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Is Payment a Benefit?

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Abstract

What I call "the standard view" claims that IRBs should not regard financial payment as a benefit to subjects for the purpose of risk/benefit assessment. Although the standard view is universally accepted, there is little defense of that view in the canonical documents of research ethics or the scholarly literature. This article claims that insofar as IRBs should be concerned with the interests and autonomy of research subjects, they should reject the standard view and adopt "the incorporation view." The incorporation view is more consistent with the underlying soft-paternalist justification for risk-benefit assessment and demonstrates respect for the autonomy of prospective subjects. Adoption of the standard view precludes protocols that advance the interests of subjects, investigators, and society. After considering several objections to the argument, I consider several arguments for the standard view that do not appeal to the interests and autonomy of research subjects.

Keywords

payment; risk/benefit assessment; paternalism; autonomy

INTRODUCTION

The purpose of this article is to examine one corner of the more general debate over the ethics of offering financial payment to research subjects: Should IRBs regard financial payment as a benefit to subjects in risk/benefit assessment? This question does not arise if offering financial payment to research subjects is categorically unethical or always compromises informed consent. But many think that whereas it is ethically permissible to offer financial payment if an IRB first determines that the risks of participation in research are reasonable in relation to the anticipated benefits, the IRB should not consider financial payment as a benefit in making that assessment. Call this the *standard view*.

Despite its (near) universal acceptance, I know of *no* sustained defenses of the standard view. Indeed, even unsustained defenses are hard to come by. Most documents simply assert the principle or policy, although a few policy statements appeal to what is thought to be an obviously unacceptable implication of its rejection. Such confidence is misplaced. I will argue that insofar as IRBs should be concerned with the interests and autonomy of research subjects, they should reject the *standard view* and adopt what I call the *incorporation view*. As its name implies, that view maintains that IRBs *should* incorporate the value of financial payments as a benefit to participants in assessing whether the risks of research are reasonable in relation to the anticipated benefits.

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This is my plan. First, I argue that the general practice of prospective risk/benefit assessment is best justified by an appeal to soft-paternalism. Second, I argue that the incorporation view is more consistent with this justification than the standard view. Third, I consider several objections to my argument for the incorporation view. Finally, I consider arguments for the standard view that do not appeal to the interests and autonomy of research subjects.

RISK BENEFIT ASSESSMENT

The reigning regulatory and ethical frameworks for clinical research emphasize the protection of research subjects. They seek to allow the pursuit of generalizable knowledge only when it is compatible with respect for the rights and welfare of individuals. Although informed consent was given pride of place in the wake of the Nazi "experiments" and other infamous examples of nonconsensual research, the current regulatory system – especially prospective risk/benefit assessment by independent ethics committees – is directed to protecting human subjects from protocols that pose undue risks of harm before subjects have the opportunity to consent to participate.

Now there is a genuine question as to whether and why prospective risk/benefit assessment by independent ethics committees is necessary at all. On its face, medical research is an interaction between researchers and subjects and it would seem that *any* interference into this interaction requires justification, particularly if we are committed to respecting the autonomy of subjects. Moreover, even if it were thought necessary to insure that subjects give informed consent by monitoring consent forms and the consent process, why should IRBs go beyond that mission and seek to prevent what would otherwise appear to be consensual transactions between researchers and subjects? The answer is simple: those transactions would not be *sufficiently* consensual because otherwise competent adults may find it difficult to protect their own interests in assessing the risks and benefits of participation in research. Most prospective subjects lack the requisite scientific and clinical knowledge to evaluate the risks and potential benefits of participation. In addition, and technical knowledge aside, patient/subjects are vulnerable to distortions of judgment such as the "therapeutic misconception" where they mistakenly assume that research interventions are designed to benefit them. And patient-subjects who are desperate for the chance of medical benefit from access to experimental treatment may overestimate the benefits and underestimate the risks of research participation.

Although the discourse of research ethics has been loathe to call a spade a spade, the protections offered by prospective risk/benefit assessment should be seen as fundamentally paternalistic, albeit a form of justified paternalism.[1] But there is paternalism and there is paternalism. To use Joel Feinberg's terminology, a limitation of B's liberty is based on *soft* paternalism when it is justified on the grounds that B decision-making is substantially impaired, that is, when we have reason to suspect that the agent lacks the information or capacity or special knowledge to protect her own interests.[2] So even Mill, who maintained that the state was generally not justified in interfering with an individual for "his own good," endorses soft paternalism in his famous bridge example: "If either a public officer or anyone else saw a person attempting to cross a bridge which had been ascertained to be unsafe, and there were no time to warn him of his danger, they might seize him and turn him back."[3] It is soft-paternalism when the state requires that patients get a prescription before using certain drugs given that most of us do not have the knowledge to properly self-medicate. In contrast, *hard* paternalism involves restricting the freedom of persons to protect them "from the harmful consequences even of their fully voluntary choices and undertakings."[4] It is hard paternalism if A prevents a competent and informed B from climbing Mt. Everest because A believes it to be too dangerous or if physicians require adult Jehovah's Witnesses to receive blood transfusions when medically indicated.

