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The Right to Withdraw from Research*

ABSTRACT. The right to withdraw from participation in research is recognized in virtually all national and international guidelines for research on human subjects. It is therefore surprising that there has been little justification for that right in the literature. We argue that the right to withdraw should protect research participants from information imbalance, inability to hedge, inherent uncertainty, and untoward bodily invasion, and it serves to bolster public trust in the research enterprise. Although this argument is not radical, it provides a useful way to determine how the right should be applied in various cases.

It is universally accepted that participants in biomedical research have the right to withdraw from participation at any time, except, perhaps, when withdrawal would constitute a threat to their health or the health of others. The right to withdraw is encoded in nearly every document on the requirements for ethical conduct of research on humans, including the U.S. Code of Federal Regulations governing all federally-funded research, the Common Rule (45 CFR 46); the Declaration of Helsinki (WMA 2008); the 2002 research guidelines of the Council for International Organizations of Medical Sciences (CIOMS 2002); and the Belmont Report (National Commission 1979). Presumably, if codification of the right in these guidelines were meant merely to prevent investigators from physically compelling subjects to remain in a trial, they would be unnecessary as such protections are already afforded in common law. After all, even if consent to participate in a trial constituted a promise or contract to complete the trial (barring unforeseen adverse events), the

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U.S. legal system does not ordinarily require a party to perform a specific act ("specific performance"), although one can be required to compensate another party for breach of contract (American Law Institute 1981). So the crucial issue is not whether subjects can be physically coerced into completing a trial. They cannot. To use the language of CIOMS as a framework, the question is whether and why subjects have the right to withdraw *without penalty or the loss of benefits to which the subject is otherwise entitled*. (We often use "right to withdraw" as shorthand for this more elaborate formulation).

Despite its near universal acceptance, it is not clear how the right to withdraw is best understood. Is it a moral right? Is it a legal right? Is it an inalienable right? It is also not clear what moral principles *justify* that right. Given that there are many areas of life in which one can make binding commitments, why *should* participants be guaranteed a right to withdraw without penalty if they give robust informed consent to be penalized? The practical implications of the right are also far from clear. Can investigators exclude from research those who have withdrawn from previous trials? Can they ask participants to provide reasons for withdrawing or try to persuade participants to remain in a protocol? Can they give monetary inducements to motivate participants not to withdraw? Does the right to withdraw from research give one the right to withdraw data about oneself or one's tissue samples at any time subsequent to completion of participation?

In contrast to the extensive literature on the principle of informed consent, the right to withdraw has received relatively little scholarly attention. It is not clear why this is so, although we suspect that many think that its meaning, justification, and implications are obvious and uncontroversial and, hence, that such extensive analysis has been deemed unnecessary. We disagree. It is important to have a sound moral and conceptual foundation for such a key feature of the regulation of research on human subjects. Without such a foundation, it is difficult to discern what the particular implications of the right to withdraw should be.

The purpose of this paper is to help to rectify this theoretical gap. We first provide a conceptual analysis of the right to withdraw and explain how that right is best understood. We then propose a justificatory framework for the right to withdraw. Finally, we discuss several implications of the right understood and justified in this manner. To foreshadow that discussion, we argue that it is an open question as to whether research subjects

should never be permitted to agree to be penalized for withdrawing. It is also an open question as to what counts as a *penalty* for withdrawal. We argue that withdrawal from research should, in some cases, carry greater consequences than is commonly thought.

RIGHT TO WITHDRAW

As Wesley Newcomb Hohfeld (1919) once argued, the notion of a "right" can refer to several different normative relations–liberties, claims, powers, and immunities. And so the deceptively simple "right to marry" involves a liberty right (A is not under a duty to marry), a power right (A can alter B's marital status with B's permission), and an immunity (no one can alter A's marital status without A's permission). The finer points of Hohfeld's framework are not of concern here. For present purposes, it is more important to note that one can speak of rights in several domains: legal, moral, and institutional. Legal rights pertain to what actions are required, permitted, or prohibited as a matter of positive law. Moral rights pertain to what kinds of actions are morally imperative, permissible, or impermissible. Moral and legal rights often overlap. We have both the moral and the legal right not to be battered or killed. But one can have a moral right to do X but lack a legal right to do X, and vice-versa. People may have a moral liberty right to practice the religion of their choice wherever they live, but people have a legal liberty right of freedom of religion only in those societies whose laws recognize such a freedom. People may have a legal right to forbid others from crossing their property, but lack the moral right to do so. We may say that one has an institutional right when the rules of an institution specify certain rights, although such need not be moral or legal rights. So professional tennis players may have an institutional claim right to challenge a specified number of line calls per set, although neither morality nor law specifies such a right (Thomson 1990). A legal right is a type of institutional right.

For present purposes, the important question is not whether people have a legal or institutional right, but whether they *should* have such a right. And given that distinction, it is important to recognize that one can have a *justified legal or institutional right* to do that which is *morally wrong*. This does not mean simply that there can be—as a matter of positive law—a legal right to perform an act that is morally wrong, such as giving a speech in which one denies that the Holocaust ever happened. There may be persuasive *moral* reasons to give people legal protection against

interference with such speech. So people may have a *justified* legal right to engage in wrongful speech. (For a more general discussion of the moral right to do wrong, see Jeremy Waldron (1981).)

