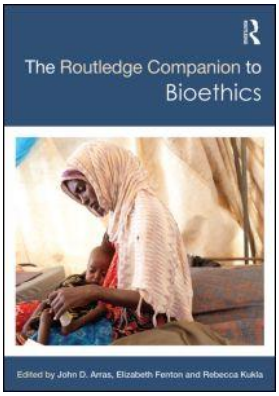

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THE ETHICS OF INCENTIVES FOR PARTICIPATION IN RESEARCH

What's the Problem?

Alan Wertheimer

The purpose of this chapter is to ask whether it is ethical to provide financial or medical incentives to people to motivate them to participate in research. It is best to put this issue in a wider context.

The ethics of medical research with human subjects raises genuine moral worries not to be found in the ethics of medical care. At the most general level, the core problem of medical (therapeutic) ethics is to determine what we can ethically do to people *for their benefit*. By contrast, the core problem of research ethics with human subjects is to determine what we can ethically do to people by using them as means to produce generalizable knowledge (Wertheimer 2011: ch. 1).

And clinical research really uses people as means. No Kantian abstractions necessary here. Researchers inject substances, draw blood, perform lumbar punctures, intubate trachea, withdraw medication for schizophrenia, perform sham arthroscopic surgery, extract and store tissue, and expose healthy volunteers to malaria-infected mosquitos. Although subjects may occasionally or even often receive medical or collateral benefits from participating in research, they emphatically do not benefit from many component procedures (for example, blood draws and lumbar punctures) that are designed to test study hypotheses.

The difficulties involved in recruiting subjects into clinical trials illustrate this problem. More than one trial in five sponsored by the National Cancer Institute failed to enroll a single subject, and only half reached the minimum needed for a meaningful result (Ramsey and Scoggins 2008). Among adults diagnosed with cancer, fewer than 5 percent participate in trials. It seems reasonable to assume that more and faster completed studies would yield greater progress in the treatment of cancer, and similar things could be said about other diseases or improvements in people's quality of life.

Although it would be desirable to facilitate recruitment of subjects into clinical trials, it is generally thought that it is unethical to enlist people in research without their valid consent. As the Nuremberg Code (1949) puts it, "The voluntary consent of the human

subject is absolutely essential" (Emanuel et al. 2003). On analysis, this simple view is false. For example, most think it is ethical to conduct observational social and behavioral research without any sort of consent as when psychologists sought to determine whether wealthy drivers (as indicated by their cars) behaved more unethically than less wealthy drivers (Piff et al. 2012). It is also thought that it is ethical to conduct minimal risk social and behavioral research without informed consent when subjects must be deceived if research is to produce scientifically valid data. Indeed, Federal Regulations explicitly allow for waivers of informed consent under these very sorts of conditions (45 CFR § 46.116(d)).

Consent is more likely to be required in biomedical research, but there are exceptions there as well. Even if we set aside cases in which surrogates consent for the subject (for example, children), there are special circumstances, such as emergency research in which research may be justified even though no sort of consent is possible. Research without consent may also be justifiable when it involves public health surveillance, collection of data from health records, or cluster randomized trials when it is impractical or impossible to seek everyone's consent.

These exceptions to the Nuremberg principle deserve more attention than they receive. If much research can be ethically permissible without valid consent, it is a puzzle why informed consent is typically regarded as a *sine qua non* of ethical biomedical research. And this is especially so when we consider the general problem of recruiting research subjects (Wertheimer 2011: ch. 2).

Although it is rarely discussed in these terms, participation in research often constitutes a classic collective action problem. It is in the *ex ante* interest of most people that research be conducted, but participation in actual research can be contrary to the interests of each individual. *Ex ante*, we may all be better off if all of us do our fair share of participation in research. But the knowledge generated by research is a *public good*, i.e., it is a good that is available to all whether or not one contributed to it. And to the extent that people are self-interested, they will seek to reap the benefits of research without paying the costs. Precisely for that reason, we often rely on the use of coercion to solve collective action problems in many contexts. We tax citizens to pay for public goods, including funding research that generates knowledge that is available to all. We require that cars come equipped with catalytic converters. We can at least ask: Why not require people to participate in biomedical research in much the same way?