As a general proposition, it is much easier to defend soft-paternalism than hard-paternalism if the later can be justified at all. It is of capital importance to distinguish between decisions that reflect genuine impairments or incapacities and those that are based on values or ends with which we may not agree. Although hard paternalism might be justified on the grounds that it can be more important to protect or promote a person's welfare than to show respect for her autonomy or judgment, it generally fails to show appropriate respect for an individual's right to determine the values by which she lives. Indeed, on the assumption that a person's values and preferences help to determine what is in a person's interests, most putative cases of hard paternalism turn out not to be paternalistic at all – for intervention may not actually advance the person's interests properly understood. By contrast, soft-paternalism is consistent with respect for a person's values and ends even if it is prepared to override a person's decisions. After all, we can assume that Mill's bridge crosser does not desire to fall into the river.

Some interventions or policies that are justified on paternalistic grounds are more visible than others. We know that the state is requiring us to wear seat belts or motorcycle helmets or that it prohibits us from swimming without a lifeguard or get a prescription before we can obtain a medication. By contrast, we may not know what drugs we cannot take because they were not approved by the FDA. Similarly, prospective subjects do not know which opportunities for participation or opportunities for payments are not available to them because they were not approved by an IRB or were never submitted to an IRB because investigators or sponsors did not think they would be approved. Here, the paternalism is indirect: IRBs limit the freedom of investigators to offer opportunities for participation in order to protect the interests of participants. But whether the intervention is visible or invisible, direct or indirect, we cannot justify on soft-paternalist grounds a policy that denies people opportunities that they might *reasonably* choose and we cannot not justify denying them such opportunities on hard- paternalistic grounds if choosing them is in a person's interests properly understood.[5]

Now it might be argued that not allowing people to participate in research does not and *cannot* disrespect their autonomy because people have no autonomy based right to have the option to participate in research in the first place or to be paid to do so.[6] But even if a person does not have a right to a particular opportunity, we may fail to show proper respect for her if we deny her an opportunity for the wrong reasons. It is obviously wrong to deny someone a job on the basis of her race even if she has no right to the job itself. Similarly, it may be wrong to deny someone the opportunity to participate in research in exchange for (a certain level of) payment even if she has no right to be presented with that opportunity. And this is so even if the person would never know that the opportunity was not made available and has numerous other opportunities available to her. We may well be able to justify a risk/benefit assessment process that denies such opportunities to prospective subjects on soft-paternalist grounds. But such interventions must be justified.

Although the language varies slightly, there is little disagreement among the canonical statements of research ethics with respect to the principal criterion for risk/benefit assessment with respect to subjects who can consent (there are stricter rules for subjects such as children who cannot consent). According to The Common Rule, " Risks to subjects are reasonable in relation to anticipated benefits, if any, *to subjects, and the importance of the knowledge that may reasonably be expected to result*."[7] (emphasis added) The Declaration of Helsinki includes similar wording.

> Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to *the subject or to others* … Medical research involving human subjects

> should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject.[8] (emphasis added)

The Belmont report states that research must "be justified on the basis of a favorable risk/benefit assessment …"[9]

Let us refer to the general and universally accepted principle as the *Reasonable Risk Criterion (RRC)* or what is somewhat misleadingly referred to as a favorable risk/benefit ratio. (The idea of a "ratio" is misleading because the question is not whether the weighting of risks and benefits is 1:2, or 2:3, but whether the benefits "outweigh" or "justify" the risks.) Sven Ove Hansson says that "the received ethical approach to clinical trials … [does] not allow a person to sacrifice her own interests by taking part in a clinical trial that is beneficial to the wider community… "[10] This cannot be right. If Hansson were correct, research ethics would have relatively little to worry about – for there would be no ethical tension between the interests of subjects and those of the wider community not to mention that much Phase I research with healthy volunteers would be impossible. But contrary to Hansson's claim, all the relevant documents adopt an *aggregative view* of *RRC* with respect to subjects who can give informed consent. They place no *de jure* or principled limitation on the risks to which subjects may be exposed so long as the "importance of the knowledge" or the expected benefit of research is sufficient to outweigh or justify those risks.