In the context of research, the right to withdraw without penalty is best understood as a legal or institutional right; it is recognized both by legal institutions (as with the Common Rule) and by nonlegal organizations such as the WHO (Declaration of Helsinki) and CIOMS (Ethical Guidelines) that have considerable force with researchers and institutional review boards (IRBs) and specific policies of institutions in which research is performed. To say that subjects have a right to withdraw without penalty is equivalent to saying that researchers are under an institutional duty to refrain from imposing a penalty or a loss of benefits to which a participant is otherwise entitled were she to withdraw from a study. For brevity, we will refer to the right to withdraw as an institutional right, although it clearly has legal dimensions as well. We also will bracket the question of whether there is a moral right to withdraw as such, and instead focus on whether there are moral reasons to institutionalize such a right.

We generally will not distinguish between a penalty and the loss of a benefit to which one is otherwise entitled. These are two sides of the same coin. One could penalize someone by taking away property they already possess, as when a police officer penalizes a speeder by issuing a ticket that compels the speeder to pay a fine. Another way to penalize someone is to deprive them of benefits to which they would otherwise be entitled, as when a company docks an employee's pay based on poor performance. Note that there are many benefits to which people are not *otherwise* entitled; thus, failing to provide a person with a benefit does not necessarily penalize her. For example, to say that A has the right to "quit her job without penalty" does not ordinarily mean that A is entitled to be paid if she quits. Similarly, to say that A has a right to withdraw from research does not necessarily mean that she is entitled to the compensation or ancillary care that is offered to trial participants.

INALIENABILITY

Although the right to withdraw is generally understood as an *in*alienable right, it is not obvious that this view is correct. Most rights are—and should be—considered alienable if people give valid consent to waive a right, in part because people may have aims or interests that can best or only be served if they are allowed to waive a right (Kuflik 1986). It is an interesting and important question as to what justifies treating a right as

morally or legally inalienable, given that respect for a person's autonomy should—at least as a default position—allow her to waive a right if she prefers to do so. For example, A can waive some of her rights to free speech by signing a confidentiality agreement as a condition of employment.

Similarly, it is at least arguably the case that not to allow participants to agree to pay a penalty if they should withdraw from a trial fails to respect those individuals' autonomy and may preclude a win-win agreement. For example, consider a trial of an experimental drug for which there is very high demand in the study population. The trial requires a blood draw at one-month and six-month intervals after the last administration, and a subject's participation would be useless for research purposes without the blood draws. Because the investigators do not have funds to provide completion bonuses, the investigators are unwilling to start the trial unless the subjects agree to pay a substantial penalty if they fail to show up for these blood draws. Treating the right to withdraw without penalty as inalienable precludes such agreements to the detriment of both researchers and subjects.

That said, our society does and probably should treat some rights as inalienable. In some cases, rights are treated as inalienable out of concern for preserving the individual's status as an autonomous person. So we do not and probably should not allow individuals to make a contract to become another's slave or to waive a right to sue for divorce as a condition of marriage. In other cases, we treat a right as inalienable because the right would lose its value if it were alienable. Consider the right to be paid (or the duty to pay) a minimum wage. If an individual could waive that right with proper consent, then the law would effectively say "You must be paid a minimum wage unless you agree to accept less." That would render the minimum wage completely ineffectual. Similarly, if subjects could waive the right to withdraw without penalty by giving informed consent to pay a penalty if they withdraw, the right arguably would not offer any substantial protections.

Eric Chwang (2008) has argued that participants generally have the *moral* right to waive their right to withdraw. We are not so certain. Fortunately, we need not determine whether the right to withdraw is *morally* inalienable. For if, as we maintain, the right to withdraw is best conceived of as an *institutional* right, society may (or may not) be justified in adopting institutional policies that do not permit subjects to waive their right to withdraw without penalty even if it would otherwise be morally permissible or desirable for them to be able to do so.

JUSTIFICATION

Establishing how the right to withdraw is best understood does not explain whether and why laws and institutions should recognize it. The most contentious debates about rights often center on this justificatory rather than conceptual question. Everyone understands what it *means* for homosexuals to have the right to marry or for women to have the right to have an abortion or for someone to have a right to give a speech denying the Holocaust. The interesting ethical question is whether the law should recognize such a right—note, e.g., that it is illegal in Germany to deny publicly that the Holocaust occurred.

Similarly, assuming our conceptual analysis is roughly correct, the interesting ethical questions are whether and why society should recognize an inalienable legal or institutional right to withdraw without penalty. We first consider several possible candidates for such a justification, and then offer to our own account.

SUPEREROGATION

Robert Levine (1998, p. 113) has suggested that because participation in research is always supererogatory, it follows that participants have a right to withdraw:

> All ethical codes and regulations require that subjects should always be at liberty to withdraw without prejudice; none suggest any limits to this freedom. This requirement derives from the assumption that the subject is always doing something for the good of others; such supererogatory acts are generally not considered obligatory.

On this view, since participants are under no moral duty to enter research, they are never under a moral duty to remain in research. The codification of the right to withdraw attempts to ensure that such a moral right is protected.

As Levine concedes, this justification for the right to withdraw is problematic. First, even if one's decision to *start* an activity is supererogatory, one may acquire moral obligations to *continue* the activity. For example, even if it is supererogatory for A to agree to help his friend move a bureau, he has an obligation not to abandon the effort as they are carrying it down the stairs. Similarly, the moral freedom to enroll in research is compatible with acquiring an obligation to continue with such research once it has begun (Edwards 2005). Surely, subjects may have a *prima facie*

moral obligation to show up for post-intervention blood draws even if they were under no obligation to enter the study in the first place. So if one can acquire an obligation not to withdraw from research even if participation were otherwise supererogatory, the supererogation argument for the right to withdraw will not work.

