will be following, but of course, everyone knows, there's *shades* of pressure around your proper ethical behavior which may be trying to push or negotiate certain decisions that the physician is making or certain opinions that they're forming, to comply or go along better with others who are pressuring him/her. (Physician Investigator E)

None of this is to say that physicians look charitably on cases of fraud that emerge in the industry. Quite the contrary, physicians report that fraudulent behavior provides so much fodder for the mainstream media that they taint the whole clinical trials industry. As one physician vented,

There are frauds out there. There are many mistakes being made, and [the media] identify the poor kid [Jesse Gelsinger] who died in that Philadelphia experiment with the gene therapy, and they identify that *louse* in California [Robert Fiddes] who was making up patients and running away with the bank, and they identify somebody else. And *three* bad stories create a picture of an industry where there are literally *tens of thousands* of studies going on. How does *that* represent the whole industry? And yet that's what the public perceives; that's what *Congress* perceives; and then it creates this hailstorm of controversy and scrutiny... It winds up then creating a very bad shiner for the industry that to an extent is very difficult to overcome, and it makes people feel bad who are trying to do a good job and working in the industry. (Physician Investigator D)

Thus, fraud is not within the realm of the acceptable. It is clearly unethical for physicians to make up human subjects, but what about radically altering subjects' data such as test results? The problem is that what tends to constitute *indisputable* fraud in the industry is *getting caught* manipulating the data or the study protocols.

Of course, it is also worth noting that physicians' orientation toward research ethics — following the study protocols provided by pharmaceutical companies — also shapes their perceptions of how financial interests can impact upon their clinical decisions. In general, physicians fall into two financial categories: those who are salaried and those who are paid according to their performance. What is interesting is that physicians falling into either category tend to think their mode of payment makes for more ethical practices than the other group.

On one hand, physicians who are salaried tend to think that this payment system reduces the possibility of many ethical breaches. From their perspective, if their salaries do not depend on the number of human subjects they enroll or retain in studies, there is less reason to allow flexible interpretations of the study protocols and subjects' test results. It also means that physicians who maintain private practices do not need to hustle their own patients into clinical trials in order to get paid as investigators. As one salaried physician explained, "I'm on salary, I don't get paid according to how many subjects I put on a study. That's a no-no, and I wouldn't even want to do that. As such, I have some freedom of not feeling pressure to try to have any of my patients become subjects." (Physician Investigator D).

On the other hand, physicians who are not salaried tend to think incentivized payment systems make them more conscientious investigators for the pharmaceutical industry. For them, it is not a question of their pay influencing their decisions about individual subjects. Instead, they see their uncertain pay as motivating them to work harder and to put more energy into the clinical trials they conduct. One such physician argued, "Somehow if you're not individually [financially] invested in what's going on at your site, you tend to let things ride and things aren't as strong. Whereas if that's where your bread and butter comes from, then it's important to you" (Physician Investigator A). Another physician who acknowledged that money has the potential to influence research practices also argued that the same payment system holds unethical behaviors in check. From his perspective, money could motivate physicians and research staff to bend the rules of the study protocols, but at the same time, physicians are also always concerned about getting the next study and fudging the data could cost them much more revenue in the long term if not put them out of business altogether:

I can see that anytime you combine money with judgment and ethics, the money will win sometimes

and ethics will win sometimes... What I don't think [money] does much, and I'm sure it probably does some of the time, is have marginal or truly not qualified patients put into the study. The same incentive of putting them in is *already* there; [the sites are] getting paid \$1600 to \$20,000 a patient depending on the study, *anyhow*. An additional \$5 or \$2000 or something like that isn't going to change the ethics of the site... But regarding the ethics of the site, if you get a bad reputation, then it's *harder* to do well in this business, particularly if the reputation is deserved. I'm not saying it's impossible, but it *is* harder. (Physician Investigator C)