For present purposes, I set such concerns aside. The question remains as to how we can ethically recruit people to participate in socially valuable biomedical research that is consistent with our commitment to requiring consent. There seem to be at least four alternatives. First, we could simply accept a slower pace of medical research as the price we pay for accepting the values secured by consent. Hans Jonas famously argued that avoidable illness and death are regrettable but not of overarching moral significance because "progress is an optional goal" (Jonas 1969: 224). Second, we could do more to encourage altruistic participation or to educate people about the benefits of receiving medical care in a research context. Third, investigators can give people financial incentives to participate such that the value of the payment exceeds the disvalue of the risk and burdens of participation. Fourth, investigators can take advantage of the fact that participation may be in a person's medical interest, as when participation is the only means of gaining access to an experimental intervention or, more problematically, when subjects do not have access to or cannot afford medical care. This explains one reason why pharmaceutical corporations have increasingly conducted their research in less developed countries in Eastern Europe, South America, Asia, and Africa.

Bioethicists have viewed some of these strategies for recruiting subjects with considerable suspicion. Carl Elliott (2008: 40) maintains, "Ethicists generally prefer that subjects take part in studies for altruistic reasons." As John Harris (2005: 246) puts it, "Most research ethics protocols and guidelines are antipathetic to inducements." Australian policy states that "volunteers may be paid for inconvenience and time spent, but such payment should not be so large as to be an inducement to participate" (Wilkinson and Moore 1997: 373). With respect to research in developing countries, many have claimed that this practice is grossly exploitative—"Residents of impoverished, postcolonial countries, the majority of whom are people of color, must be protected from potential exploitation in research. Otherwise, the abominable state of health care in these countries can be used to justify studies that could never pass ethical muster in the sponsoring country" (Lurie and Wolfe 1997: 855).

So is it ethical to provide financial or medical incentives to people to motivate them to participate in research? In particular, does the use of financial or medical incentives constitute coercion or undue influence and thereby compromise the validity of consent? I will argue that offering incentives does not compromise the validity of consent. But even if people can give voluntary informed consent when participation is in their financial or medical interests, it may be wrong to exploit their financial or medical needs. And so I shall consider whether the use of incentives can constitute exploitation and whether that is a good reason to prohibit the use of such incentives.

Coercion

David Rothman has remarked that when investigators recruit lower-income patients who either need the money or cannot afford conventional treatment, it is "coercion through lack of income" (Rosen 2012: 40). Although one can legitimately use the word coercion in different ways and for different purposes, we must be careful when we claim that the use of financial incentives is coercive. Words have consequences. In a recent study of institutional review board (IRB) members' views of coercion, one of the respondents noted that "Coercion has come to mean something more along the lines of simple influence in the IRBs I have worked with—not the meaning it has in other contexts" (Largent et al. 2012: 4). This statement suggests that this respondent's IRB has adopted an excessively expansive account of coercion that may be used inappropriately to limit the activities of researchers and prospective subjects.

So what constitutes the sort of coercion that invalidates consent? *The Belmont Report*, upon which many rely for authoritative guidance, gets it basically right: "Coercion occurs when an overt threat of harm is intentionally presented by one person to another in order to obtain compliance" (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1978). It is worth emphasizing that this definition states that coercion requires a *threat* of harm. I have argued elsewhere for a minor modification of Belmont's suggestion. Putting aside some minor complications, A coerces B to consent to do X only if A proposes to violate B's rights or not fulfill an obligation to B if B chooses not do X (Wertheimer and Miller 2008).

On this view, A does not coerce B to do X if A offers to give a benefit to B if B consents to do X. Threats are coercive but genuine offers are not. Threats reduce the options available to the target, whereas offers expand them, and one does not coerce another when one's proposal expands the options available to her. Ruth Macklin has said that the question as to how large a payment constitutes a coercive offer is one for "which no

clear answer is forthcoming" (Macklin 1989: 3). I disagree. A clear answer is forthcoming: Genuine offers do not coerce.

Those who think that offers can coerce sometimes appeal to the well-known phrase from *The Godfather*—"My father made him an offer he couldn't refuse." But Don Corleone's proposal was coercive not because it was an exceptionally attractive offer, but because it was a paradigmatically coercive threat—"Either your signature or your brains will be on the contract."