Second, and *pace* Levine, it is entirely possible that participation in research is *prima facie* obligatory rather than supererogatory (Schaefer, Emanuel, and Wertheimer 2009). This does not mean that informed consent is unnecessary or that subjects do not have a morally justified right to withdraw without penalty. But if this view is correct, it does mean that we cannot justify the right to withdraw by appeal to the claim that participation is supererogatory.

CONTINUAL CONSENT

One might be tempted to justify the right to withdraw by appeal to a principle of "continual consent." Consider sexual relations. Not only must the parties consent before sexual relations commence, they must consent at all subsequent times as well. Similarly, it may be thought that just as subjects must consent before research begins, they must consent at all subsequent times.

The continual consent justification, however, either proves too much, or proves too little. Suppose a furniture maker agrees to produce 500 beds for a hotel that is about to open, on the explicit understanding that he would have to pay a penalty if he fails to deliver the beds before June 1. It might be thought that the furniture maker has not provided continual voluntary consent to comply with the contract if he produces the beds only because he will be penalized for failing to deliver. If continual consent is a requirement for all contracts, then contracts that specify a penalty for nonfulfillment should be banned just as we ban penalties for withdrawing research participation.

If the furniture maker's contract should in fact be banned because it fails to provide continual consent, then the continual consent justification for the right to withdraw is much more radical than is appropriate. It would be impossible for individuals to seek remedy for breach of contract, since doing so would constitute a penalty for withdrawal, making the initial contract unenforceable. The consequences of such a policy would be disastrous, as it would effectively eliminate the possibility of contractual arrangements. Additionally, this interpretation implies that it

is impossible to legitimately consent to pay penalties—which itself seems to make a mockery of one's autonomous ability to make meaningful commitments.

On the other hand, if the furniture maker's contract to deliver on pain of penalty is ethically permissible, then it is unclear what continual consent has to say about the permissibility of penalties for withdrawing from research. The continual consent model does little in itself to provide reason to treat research any different from private contracts where penalties are not especially noteworthy. It must be shown that participation in research more similar to sexual relations than to ordinary commercial arrangements. Later in the paper, we discuss some plausible reasons that withdrawal from research should in fact be treated differently. As we indicate, those reasons do not rest on protecting a singular notion of "continual consent." Rather, we offer a pluralistic or multi-reason justification for institutionalizing a right to withdraw from research without penalty.

INCENTIVES

Providing a right to withdraw without penalty could be justified as a way to encourage prospective subjects to enroll in trials, just as retailers allow refunds of purchases to encourage consumption. From this perspective, however, there is no need to *mandate* that researchers state that subjects have a right to withdraw without penalty. Just as some retailers—e.g., L.L. Bean—find it profitable to allow customers to return their merchandise for a full refund at any time while other retailers find more restrictive return policies appropriate, researchers would grant such a right on their own if and when it serves their interests to do so.

SPECIAL ASPECTS OF RESEARCH

Given that the foregoing justificatory strategies are not convincing, the most plausible justification for the right to withdraw without penalty will have to arise from other special features of research on human subjects. Society does not prohibit agreements that include penalties for withdrawal in other contexts, such as agreeing to perform a concert, rescheduling a nonrefundable airline ticket, or cashing in a two-year certificate of deposit before it comes due. So if we are to justify a right to withdraw from research without penalty, the task is to show why research is different from contexts in which penalties for withdrawal are permissible.

Although the following set of reasons is by no means exhaustive, there are at least four reasons for extending such special protection that are *internal* to the research process, arising from the interests of research participants: information asymmetry, uncertainty, hedging asymmetry, and bodily integrity. There is also one reason *external* to the research process: the interest of society in sustaining public trust in clinical research. These five reasons independently justify institutionalizing a right to withdraw from research. They also reinforce each other. Society would worry less about protecting people from decisions regarding their body if there were less informational asymmetry and uncertainty. And so information asymmetry and uncertainty are more worrisome when the consequence is a violation of bodily integrity. The scope and strength of the right to withdraw is, then, contingent on the degree to which these reasons are operative in the research context.

Some readers may be disappointed that we do not provide a neat and simple justification for the right to withdraw from research. We, too, would have preferred a justification that had the following form: "Because research is X, subjects must have a right to withdraw without penalty." Unfortunately, we do not think there is any such sort of justification for the right to withdraw, and so we hope that our pluralistic justification makes up in plausibility and soundness what it lacks in simplicity.

INTERNAL JUSTIFICATIONS FOR A RIGHT TO WITHDRAW FROM RESEARCH

Information Asymmetry

Compared with subjects, investigators in clinical research have much greater knowledge and expertise related to the trial, its procedures, the nature of the risks and benefits, and so on. An unscrupulous researcher could use this asymmetry to mislead subjects about the level of risk in a study. Although oversight of the initial consent process is meant to mitigate this asymmetry and prevent such abuses, the right to withdraw can act as a failsafe in case such oversight fails. Even if all parties are acting in good faith, no plausible amount of information in a consent form will ever put subjects on an equal playing field with the researchers in terms of knowledge about the risks and benefits of participation.

Information asymmetry is also worrisome in the context of commercial contracts (Trebilcock 1993). Interestingly, when contracts rooted in informational asymmetry lead to substantial harm, courts may forgive the ill-informed party of contractual obligations. Although such *ex post* and

ad hoc determinations may be appropriate in contract law, the information asymmetry in research may be so pervasive that it is better to immunize subjects *ex ante* against being penalized for withdrawal.