In spite of their differences, private-sector physicians regardless of the system of payment they fall under are aware both of the bad press and the attitude of the bioethics community regarding financial “conflicts of interest.” In response to these outsider perspectives on their work and on the industry as a whole, physicians tend to coalesce around the same position: that it is impossible to separate the business from the research no matter what. The point for many of these physicians is that the framing of financial conflicts of interest implies that there is a pure state of research that will not be influenced by any monetary pressures. Physicians interpret this framing of the financial aspects of their work as both naïve and as a problem that is not unique to clinical trials work. One physician who is salaried articulated his opinion about the additional scrutiny on researchers: “There’s a higher level of significance, perceived *ethical* significance, that goes along with people’s health. If there are intentional fraudulent behaviors — even compared to if you’re screwing around with other people’s money, which nobody likes” (Physician Investigator D). In his view, these financial issues are endemic to all industries and all types of work, but because the clinical trials industry is dealing with human health and illness, there is an increased scrutiny to the impact of financial matters on physicians’ ethical conduct.

Conclusion

This paper has illustrated the ways in which private-sector physicians construct ethical codes of conduct in their clinical trial work. Rather than perceiving their ethical responsibility solely in terms of the patients/subjects they enroll in studies, physicians primarily envisage ethics in terms of adhering to the study protocols that pharmaceutical companies hire them to conduct. This does not mean that physicians do not take

seriously their responsibility to safeguard human subjects, but rather than seeing that as their primary ethical obligation, it is merely part of the good conduct of the study protocols. Although physicians are not immune to the critiques of the bioethics community and the mainstream media regarding their work, they construct their sense of what is ethical through their everyday practices in the clinic in relation to the needs of the pharmaceutical industry and their own business bottom-lines. That financial conflicts of interest may cause some ethical breaches is to be expected from bioethics reports on the matter, but what those scholars miss are the ways in which financial interests can also motivate physicians to conduct studies ethically. The interest of future business and future prosperity also profoundly shape the decisions that physicians make about present studies.

This paper is not meant as an apology for the financial arrangements that are prevalent in the clinical trials industry. From a more normative position, contract research is fraught with ethical dilemmas that are not captured within physicians’ own construction of research ethics and need to be explored in further detail in future research. Instead, this paper is meant to show the continuities and differences in the ethical norms and practices of physicians in the role of investigators. Although it is unclear the extent to which private-sector physicians, who make up the vast majority of pharmaceutical investigators, differ from their academic counterparts engaged in the same or similar clinical trials, this empirical research indicates how research ethics gets articulated and defined by the largest segment of researchers in the U.S.

Even before the development of a codified system of research ethics, physicians were guided by tacit and contextualized rules of ethics. While much has changed in how and where research is conducted from the mid-20th century, what has not changed is that physicians continue to develop their own codes of ethics in response to their professional roles and responsibilities. What is different today is that private-sector physicians’ construction of ethics is shaped by their obligations to pharmaceutical companies rather than to human subjects or to science more generally.

Physicians are not unaware of conflicts of interest between patient care and pharmaceutical research, yet they may see these conflicts as irreconcilable on their own terms. Instead, physicians construct their ethical conduct in terms of producing data in lines with study protocols and fulfilling their contracts with pharmaceutical companies. This orientation defines “ethical” practice

in a more clear-cut way because it requires that physicians simply follow pharmaceutical companies' instructions. In contrast, a focus on ethics in relation to patients' subjects requires physicians to navigate significant clinical, as well as ethical, ambiguity. Given that the field of bioethics disagrees about solutions to conflicts of interest and ethics in human subjects research, it is no wonder that physicians choose to redefine the problem of clinical ethics in such a way that, for them, it can be resolved.

Appendix. Demographic information for quoted informants

- Physician Investigator A: male, 60–70 years, internal medicine, 20+ years in industry
- Physician Investigator B: female, 35–45 years, pediatrics, 3 years in industry
- Physician Investigator C: male, 40–50 years, neurology, 10 years in industry
- Physician Investigator D: male, 40–50 years, rheumatology, 15 years in industry
- Physician Investigator E: male, 30–40 years, internal medicine, 1 year in industry
- Physician Investigator F: male, 45–55 years, family medicine, 2 years in industry.

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