Now to say that offers do not coerce is not to deny that offers can be seriously immoral:

> *Bribe*. A, a police officer, stops B for speeding. B offers to give A $100 if B does not write a ticket. A accepts.

It is immoral for B to offer a bribe to A and it is immoral for A to accept a bribe, but B's offer hardly coerces A in a way that negates or reduces A's responsibility for accepting it. Similarly, if A offers to pay B $10,000 to kill C, B could hardly claim that A coerced him into killing C by offering a financial incentive.

In a recent study we found that many IRB members were in the grips of serious misconceptions about the concepts of coercion and undue influence. For example, some respondents thought that offers of payment were coercive or unduly influential when they motivated people to agree to participate when they would otherwise not do so, a view that is incorporated in the Australian policy noted above (Largent et al. 2012). This view is dubious. There are numerous ways of motivating people to do things that they would otherwise not do, and most of them do not involve coercion or anything morally problematic. If A persuades B to give blood or go to a movie or invest in a mutual fund when B would otherwise not do so, it is clear that B has not been coerced. The same is true for offers. If A offers the teenager next-door $20 to mow his lawn, we would not say that the teenager has been coerced.

Another popular view claims that A coerces B to do X when A's proposal leaves B with "no reasonable alternative" but to accept A's proposal. This is a natural but deeply mistaken view. It is a natural view because one generally has no reasonable alternative but to succumb to a coercive proposal. Consider the paradigmatic case in which A (a gunman) says to B, "hand over your wallet or I'll shoot you." Although A has been coerced to hand over his wallet and although B has no reasonable alternative but to do so, it does *not* follow that B has been coerced *because* he has no reasonable alternative.

To see this, simply note that there are many situations in which people choose options because they lack reasonable alternatives without being coerced. Arthur Caplan accepts the "no reasonable alternative" view when he claims that illness is coercive. But we do not say that a patient who agrees to surgery or chemotherapy because the only alternative is death has been coerced to consent or that her consent to treatment is involuntary or invalid. Nor do we describe people as coerced if they take an unpleasant job in order to provide for their families if their only alternative is to remain unemployed.

Now consider the person who consents to participate in research in exchange for payment because her background conditions are very poor. David Rothman (2000) writes, "abject poverty is harsh enough without people having to bear the additional burdens of serving as research subjects." If research participants are *benefiting* from participation all things considered, we might just as well say that abject poverty is harsh enough without denying people the opportunity to make their lives somewhat less

miserable by participating in biomedical research and receiving financial payments or medical care that they would not otherwise receive. We can grant that people "do not have enough options and that society has been unjust to them in not extending more options, while nonetheless respecting and honoring the choices they actually make in reduced circumstances" (Nussbaum 1998: 721).

I suspect that many concerned with the protection of research subjects accept a form of "research exceptionalism" whereby factors that would not compromise the validity of consent in other contexts are thought to be worrisome in the context of research. After all, we allow people to assume high-risk jobs such as police work, military, fire-fighting, timber cutting, lobster fishing, structural steel work, coal mining, and professional football. We do not think that people are coerced by the offer of payment into accepting such risks, and, similarly, we should not think that prospective subjects are coerced by the offer of payment.

What would constitute coercion to participate in research? If a doctor were to implicitly or explicitly threaten to abandon a patient if he does not agree to participate in research, then the patient's decision is coerced and involuntary. If a patient were to mistakenly *fear* that he would be abandoned if he did not agree, then we might say that his decision to participate is involuntary although he has not actually been coerced. But those sorts of situations aside, we should probably simply abandon the concern that offers of payment or medical care are coercive.

Undue Influence

Even if offers of payment or medical care do not coerce, they could constitute undue influence and thereby invalidate consent. But what sort of influence is undue in that way? *The Belmont Report* states that "Undue influence, by contrast [with coercion], occurs through an offer of an excessive, unwarranted, inappropriate or improper reward or other overture in order to obtain compliance" (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1978). Unfortunately, this account is not helpful. It does not specify when or for what reasons an offer should be considered excessive, unwanted, inappropriate or improper, or indicate why such offers compromise the validity of consent.