Uncertainty

Even if there were no asymmetry between investigators and subjects with respect to a study's risks, burdens, and benefits, the risks and burdens of participation in research may be systematically more uncertain than the risks and burdens in many other contexts. The highly subjective and variable nature of the burdens and inconveniences of participation could result in even the most discerning subject consenting to participate in a study in which those burdens and inconveniences turn out to be much greater than she could reasonably have anticipated. Given that informed consent is insufficient to protect subjects from misjudging the full costs of participating in a study, society may prefer to protect individuals from the consequences of their nonculpable misjudgments. There is a degree of paternalism in offering such protection, but we think such paternalism is justifiable (Miller and Wertheimer 2007).

We find similar protections in some other contexts. It is precisely such concerns about uncertainty and the subjective value that consumers derive from products that motivate mandated product return policies in some jurisdictions. In the U.S., such uncertainty motivates laws that mandate a three-day "cooling-off period" after making a purchase from a door-to-door salesman. The salesman cannot say, "I'll give you a discount if you waive the cooling off period." In Europe, a recently proposed mandate on full refunds for purchases made over the phone or internet is similarly justified by the inherent uncertainty in making such purchases. Because it is difficult for consumers to know whether a product is worthwhile without seeing it in person, the mandated return policy protects consumers from this uncertainty (Ben-Shahar and Posner 2010). For similar reasons, the right to withdraw without penalty protects subjects from having to pay for withdrawing from a trial in which the burdens and inconveniences could not be anticipated by reasonable people.

Hedging

Hedging involves accepting a relatively small cost in order to avoid especially bad outcomes, or having a pool over which risks counterbalance.

Insurance is the most typical form of hedging, but one can sometimes hedge by diversifying investments. Instead of putting all of one's resources in one stock, one buys a smaller number of shares in a large number of stocks so that one company's catastrophe does not ruin one's finances.

Although researchers can hedge against withdrawal by subjects by over-recruitment, subjects have no effective mechanism by which to hedge against unwanted risks and burdens. Subjects cannot be expected to pool risks and burdens by enrolling in a large number of trials, and the highly subjective nature of potential burdens makes a private insurance market untenable. And so the total risk to subjects is reduced by stipulating that they are entitled to withdraw without penalty.

Bodily Integrity

Society often treats a person's body as having special moral significance. For this reason, people's bodies are offered greater protection than their external resources, and society is more likely to restrict what people can do with their bodies than with their external resources. To use Ronald Dworkin's (1983, p. 39) phrase, our society tends to draw a "prophylactic line" around the human body that makes the body relatively inviolate. Thus it is widely held that it is permissible for governments to tax individuals' property or even seize it via eminent domain but not to take individuals' organs (even with compensation). Although one can consent to encroachments on one's property (it is not trespass if one consents), one cannot consent to battery outside of athletic and medical contexts (Bergelson 2010). And although people can sell their property with relative ease, our society prohibits the sale of organs. There is not space here to provide a proper justification for this special concern over bodily integrity. Given the widespread acceptance of the value of bodily integrity, however, it is important to consider how it serves to help justify the right to withdraw from research without penalty.

Because invasions or uses of the body are treated as morally suspect, it seems desirable to protect people from having to choose between continuing to accept invasions (or uses) of their bodies and having to pay a penalty. Given the potential defects in decision making about enrollment in trials just discussed, it may be desirable to provide subjects with greater protection when those mistakes impact the body than when similar mistakes would affect their property.

EXTERNAL JUSTIFICATION: PUBLIC TRUST

In addition to the internal justifications that we have considered, the right to withdraw can be justified as a mechanism to bolster the public's trust in researchers and the research enterprise. We do well to remember that the U.S.'s current regulatory framework originated from ethical scandals like the Tuskegee syphilis study. Policymakers were and are concerned not only to protect subjects from exploitation and abuse, but to promote the public's trust in the research enterprise. Even if those involved in the research enterprise have "learned their lesson" and are unlikely to engage in unethical research, protective policies help to assure the public that subjects will not be mistreated. Other kinds of regulation, including privacy protections surrounding the use of genetic information and disclosure by researchers of potential conflicts of interests, are explicitly justified by appeal to concerns about public trust (Annas 2002; Hudson 2007). Institutionalizing the right to withdraw without penalty can serve a similar purpose.

At the same time, it is worth remembering that public trust goes both ways. If we are willing to take positive effects on the public's trust into account when justifying the right to withdraw, we also need to account for the potentially negative effects on the public's interests from institutionalizing a right to withdraw without penalty. In particular, it is possible that ensuring subjects have the right to withdraw will slow down the development of novel medical diagnoses and interventions. The general right to withdraw without penalty, like other restrictions on research, is most likely a cost the public is willing to bear, but it is important to keep in mind the burdens as well as the benefits of regulation when determining particular implications of the right to withdraw.

A JUSTIFIED INSTITUTIONAL RIGHT TO WITHDRAW

Recall that our pluralistic approach to the justification for the right to withdraw advances five reasons in support of such a right, none of which are strictly necessary, but in which the cumulative weight of these reasons provides a sound foundation for that right. An advantage of this multi-reason approach is the ability to justify institutionalizing a right to withdraw even if the strength or applicability of one or more of the five reasons is disputed. For instance, some commentators recently have argued against the view that the body deserves special moral protection.

Cecile Fabre (2006) has extended this argument to justify involuntary organ procurement by the government and the sale of organs. If such arguments are correct, our argument for the right to withdraw becomes somewhat weaker, but it still might be strong enough. The other facets to the argument might well be sufficient, just as the three-day cooling off period—which is a kind of right to withdraw from purchases—can be justified without appeal to bodily integrity.