Now the aggregative view does not require that all interests count *equally*. For example, the Belmont Report suggests that "the risks and benefits affecting the immediate research subject will normally carry special weight."[11] At the same time, the Belmont Report adds that "interests other than those of the subject may on some occasions be sufficient by themselves to justify the risks involved in the research, so long as the subjects' rights have been protected."[12] People may, of course, refuse to enroll in trials in which they would be put at risk for the benefit of society or enroll only if they are adequately compensated for undergoing such risks, but that is a different matter.

Although there are questions as to what counts as a harm or a risk for the purpose of applying RRC (as contrasted, say, to the burdens and inconveniences of participation), the more important question, for our purposes, is what should count as a benefit to the subject. Here we can distinguish between *the prospect of direct medical benefit* and a heterogeneous class of *adjunctive* or *inclusion* benefits. Research that is focused on the development of treatments or diagnosis may provide the prospect of direct medical benefit to the subjects when they receive (or have a chance of receiving) the intervention or diagnostic technology under investigation. Adjunctive or inclusion benefits may include "free goods or services provided as an enrollment incentive; diagnostic testing and standard treatments provided on-study at no cost to participants; the opportunity to be monitored closely by disease experts."[13] Lynn Jansen argues that altruistically motivated subjects benefit from their contribution to the scientific goals to which they contribute.[14] And, of course, subjects may regard payment as an inclusion or adjunctive benefit for participation. Although we might ask whether IRBs should regard all adjunctive or inclusion benefits in its risk/benefit assessment, I will focus on payment. If IRBs should not regard payment as a benefit, there remains the question as to whether they should count other adjunctive benefits, but if – as I shall argue – they *should* regard payment as a benefit, my argument would probably apply to the full range of adjunctive benefits.

THE STANDARD VIEW

Although the canonical documents are mostly silent as to what IRBs should count as a benefit to subjects, the standard view maintains that IRBs should completely ignore or exclude the value of financial payments to participants in its risk/benefit assessment. If an

IRB determines that a protocol satisfies RRC, then IRBs may permit investigators to offer financial payment to subjects so long as such payment is not coercive and does not constitute undue influence. But IRBs should not regard the value of payment to the subject as a benefit that offsets risk. As NIH policy puts it, "The IRB should not view remuneration as a benefit to offset research risks in deciding whether a protocol should be approved."[15] In a more expansive statement, a New York State Task force states that from the IRB's perspective, there are only two types of benefit: (1) direct medical benefit or "any direct enhancement to the health and well-being of the individual subject; (2) the prospect of increasing knowledge of benefit to society."[16] The Task Force acknowledges that " … there are certain aspects of research [for example, payment] that *subjects* are likely to perceive as benefits," but adds that "they do not constitute the *type* of benefit that IRBs should consider in evaluating the risk-benefit ratio of a protocol."[17] (emphasis added)

Although the standard view has become a virtual mantra in research ethics, *no* document contains an argument in its defense. As guidelines for IRBs, that is not surprising. IRBs do not need to know the philosophical justification for the policies that they are meant to follow. They need to know – in broad terms – what to do. It is somewhat more surprising that the scholarly literature also contains little defense of that view. For example, the important article by Emanuel, et. al. – "What Makes Clinical Research Ethical" simply states that "extraneous benefits, such as payment, or adjunctive medical services … cannot be considered in delineating the benefits compared with the risks," although it adds as a justificatory assertion that "otherwise simply increasing payment or adding more unrelated services could make the benefits outweigh even the riskiest research."[18]

Unfortunately, this "otherwise" justification assumes precisely what is at issue, namely, that it would be wrong to allow the value of payment (or other benefits) to subjects to justify risks that are otherwise unacceptable. One can't argue that X is wrong because it might lead to Y when it is not obvious that Y is wrong. And why shouldn't it be ethically permissible to ask people to assume greater risks by offering them what they reasonably regard as greater and sufficient benefits if they do so? After all, in the realm of medical treatment, it is perfectly justifiable to allow patients to consent to risks that would "otherwise" be unacceptable (as in chemotherapy) for the sake of medical benefits. Why is it not similarly permissible to allow subjects to accept risks that would otherwise be unacceptable for the sake of financial gain?