I think that A's offer of payment is best understood as undue influence if and only if it is so attractive that it distorts subjects' evaluation of the risks and benefits of participation. The Office for Human Research Protections (OHRP 2011) guidebook for IRBs implicitly endorses this view when it says "Offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment." For reasons noted above, it hardly makes sense to say that an incentive is unduly influential just because it gets people to consent when they would otherwise not do so. Once again, on this view an inducement is *not* morally problematic if it is *genuinely* too good to refuse. It is problematic if it would be refused if the agent's judgment were not blinded or clouded or impaired.

In principle, an agent's decision-making could be distorted by the offer of inducements in at least two ways. An agent may experience *tunnel vision* when the lure of the payment causes the agent to ignore or give inadequate consideration to other relevant interests. An agent may experience *decisional myopia* when the lure of the inducement causes her to overweight the short-term benefits and underestimate or underweight the long-term costs of participation. Distortion of judgment is the key (Wertheimer 2011: ch. 4).

The Council for the International Organization of Medical Sciences worries that the offer of monetary payments may "induce prospective subjects to consent to participate

in the research *against their better judgment*" (CIOMS 2002). But what does that mean? The phrase "against one's better judgment" sometimes conveys that we do something reluctantly. For example, a professor might say to a student, "It's against my better judgment but I'll grant your request for an extension on your paper." The professor does not think that he acts involuntarily or that he is not responsible for his decision. A's offer of money (or medical benefits) may motivate B to do something that *would* have been against her better judgment in the absence of the value of the offer, but that does not show that acceptance of the offer is against her better judgment *given* the value of the offer to her.

It is sometimes argued that an offer constitutes undue influence or compromises voluntariness if it is so large or in excess that it is irresistible in this context. Once again, we must be careful. We cannot say that an offer is irresistible just because one finds it hard to reject it, for that is true of all choices for which we have strong desires. We might say that a proposal is irresistible just in case no reasonable person (in that person's situation) would reject the proposal, as when a person of modest means is offered $1,000 to mow a lawn. On that view, however, there would be nothing wrong with making an irresistible offer and no reason to question the validity of the consent.

Grant and Sugarman (2004: 728) argue that while incentives are always designed to motivate "someone to do what they otherwise might not," there is something ethically suspect about using an incentive to get "someone to do something to which they are *averse* . . . And the ethical problem is multiplied where the aversion is a principled one or a matter of moral scruple."

I'm not sure I understand the distinction between (1) getting someone to do something they would otherwise not do in the absence of an incentive, and (2) getting someone to do something to which they are averse. If I would not work unless I were paid for doing so, does it not mean that I am averse to working without being paid? Grant and Sugarman might say that I'm not averse to teaching college students but I might be averse, say, to teaching middle school students or mowing lawns. I don't think this reply will work. For whatever sum of money that would be sufficient to motivate me to teach college students (to which I would be averse in the absence of being paid that sum), there is a greater sum that would be sufficient to motivate me to teach middle school or mow lawns.

Grant and Sugarman (2004: 728) might claim that things are different if the aversion is "a principled one or a matter of moral scruple," as for example, if one tried "to induce religious people to work on the Sabbath by offering large incentives." This is tricky. It does seem perverse to offer Mormons (whose religion prohibits consumption of caffeine) a large cash incentive to participate in a study of the effects of caffeine on the brain (the research may require people who have never consumed caffeine), even if there is nothing intrinsically wrong with the consumption of caffeine. But I am not sure to what extent this intuition is defensible.

First, people do not all place the same weight on their moral commitments as contrasted with their non-moral interests. Second, and more importantly, even if an offer may motivate B to violate *one* of her moral values, people have multiple values and commitments. Consider this case:

> *Family.* A wants to hire B. The job would require that B spend much of her time traveling. B tells A that she is reluctant to accept because she thinks she has an obligation to her spouse and children to work close to home. A raises the offer. B accepts.