Additionally, it should be remembered that the right to withdraw will not provide complete protection against the worries it helps to mitigate. IRBs should still seek to reduce uncertainty where possible, and there are many other strategies for bolstering public trust in research that remain as crucial as ever even with an institutionalized right to withdraw.

We have still not resolved whether the right to withdraw should be treated as inalienable. We have suggested already that an alienable right to withdraw would not offer substantial protections to subjects, because researchers could simply require subjects to waive that right as a condition of participation. But this conclusion may be too quick. Let us examine more closely what an alienable right to withdraw would amount to.

An alienable right to withdraw could serve as a signaling device, forcing researchers to explain very clearly the penalties of withdrawal to subjects. This would be akin to a law where store patrons have a right to return any merchandise at full price unless the store clearly displays their return policy (or lack thereof). Yet research, unlike store sales, already requires rigorous informed consent. Even without delineating a specific right to withdraw, any responsible IRB would be careful to ensure that subjects know about the risks of withdrawing—both to their health and potentially to their pocketbooks.

Alternatively, the right to withdraw could be a useful bargaining chip. Many rights are especially valuable because one can get something in exchange for waiving them. For instance, a person's right to a 20 dollar bill is important mostly in virtue of the fact that she can, in essence, waive that right in exchange for, say, a haircut. Similarly, the right to withdraw could be a default position that subjects can use as a bargaining chip, waiving it in exchange for greater compensation if they complete. However, research participants are not in a bargaining position; the terms of informed consent are generally non-negotiable. An alienable right to withdraw would therefore be of little use to participants.

IMPLICATIONS

Exceptions to the Right to Withdraw

We have argued that there is some moral reason to institutionalize a right to withdraw from research without penalty. Although there may be relatively few cases in which researchers and subjects might want to agree on a penalty for early withdrawal, is there reason to preclude them from doing so in every case? First, as previously noted, it is arguable that if one is to respect subjects' autonomy, one should allow them to enter into agreements that involve a penalty for withdrawal if they so choose. Paternalistic prohibitions of such choices can sometimes be justified, but one should err on the side of respecting individual autonomy. Second, there are cases in which it is in a person's interest to be able to agree to penalties. Travelers want to be able to buy cheaper nonrefundable airline tickets rather than be forced to buy more expensive tickets that are refundable without penalty. Similarly, people may want to be able to agree to a penalty for withdrawal from research if that is the only way for them to gain access to an experimental intervention or if they will thereby receive greater financial compensation for participation.

Consider a variation on the hypothetical protocol discussed above. Subjects receive an experimental intervention that is only available in the trial. The protocol requires the completion of a "quality of life" questionnaire at 1 month, 6 month, and 12 month intervals following the last intervention. Recruitment is not an issue, because people want access to this experimental intervention. Investigators are prepared to allow subjects to withdraw without penalty if they withdraw before the last intervention, but should it be permissible for investigators to propose and for subjects to consent to a financial penalty for failure to complete the questionnaire? (The subjects could be asked to post a deposit on enrollment in the trial that will be returned when they complete the questionnaire.) The study will be worthless without the post-intervention survey data, and investigators will not go forward without a penalty scheme because they reasonably fear that too many subjects would otherwise fail to complete all three of the post-intervention surveys.

This is a case in which the previously discussed justifications for a right to withdraw without penalty have relatively little force. There are no concerns about bodily integrity, as there are no physical procedures being compelled once the final intervention is completed. Continued participation is without additional risk to the subject. There is little information

asymmetry or uncertainty about the burdens or risks of completing the questionnaire. There is no need to hedge against adverse consequences. Given these assumptions, it seems sensible to allow subjects to agree to a penalty for withdrawal. The subjects want it. The investigators want it. It is a win-win situation.

For these reasons, we believe it is an open question as to whether to make exceptions for such cases. On the one hand, it might be argued that it is difficult to write policy codes sensitive to such an unique and exceptional case without also including too many cases where subjects should have the right to withdraw without penalty. Consider the prohibition of sexual relations between psychotherapists and their patients. Although there may be a few cases where such relations might be harmless or even beneficial to both parties, neither psychotherapists nor patients are well-positioned to determine when that is so. And so the benefits of a blanket nonwaivable prohibition outweigh any potential gains to the parties from allowing such waivers. One could argue that similar considerations extend to the right to withdraw from research without penalty.

On the other hand, the fact is that different categories of research already are treated in different ways. For example, the Common Rule already makes provision for a waiver of some or all elements of informed consent in some cases of research involving minimal risk when getting consent is not feasible (45 CFR 46. 116 (d)). We might, as some have argued (Chwang 2008; Edwards 2005), find it similarly possible and desirable to make provision for waiving the right to withdraw without penalty for certain categories of research. For the present, we think it sensible to regard as an open question whether subjects should be guaranteed a right to withdraw without penalty in *all* research studies.

Completion-Contingent Payments

When researchers offer financial payment to subjects, such payment can be made in two ways. In some cases, subjects are paid exclusively on a *pro rata* (per visit or per procedure) basis. In other cases, subjects receive either partial payment (a completion bonus) or all of their payment on a completion-contingent basis. Some worry that completion-contingent payment schemes may compromise the right to withdraw. Indeed, some institutions put strict limits on the proportion of payment that can be made contingent on completion (Institutional Review Board Handbook 2007, 2.1.2.; Research Administration 2010). The question is whether these worries are well founded?