THE INCORPORATION VIEW

By contrast with the standard view, the *incorporation view* maintains that IRBs *should* consider the value of financial payments as a benefit to participants in risk/benefit assessment. Consistent with the soft paternalist justification for risk/benefit assessment, the incorporation view does not take a prospective subject's judgment about the value of financial payment at its word. If IRBs have reason to believe that prospective subjects are assigning excessive weight to financial payment relative to the risks and burdens of research, then IRBs should try to count only the amount of benefit that a reasonable prospective subject would assign. I do not doubt that it will be difficult for IRBs to make such judgments, a problem that I consider in more detail below. For present purposes, let us assume, *arguendo,* that such judgments are possible and focus on the question as to whether – in principle – the incorporation view should be adopted.

There are several related reasons for favoring the incorporation view. First, the standard view can lead to sub-optimal decisions from the perspective of all relevant parties. To see this, consider the cases in Table 1, where the *subject's* benefit from participation is *negative* on the *standard* view, that is, the risks are greater than the expected direct medical benefit if

any. (If participation can reasonably be expected to be of direct *medical* benefit to the subject and the research is also socially beneficial, then it is unproblematic with respect to *RRC*.) Let us assume that we can estimate the monetary-inclusive benefit to the subject for cases in which investigators are prepared to offer payment to subjects and that we can estimate the social value of the research. Given these estimates, we assess the aggregate expected benefits of the research. In each set of cases (e.g., (1,) (1a), (1b)), the *unmodified* number (e.g. (1) or (2)) *excludes* financial benefits from the calculation as on the standard view (*SV*)) whereas the *modified* numbers (e.g. (1a) and (1b) or (2a) and (2b)) *include* the financial benefits of various magnitudes as on the incorporation view (*IV*). Consider the following set of possibilities, where + = a net expected benefit, ++ = a greater net expected benefit; − = a net expected loss; and 0 = no expected benefit or loss, and so forth.

Recall that on the aggregative view, a protocol satisfies *RRC* if it has positive overall value, that is, the social benefits are sufficient to outweigh the risks to participants. If we focus on the standard view or unmodified (SV) cases, then (1) is the *only* protocol that can be approved and to which prospective participants would even have the opportunity to consent. (2) has a similar personal risk profile to (1) (it is no more risky), but less expected social value and thus does not produce net positive overall value. Note, however, that the modified IV view versions of (2) *could* be approved as in (2a) and (2b). Indeed, if the payments are high, as in (2b), the protocol would not only be expected to be of moderate positive *social* value, but participation would be of positive benefit to the subject. As an example of high risk/high social value research, (3) is the most interesting case. On an aggregative view of *RRC*, (3) will not be approved on the standard view because the social value, considerable though it may be, is not sufficient to justify the risks to the subjects. On the incorporation view, however, IRBs might approve the protocol in (3a) and (3b). Moreover, if the payments are sufficiently high, as in (3c), the research would generate a positive expected benefit for the participants as well as substantial social value. By comparison with (3c), it seems that (3) is sub-optimal from *everyone's* perspective. Researchers want to go forward. Future patients would be better off. And prospective subjects would benefit from participation by their own reasonable lights. We should be very reluctant to adopt a policy that would bar win-win-win outcomes.

The case for the incorporation view can be put more positively. The first and principal point is actually quite simple although no less compelling for that: if subjects can reasonably regard the financial benefits of participation as greater than the risks of participation, and if IRBs should demonstrate respect for the interests and judgment of prospective subjects, there is at least *prima facie* reason for IRBs to incorporate that judgment into their own risk/benefit assessment. Not to regard payment as a benefit is inconsistent with the paternalistic rationale for prospective risk/benefit assessment. We cannot justify denying people the opportunity to participate on paternalistic grounds (hard or soft) if participating in research will actually advance their well-being. Moreover, insofar as IRBs should be committed to respecting the autonomy of prospective participants, they should not structure its risk/benefit assessments in ways that deny people opportunities that it would be reasonable for them to accept.

To see the force of the previous point, let us consider respect for autonomy in a bit more detail. There is both a negative and a positive dimension to autonomy. The negative dimension of autonomy encompasses an agent's interest in not undergoing interventions or bearing risks unless such interventions are the result of her autonomous choice. The positive dimension of autonomy refers to an agent's interest in being able to avail herself of opportunities or being able to facilitate interactions with others in order to bring about a desired result. Both dimensions are important. Consider sexual relations. It is, of course, of great moral importance that people be protected from sexual relations to which they do not

consent or give valid consent. But as the ugly story of prohibitions on homosexual sexual relations makes clear, it is of importance that people have the opportunity to engage in sexual relations with persons of the same sex.