Grant and Sugarman might argue that A is acting wrongly because he is seeking to get B to do something to which she was averse on moral grounds (her obligation to her family). I disagree. First, it might be objectionably paternalistic for A to not offer B a payment on this ground. Unless A has reason to think that his offer will distort B's judgment, A shows respect for B's autonomy by allowing B to make her own decisions in the light of her own value structure and not by preemptively short-circuiting B's decision process or opportunities. Second, people have multiple aims, projects, and obligations. B may believe that she has an obligation to spend time with her family, but she may also believe that she has a greater obligation to provide for them financially.

That is precisely why some people choose to participate in research. Consider the story of Rambha Gajre, a woman in India:

> She and her family faced eviction from their cramped, tin-roof hut if she didn't soon repay loans she used to cover life-saving medical treatment for her son . . . "Many people commit suicide and I didn't want to become one of those and I didn't want people to think I did it to avoid repaying. I have two young kids, 10 and 12 years old. What would become of them?" So Rambha did what thousands of other desperate women and men from India's slums, and across the world, now do to survive—she signed up to be a human guinea pig in drug trials for foreign pharmaceutical companies." In explaining her decision, Rambha said "I am helpless, I have to do this . . . They don't really force us, but I don't have a choice."
>
> (NBC News 2012)

This is a sad story, but it seems that Rambha knew what she was doing. She was participating in research in order to provide for her family. I am reluctant to say that her judgment was distorted or that it would have been better to deny her that opportunity.

Absent showing that participants are making irrational judgments in response to offers of financial payment, there is no reason to reject them on this ground. Moreover, although the evidence on this is limited, several empirical studies suggest that financial incentives do *not* cause subjects to be insensitive to the risks of participation (Halpern et al. 2004). Given the difficulty of recruiting subjects into socially valuable research, we should be reluctant to reject the use or even increased use of incentives as a means of facilitating recruitment when it is compatible with the principle of informed consent.

Exploitation

The concept of exploitation has also come to play an important role in discourse about the ethics of clinical research. Indeed, some bioethicists have argued that the principle of non-exploitation is the underlying rationale for many of the oft-mentioned principles of ethical research such as social value, scientific validity, informed consent, fair participant selection, and favorable risk–benefit ratio (Emanuel et al. 2000).

Accusations of wrongful exploitation in research are most frequently invoked with respect to research with vulnerable populations, such as prisoners, people on low income, and the desperately ill. The charge seems particularly poignant in the international context when poor citizens in less developed countries (LDCs) are used as subjects in research that is primarily designed to benefit those in developed countries: "the specter of exploitation is the most serious ethical issue in multinational clinical research" (Emanuel 2007: 189). Accusations of exploitation are especially applied to the growing

practice in which pharmaceutical corporations "outsource" medical research to contract research organizations that, in turn, conduct many of their studies in *LDCs*—"A huge population with a diversity of diseases that are untreated—yes, that is the 'India Advantage'" (India Resource Center).

Accusations of exploitation reached fever pitch when investigators conducted placebo-controlled trials in LDCs when proven effective treatment was available in developed countries (Angell 1997). Consider *The Short-Course ART Trial*. Placebo-controlled trials had unequivocally established the efficacy of a "long course" use of the antiretroviral drug zidovudine for reducing maternal–fetal transmission of HIV (Connor et al. 1994; Lurie and Wolfe 1997). The protocol involved administering the drug orally to women who were HIV positive during pregnancy, administering the drug intravenously during labor, and subsequently administering the drug to the newborn infant. Unfortunately, the efficacy and use of the long course regime could not be confidently extrapolated to LDCs. First, the drug might not be as efficacious in LDCs due to differences in immune status and breastfeeding practices. Second, even if the long course regime proved to be efficacious in LDCs, many thought that its use was not administratively or economically feasible. It would prove too expensive, compliance with the regime would prove virtually impossible for many women, and many LDCs lacked the medical infrastructure, such as refrigeration, to support its administration. Given these facts on the ground, investigators wanted to determine whether a cheaper and simpler "short course" use of zidovudine would be reasonably effective in reducing maternal–fetal transmission of HIV even if it would not be *as* effective as the long course regimen.