Compare two proposed payment schemes for a protocol. In the first, subjects receive financial payment only if they complete the study or must be withdrawn because of adverse effects. In the second, subjects are paid *pro rata*. Assuming a fixed budget for payment, the completion-contingent payment schedule will give less to those who withdraw than the *pro rata* schedule. However, given that the payments that would have been made to those who withdraw would then be available to those who complete, it follows that those who complete the study would receive *more* compensation under the completion-contingent schedule than under the *pro rata* schedule. Thus, some subjects could benefit significantly from allowing completion-contingent payment.

Is such a payment scheme compatible with the right to withdraw without penalty or loss of benefits to which subjects are otherwise entitled? Failing to pay a subject who withdraws is not a penalty. And given that researchers are not required to pay subjects at all, a completion-only payment schedule does not deprive subjects of benefits to which they are otherwise entitled. But that may be too quick. It may be argued that if subjects are paid at all, fairness requires that all research participants be paid the same amount of money for the same amount of work done or time spent. And if subjects have a right to be treated fairly, then we can argue that such payment schedules deprive subjects of something to which they are otherwise entitled.

We do not think that fairness requires that subjects be paid *pro rata* on a per procedure or per visit basis. First, and almost by definition, fairness goes *both ways*. Since a subject's participation may be of no value to the investigators if the subject does not complete participation in the trial, it is arguably unfair to require investigators to pay for labor that has no value to them. If A hires B to paint A's portrait, fairness does not require that A pay B for his labor if B quits before the painting is completed given that a partially completed portrait may have no value to A. Second, we generally think it is permissible to offer people incentives for completion if the terms of the arrangement are clear at the outset. We do not think it unfair if a real estate company pays its agents on a commission basis rather than an "hours worked" basis. The same opportunity is made available to all agents. So absent a convincing argument to the contrary, we see no reason to think that completion-contingent payment schedules are unfair.

Alternatively, one might claim that completion-contingent payment constitutes an undue inducement to remain in a trial and thereby compromises the right to withdraw (see, e.g., FDA 2009; Borror 2002). It is

true that completion-contingent payment or completion bonuses may induce subjects to remain in a trial. (*Pro rata* payment also gives subjects an incentive not to withdraw.) However, neither regulations nor ethical principles prohibit providing inducements for enrollment or for completion. They only prohibit *undue* inducements. It is not true that there is undue inducement whenever compensation gets someone to do something they would not otherwise do. If A offers B $50 to mow his lawn, it is not an undue inducement if B makes a reasonable judgment that the value of $50 is greater than the disvalue of mowing A's lawn. On the most plausible view, such payment schedules would constitute an *undue* inducement only if they were to *distort* a subject's judgment about the benefits and risks of continued participation. The mere fact that a subject would withdraw if paid on a *pro rata* basis does not show that she is making an unreasonable judgment that it is worthwhile to complete the study in order to receive the completion-contingent payment.

Still, it might be argued that completion-contingent payment takes unfair advantage of subjects' belief that they will *not* want to withdraw. Manufacturers offer rebates rather than discounts precisely because purchasers vastly overestimate the likelihood that they will bother to complete the paperwork—e.g., clipping the UPC bar code, keeping the receipt, completing a form, etc. In a similar way, the offer of completion-contingent payment to subjects may take advantage of the fact that subjects overestimate the likelihood that they will complete a study.

Two points. First, there is an interesting question as to whether commercial rebates are unethical if they take advantage of such decisional errors. We set that issue aside. Second, although the rebate's main purpose is to take advantage of people's irrationality, this is not so with completion-contingent payment. Instead, the completion-contingent payment is meant to provide participants with an incentive to finish the study and to provide payment based on the value of data collected (withdrawn data may be useless). Researchers, unlike rebate-offering companies, would be perfectly happy if subjects were completely aware of their odds of withdrawing. In any event, instead of banning completion-contingent bonuses in the name of the right to withdraw, the proper response here may be for IRBs to pay special attention to the purpose and function of such bonuses. Special efforts could be made to combat subjects' irrationality directly, for instance by informing participants of the expected withdrawal rate. This issue deserves more attention.

Participation in Other Trials

Respecting a subject's right to withdraw without penalty does not entail that it would be improper to exclude an individual from a trial because she had withdrawn from a previous study. Subjects are entitled to a fair selection process, but they are not entitled to participate in a given trial. Fair selection requires that, if a subject is to be excluded from a study, it must be for relevant reasons. But given that researchers have a legitimate interest in completing studies quickly and efficiently, it may be quite appropriate for researchers to use a history of withdrawing from studies as an exclusionary criterion. That is not to say that researchers can legitimately exclude certain groups—regardless of individual history—from research based on aggregate likelihood of withdrawal; such a practice might end up denying certain disadvantaged populations access to research. Focusing on individual history, however, would not have such a broad discriminatory effect.

Pressure

Some have argued that having a right to withdraw implies that subjects should not be asked why they are withdrawing from a trial because the prospect of being asked such questions constitutes pressure to remain *in* the trial or because being asked such questions constitutes a *penalty* for withdrawal *from* the trial (Herxheimer 1988).

Although the prospect of having to answer such questions may motivate some subjects to remain in a study, not all forms of pressure are impermissible. It is a mistake to assume that individual autonomy is so fragile that it would be violated by the prospect of having to explain one's decisions. So long as the prospect of answering questions does not cause subjects to reasonably believe that they will suffer palpable and illegitimate adverse consequences should they withdraw, it does not seem to constitute excessive pressure.

But suppose a subject does withdraw. Does having to answer such questions constitute a *penalty*? We think not. First, although such questioning may lead some subjects to feel guilty, there may be some cases when subjects are morally obligated to remain in a study. When feelings of guilt are appropriate, subjects cannot be entitled not to be made to feel guilty. Second, we do not believe that experiencing such feelings as a consequence of being asked why one has withdrawn can reasonably be understood as a penalty for withdrawal.

Do investigators violate the right to withdraw by trying to *persuade* subjects to remain in a trial? In general, giving people reasons to behave in one way or another is quite compatible with—indeed it epitomizes—respect for their autonomy. In this case, however, there are dangers. When one party has more knowledge and perhaps more status than the other party, persuasion may become more akin to bullying. The researchers may stress the reasons that the subject should remain in the study and will be insufficiently appreciative of the subject's reasons for contemplating withdrawal. The process also may cause the subject to believe that there will be palpable and illegitimate costs to withdrawal—even if that belief is false and even if the researchers have not suggested or implied this. In addition, subjects could become overly deferential to researchers' apparent authority, remaining in a trial because a researcher's suggestions seemed more like orders. It is unclear whether these potentially troublesome effects of are sufficient to justify a policy of prohibiting all attempts to persuade subjects not to withdraw. This question merits further empirical and moral analysis.

Effects on the Doctor-Patient Relationship

Some irony arises when contemplating the effect of withdrawal from research on the doctor-patient relationship. On the one hand, it is arguable that the most important protection provided by the right to withdraw is to ensure subject-patients that they will not be deprived of treatment to which they would otherwise be entitled. On the other hand, it is arguable that subjects do not actually need the protection offered by the right to withdraw. After all, it is against professional codes for doctors to make continued treatment contingent on performance of certain actions, outside of direct remuneration. Having a regulation that prevents physicians from taking such factors into account during treatment hence does not technically provide any additional protections to subjects.

Yet even with such pre-existing rights, it is reasonable to institutionalize a specific right in order to give subjects additional assurance that they will not be abandoned or deprived of treatment if they withdraw from a trial. In addition and of equal importance, requiring researchers to tell patients (orally or in writing) that they have such a right may help to remind physicians and researchers of *their* obligations.

All that said, two points should be made. First, not continuing to provide an experimental intervention subsequent to withdrawal does not deprive the subject of anything to which she was otherwise entitled.

Second, it is simply impossible to protect patients from the possibility that their physicians might disapprove of their withdrawal and that this could affect the physician's beliefs and feelings about the subject. We do not deny the significance of those reactions. Patients want to be liked and respected by their physicians—and this is so even when they do not think that their *treatment* will be affected by their decision. A "good doctor" will be sensitive to those desires. Nonetheless, it is absurd to think that a subject's *rights* are violated just because a physician may disapprove of his decisions.

Withdrawing Data

Subjects may complete a trial, but subsequently wish to have their data or tissue samples destroyed. Does the right to withdraw extend to such a request? The answer is not clear. According to federal guidelines, the use of data about a subject constitutes participation *by* the subject if the investigators are using identifiable private information (45 CFR 46.101 (b) (4)). The regulations aside, our justifications for the right to withdraw from research without penalty do not necessarily work to justify allowing participants to withdraw data or samples after they have been obtained. Whereas the right to withdraw is designed to protect the subject's autonomy and to protect them from harmful consequences, the question here concerns issues of control.

Although we do not think that our justification for the right to withdraw without penalty can be made to cover the control of information without considerable distortion, there may be one or more distinct justifications for the right to control that information, and it is useful to spend some time examining possible reasons for a right to control data or bodily tissue.

The Irish Council of Bioethics (2009) recently claimed that an individual's biometric data is an intrinsic element of that person and so should be protected by bodily integrity. This view is not plausible. An individual's bodily integrity is limited to their flesh and bone, not the information about it. It is one thing to touch another person without her consent, but quite another to convey information about her without her consent. As for tissue samples, we do not consider ourselves strewn about the floor when our hair is cut at the barber's. Only the flesh and bone physically connected to the individual lies within the "prophylactic boundary" and merits a special degree of protection. Thus concerns about bodily integrity do not offer a compelling reason to give subjects control over data and samples upon completion of a trial.

Even if the arguments in defense of a right to withdraw from participation in a trial do not justify a right to withdraw one's data and samples, there are at least three different reasons that might justify the latter right. First, people may be concerned about discrimination on the basis of their genetic information. For that reason, the recently passed Genetic Information Nondiscrimination Act (GINA) attempts to reassure people that genetic information will not be used to determine employment or health insurance eligibility. Concern over potential sample identification, stigma, and/or paternity claims remains, but these risks are remote so long as samples are handled responsibly in accordance with current law.

Second, there are concerns about privacy. Although such concerns are relatively minimal when data is de-identified, some valuable research requires the ability to link research data with current clinical data and may pose a greater threat to privacy. It is unclear as to how to strike the right balance between the value of privacy and the value of such research. But even if privacy concerns are sufficient to justify a strong right to remove data about oneself from a study, such a right would not be derived from a general right to stop participating in a study.

Third, it may be thought that subjects have a property right in their tissue and a claim on any financial benefits obtained from the use of their tissue. Although the California Supreme Court argued against that view in *Moore v. California* (*Moore v. Regents of the University of California* 51 Cal. 3d 120 (1990); 271 Cal. Rptr. 146 (1990); 793 P.2d 479 (1990)), that does not settle the ethical question or whether laws should be drafted that would give subjects some ownership rights in their tissue. Regardless of how that issue is settled, however, it will not necessarily be resolved by reference to the reasons that justify a subject's right to withdraw from participation in research without penalty.