It would have been ethically impossible to conduct a placebo-controlled trial (PCT) of the short course regimen in a developed nation where the local standard of care would have included the long course regimen. It would not be approved by an IRB and even if it were approved, women would not consent to participate if the long course were available. By contrast, it was ethically feasible, many argued, to recruit subjects to a PCT of the short course treatment in an LDC where the local standard of care was to receive no treatment at all. In effect, the investigators offered subjects a 50 percent chance of getting treatment where the subjects would otherwise have received nothing. The placebo-controlled trials were conducted but were widely condemned as unethical and exploitative because the investigators deliberately withheld a proven effective intervention from those in the control group.

Exploitation in clinical research is a large topic with many dimensions. The question I want to focus on here is this: Is there reason to prohibit research just because it is exploitative? To begin, it is crucial to distinguish between types of exploitation on two axes. First, we can distinguish between *harmful exploitation* and *mutually advantageous exploitation*. By harmful exploitation, I refer to those cases in which the exploiter gains by harming the exploitee. By mutually advantageous exploitation, I refer to those cases in which both parties—including the exploitee—reasonably expect to gain from the transaction as contrasted with the pre-transaction position (Wertheimer 1996, 2011: ch. 5).

We can similarly distinguish between *non-consensual exploitation* and *consensual exploitation*. By consensual exploitation, I refer to cases in which the exploitee gives valid consent in the sense that she is competent, has adequate information, and is not coerced.

These two distinctions overlap but are not equivalent. There can be cases of mutually advantageous but non-consensual exploitation. There can also be cases of harmful but consensual exploitation, as when a self-loathing B allows A to benefit by harming her. Nonetheless, because these distinctions tend to converge, I shall rely on the distinction

between harmful non-consensual exploitation and mutually advantageous and consensual exploitation.

Now it is not easy to explain how and when a mutually advantageous and consensual transaction is exploitative. When does A take unfair advantage of B? Consider *Umbrella*.

> *Umbrella*. A, a storeowner, normally charges $10 for an umbrella. B, who is wearing an expensive suede jacket, wants to buy an umbrella from A. A sees that it is pouring and tells B that the umbrella will cost $50.

The transaction is mutually advantageous because it is better for B to buy the umbrella for $50 than not to do so. It is arguably consensual because B understands that to which she is consenting, because it is rational for B to consent, and because A's proposal is not coercive, i.e., A does not threaten to violate B's rights if she declines. Nonetheless, it seems that A is taking unfair advantage of B. But what is the criterion of unfairness? Some say that a transaction is exploitative when the exploiter gains much more than the exploitee. But contrary to what is often supposed, the exploited person usually gains *more* utility from a transaction than the exploiter. For example, the utility gain to B (who preserves an expensive jacket worth $1000) is probably much greater than the utility gain to A (who gets, say, $40 more than usual). Indeed, it is precisely because the exploiter stands to gain relatively little that he can threaten to walk away from the transaction.

Let us assume for the sake of argument that the terms of *Umbrella* are exploitative. The important question for our purposes is whether we should endorse the principle that A should not be able to sell the umbrella to B for $50 or that B should not be able to buy it. In the present context, we must determine whether investigators should not be permitted to exploit research subjects by offering inadequate benefits to them *if* the subjects benefit from participating in research because they receive medical care or financial payment and if they are giving valid consent to participate.

What could justify not allowing the parties to enter into a mutually advantageous consensual transaction? This issue is too complicated to be answered here. In general, I think that we should be very reluctant to interfere with transactions between investigators and subjects if participation is beneficial to the subjects and they give valid informed consent. And that includes participation in placebo-controlled trials in which subjects consent to participate in order to get a 50 percent chance at receiving at medical care. Although I am not convinced that the short course trial actually did exploit the subjects, we can concede for the sake of argument that the subjects were treated unfairly and still maintain that it is best to allow the research to take place. We may object to and work to change the circumstances that render it reasonable for people to consent to participate in exchange for medical care or what strikes us as inadequate financial compensation, but, as a general principle, we do the people of LDCs no favor if we deny them the opportunity to participate in research when they are better off if they do so.

To put the previous point slightly differently, it is sometimes right to allow people to do an act that is wrong. It may be right to allow people to engage in wrongful or hateful speech. And it may be right to allow one person to exploit another if the exploitee benefits from the exploitation and consents to it.