CONCLUSION

We have argued that the right to withdraw without penalty is best understood as a justified institutional right that, as a matter of course, prevents subjects from entering into research protocols that might otherwise include penalties or the loss of entitled benefits for withdrawal. We should provide such protection to subjects because of the information asymmetry, inherent uncertainty, and inability to hedge surrounding agreements that involve a potential violation of their bodily integrity. In addition, institutionalizing such a right promotes greater trust in the research enterprise.

We have left several matters open and unresolved. Some might object that our analysis provides too little protection to subjects who wish to withdraw from research, overlooking extra reasons to provide a right to withdraw that would justify more stringent restrictions than we ultimately suggest. Others may respond from the opposite direction, arguing that research is not so special that it subjects need a right to withdraw, or that other policies like extra compensation could address the five problems we raise more adequately than a broad right to withdraw. Although there is not space here to delve into these issues, we wholeheartedly welcome such discussions. What is and is not entailed by the right to withdraw deserves much greater attention than it has heretofore received.

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REFERENCES

American Law Institute. 1981. Restatement (Second) of Contracts, Section 359. Available at *http://www.lexinter.net/LOTWVers4/adequacy_of_damages.htm#§359._EFFECT_OF_ADEQUACY_OF_DAMAGES*, accessed 27 November 2010.

Annas, George J. 2002. Medical Privacy and Medical Research—Judging the New Federal Regulations. *New England Journal of Medicine* 346: 216–20.

Ben-Shahar, Omri, and Posner, Eric A. 2010. The Right to Withdraw in Contract Law. In *John M. Olin Law & Economics Working Paper*. (2nd Series.) Chicago: University of Chicago. Available at *http://www.law.uchicago.edu/files/file/514-obs-eap-withdraw.pdf*, accessed 23 November 2010.

Bergelson, Vera. 2010. Consent to Harm. In *The Ethics of Consent: Theory and Practice*, ed. Alan Wertheimer and Franklin G. Miller, pp. 163–92. Oxford: Oxford University Press.

Irish Council for Bioethics. 2009. *Biometrics: Enhancing Security or Invading Privacy?* Dublin: Irish Council for Bioethics.

Borror, Kristina C. 2002. RE: Human Research Subject Protections Under Federal-Wide Assurance FWA-93. Letter to Gregory W. Siskind, M.D., and David P. Hajjar, Ph.D., 4 April. Office of Human Subjects Protection, Department of Health and Human Services. Available at *http://www.hhs.gov/ohrp/detrm_letrs/YR02/apr02k.pdf*, accessed 28 November 2010.

Chwang, Eric. 2008. Against the Inalienable Right to Withdraw from Research. *Bioethics* 22: 370–78.

CIOMS. Council for International Organizations of Medical Sciences. 2002. International Ethical Guidelines for Biomedical Research Involving Human Subjects. Geneva, Switzerland.

Dworkin, Ronald. 1983. Comment on Narveson: In Defence of Equality. *Social Philosophy and Policy* 1: 24–40.

Edwards, Sarah J. L. 2005. Research Participation and the Right to Withdraw. *Bioethics* 19: 112–30.

Fabre, Cecile. 2006. *Whose Body Is It Anyway? Justice and the Integrity of the Person*. Oxford, U.K.: Clarendon Press.

FDA. 2009. Information Sheet Guidances, Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Payment to Research Subjects. Available at *http://www.fda.gov/RegulatoryInformation/Guidances/ucm126429.htm*, accessed 23 November 2010.

Herxheimer, Andrew. 1988. The Rights of the Patient in Clinical Research. *Lancet* 12: 1128–30.

Hohfeld, Wesley Newcomb. 1919. *Fundamental Legal Conceptions as Applied in Judicial Reasoning*. New Haven: Yale University Press.

Hudson, Kathy L. 2007. Prohibiting Genetic Discrimination. *New England Journal of Medicine* 356: 2021–23.

Institutional Review Board Handbook. 2007. *The Institutional Review Board Handbook: Policies and Guidelines*. Syracuse University. Available at *http://orip.syr.edu/forms/THE%20IRB%20HANDBOOK-2007.pdf*, accessed 28 November 2010.

Kuflik, Arthur. 1986. The Utilitarian Logic of Inalienable Rights. *Ethics* 97: 75–87.

Levine, Robert J. 1988. *Ethics and Regulation of Clinical Research: Second Edition*. New Haven, CT: Yale University Press.

Miller, Franklin G., and Wertheimer, Alan. 2007. Facing up to Paternalism in Research Ethics. *Hastings Center Report* 37 (3): 24–34.

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. 1979. *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects Research*. Available at *http://ohsr.od.nih.gov/guidelines/belmont.html*, accessed 28 November 2010.

XX–Research Administration. 2010. *Subject Selection, Recruitment and Compensation*. University of California, Irvine. Available at *http://www.research.uci.edu/ora/hrpp/subjectselection.htm*, accessed 28 November 2010.

Schaefer, G. Owen; Emanuel, Ezekiel J.; and Wertheimer, Alan. 2009. The Obligation to Participate in Biomedical Research. *JAMA* 302: 67–72.

Thomson, Judith Jarvis. 1990. *The Realm of Rights*. Cambridge, MA: Harvard University Press.

Trebilcock, Michael J. 1993. *The Limits of Freedom of Contract*. Cambridge, MA: Harvard University Press.

Waldron, Jeremy. 1981. A Right to Do Wrong. *Ethics* 92 (1): 21–39.

WMA. World Medical Association. 2008. *Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects*. Tokyo, Japan.