It might be thought that it is one thing to employ people in LDCs to produce running shoes for low wages if the workers benefit from doing so and quite another to employ them as subjects in a trial of a new drug for type 2 diabetes, whether they do it for money

or for access to medical treatment that they would otherwise not receive. Shamoo and Resnik (2006: w8) say "it is especially important to prevent pharmaceutical companies from using people in developing countries as cheap labor to test drugs that will only be used in the developed world, because this would constitute an egregious form of exploitation." Although they do not say what it is that makes this practice exploitative, it is not clear why we should want to prevent it. Would they seek to prevent running shoe manufacturers from using people in developing countries as cheap labor to manufacture shoes that will only be used in the developed world if what is cheap labor to us are among the better jobs available in such societies?

I have argued elsewhere that we would be justified in prohibiting exploitative transactions *if* doing so would result in transactions that are fairer (Wertheimer 2011: ch. 5). So we prohibit people from working for sub-minimum wages in the hope that employers will not refuse to employ people but will, instead, employ them at a fairer wage. If prohibiting investigators from exploiting subjects will result in fairer terms for the subjects, then we can justify prohibiting mutually advantageous and consensual transactions. But if prohibiting such transactions causes the research not to be done with those subjects to their detriment, then it is actually difficult to justify not allowing such exploitation to occur.

Conclusion

The recruitment of subjects into socially valuable biomedical research presents us with a difficult problem. Given that people's willingness to incur the burdens and risks of participation is rather limited, the progress of research is held back to the detriment of all of us. We should therefore support strategies that give people incentives to participate when they would otherwise not do so. At the same time, those strategies must be compatible with respect for the interests and autonomy of prospective subjects. In particular, we should not recruit people into research without their valid informed consent. Adhering to this principle is not without cost. Baruch Brody (2011) describes a placebo-controlled study of the benefits of arthroscopic surgery in which subjects were required to write by hand that they understood that they might be receiving "sham surgery." Although this procedure generated a "significant refusal rate," Brody maintains that this is "the price you may have to pay if you increase potential subjects' understanding." No one said that ethics comes cheap.

But the price need not and should not be more expensive than it needs to be. Many people object to the use of financial or medical incentives for participation on the grounds that they are or can be coercive or unduly influential or exploitative. I have argued that genuine incentives do not coerce and that incentives are unduly influential only if they distort the prospective subject's ability to make a reasonable determination as to whether the benefits of participation outweigh the burdens and risks of participation. Prospective subjects need protection when they are not capable of understanding the risks and burdens of participation (Wertheimer 2011: ch. 2). But they also need respect, and we do not respect people when we deny them the opportunity to participate when it is in their interest to do so.

Given that there is a tradition of research ethics that claims that participation should always be altruistic and, at its best, that participants should adopt the goals of the research as their own goals, it is not surprising that some IRB members will find it unseemly to introduce payment into the research equation (Jonas 1969). But such justifiable caution

about payment does not warrant misconceiving and misapplying the concepts of coercion and undue influence. If, as in other contexts of life, people can reasonably regard the value of payment or other incentives as greater than the risks of engaging in some activity, be it ordinary employment or participation in research, then we do not protect subjects when we preclude their activity on grounds of coercion or undue influence or exploitation.

Related Topics

Chapter 16, "The Future of Informed Consent to Research: Reconceptualizing the Process," Paul Appelbaum
Chapter 23, "Incentives in Health: Ethical Considerations," Richard Ashcroft

Bibliography

Angell, M. (1997) "The Ethics of Clinical Research in the Third World," *New England Journal of Medicine* 337: 847–9.

Brody, B. (2001) "Making Informed Consent Meaningful," *IRB* 23 (5): 1–5.

CIOMS (2002) "International Ethical Guidelines for Biomedical Research Involving Human Subjects," The Council for International Organization of Medical Sciences, guideline 7. Available at: http://www.cioms.ch/publications/layout_guide2002.pdf (accessed July 18, 2014).

Common Rule (2009) 45 CFR Part 46.

Connor, E.M., Sperling, R.S., Gelber, R., Kiselev, P., Scott, G., O'Sullivan, M.J. et al. (1994) "Reduction of Maternal–Infant Transmission of Human Immunodeficiency Virus Type 1 with Zidovudine Treatment" [electronic version]. *New England Journal of Medicine* 331: 1173–80.

Elliott, C. (2008) "Guinea Pigging," *The New Yorker* January 7, 36–41.

Emanuel, E. (2007) "The Paradox of Exploitation," in J. Lavery, C. Grady, E.R. Wahl and E.J. Emanuel (eds.) *Issues in International Biomedical Research: A Casebook*, New York: Oxford University Press.

Emanuel, E., Wendler, D. and Grady, C. (2000) "What Makes Clinical Research Ethical?" *JAMA* 283: 2701–11.

Emanuel, E. et al. (eds.) (2003) *Ethical and Regulatory Aspects of Human Subjects Research*, Baltimore, MD: Johns Hopkins University Press.

Grant, R. and Sugarman, R. (2004) "Ethics in Human Subjects Research: Do Incentives Matter?" *Journal of Medicine and Philosophy* 29: 717–38.

Halpern, S.D., Karlawish, J.H., Casarett, D., Berlin, J.A. and Asch, D.A. (2004) "Empirical Assessment of Whether Moderate Payments are Undue or Unjust Inducements for Participation in Clinical Trials," *Archives of Internal Medicine* 164: 801–3.

Harris, J. (2005) "Scientific Research Is a Moral Duty," *Journal of Medical Ethics* 31: 242–7.

India Resource Center (2004) http://www.indiaresource.org/issues/globalization/2004/indianguineapigs.html (accessed July 11, 2014).

Jonas, H. (1969) "Philosophical Reflections on Experimenting with Human Subjects," *Daedalus* 98: 219–47.

Largent, E., Grady, C., Miller, F.G. and Wertheimer, A. (2012) "Misconceptions About Coercion and Undue Influence: Reflections on the Views of IRB Members," *Bioethics* 27: 500–7.

Lurie, P. and Wolfe, S. (1997) "Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries," *New England Journal of Medicine* 33: 853–6.

Macklin, R. (1989) "The Paradoxical Case of Payment as Benefit to Research Subjects," *IRB* 11: 1–3.

Nussbaum, M. (1998) "Taking Money for Bodily Services," *Journal of Legal Studies* 27: 693–724.

NBC News (2012) http://investigations.nbcnews.com/_news/2012/03/04/10562883-in-india-oversight-lacking-in-outsourced-drug-trials (accessed July 11, 2014).

Office for Human Research Protections (OHRP) (2011) *IRB Guidebook*. Available at: http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm (accessed July 11, 2014).

Piff, P., Stancato, D.M., Côté, S., Mendoza-Denton, R. and Keltner, D. (2012) "Higher Social Class Predicts Increased Unethical Behavior," *PNAS* 109: 4086–91.

Ramsey, S. and Scoggins, J. (2008) "Commentary: Practicing on the Tip of an Information Iceberg? Evidence of Underpublication of Registered Clinical Trials in Oncology," *The Oncologist* 13: 925–9.

Rosen, G. (2012) "Studying Drugs in All the Wrong People," *Scientific American Mind* September–October: 32–41.

Rothman, D. (2000) "The Shame of Medical Research," *The New York Review of Books*, November 30.
Shamoo A. and Resnik, D. (2006) "Strategies to Minimize Risks and Exploitation in Phase One Trials on Healthy Subjects," *American Journal of Bioethics* 6 (3): W1–13, w8.
The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1978) *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (DHEW Publication OS 78-0012). Washington, DC: Department of Health, Education, and Welfare. Available at: http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html (accessed July 23, 2014).
Wertheimer, A. (1987) *Coercion*, Princeton: Princeton University Press.
Wertheimer, A. (1996) *Exploitation*, Princeton: Princeton University Press.
Wertheimer, A. (2011) *Rethinking the Ethics of Clinical Research*, New York: Oxford University Press.
Wertheimer, A. and Miller, F. (2008) "Payment for Research Participation: A Coercive Offer?" *J Med Ethics* 34: 389–92.
Wilkinson, M. and Moore, A. (1997) "Inducements in Research," *Bioethics* 11: 373–89.