Consider medical care. It is of great moral importance that people not be forced to undergo procedures to which they have not given valid consent. But it is also important that we not prevent people from availing themselves of medical procedures from which they reasonably believe they will benefit and to which they are prepared to consent. The right to accept treatment is the flip side of the right to refuse treatment. Now I am not arguing that patients have a right to demand that others provide them with treatment. And I am *not* arguing that restrictions on one's positive autonomy are typically as wrong as violations of one's negative autonomy. It is generally worse to impose an unwanted intervention than to fail to make an opportunity available. I am arguing that restrictions on one's positive autonomy are wrong enough and both dimensions of autonomy stem from the common value that people should be in control of their lives. As Richard Epstein puts it, "it is surely a big deal to tell individuals that treatments they wish to undergo are to be denied to them on the ground that someone else thinks that it is unwise for them to undergo these treatments," as, for example, if the state prohibits breast implants on the grounds that they impose risks on women and do not provide what regulators regard as a genuine benefit.[19]

Now for understandable historical reasons, research ethics has focused on the negative or protective dimension of autonomy that encompasses an agent's interest in *not* undergoing interventions or bearing risks unless such interventions are the result of her autonomous choice. So there is great concern that a subject's consent is voluntary, informed, and not distorted by the therapeutic misconception or the lure of financial incentives. And that is as it should be. But it is also of moral importance that people not be denied the opportunity to participate for what they believe or would believe are good reasons and this is so particularly so when the decisions are made within a framework that is ostensibly committed to respect for persons and the value of autonomy. If IRBs want to say: "Look, we've decided that people don't have good judgment about financial benefits and so we're not going to make certain opportunities available to them," then they are appealing to the soft-paternalist rationale with which I am broadly sympathetic. But they cannot consistently say that whereas participation in exchange for payment may be in the interests of participants, they will not regard payment as a benefit in order to protect them.

A third argument for the incorporation view emphasizes its consistency with a plausible and popular view of the assessment of harm or risks to subjects. The Belmont Report suggests that IRBs need to consider risks of "psychological harm, physical harm, legal harm, social harm, and economic harm, such as the loss of a job. Interestingly, Belmont also maintains that IRBs should consider "corresponding benefits." If IRBs should regard economic loss as a harm of participation, it would seem that they should also consider the economic benefits of participation. What's sauce for the goose and all that.

The incorporation view is also consistent with a necessary and universal feature of human decision-making, namely that it is perfectly reasonable for people to balance or make trade-offs between risks to their life or health and other benefits or goods or ends and that we allow them to do so. Although I am hardly the first person to have made this point, I restate the obvious for I think its significance for research ethics is not sufficiently appreciated. We allow people to take considerable risks engaging in activities which they enjoy, be it football, skiing, rafting, climbing Mt. Everest, and riding motorcycles (without helmets in many states). We allow people to put their family in a car and take a cross country trip or just a Sunday drive to see Grandma. We allow people to drive rather than fly if they find it

cheaper to do so, even though they put their lives at greater risk for monetary gain (or savings).

It might be thought that it is one thing to "allow" people to make such trade-offs and another thing to "invite" people to do so. Perhaps, but we do well to bear in mind that employers invite prospective employees to accept jobs that involve moderate or even very high risks of illness, accidents, and death. Police officers, soldiers, and fire fighters all face considerable risks, as do timber cutters, lobster fishermen, structural metal workers, coal miners, general aviation pilots, and hospital workers. And if there were an occupational equivalent of IRBs charged to allow people to be employed only if the benefits of employment exceeded the risks and burdens (given their situation), it would be absurd not to include financial benefits in making such calculations.

Now it might be argued that we can and should distinguish between the way in which we should count financial benefits in ordinary employment as opposed to participation in medical research. But even in the medical realm, we allow people to accept risks to their life and health in pursuit of other goods. For example, a plastic surgeon may perform breast enlargement surgery and put the patient at some medical risk for the sake of psychic or social or economic benefits to the patient, as when a cocktail waitress seeks such surgery because she believes larger breasts will generate more tips. A physician might prescribe drugs rather than surgery for prostate cancer because the patient is willing to risk a higher probability of death in order to avoid a higher probability of impotence. And I believe that a physician might conscientiously prescribe a medically less effective but less expensive therapy to patients who are financially strapped – if they are making an informed choice among the alternatives.

In response to the previous suggestion, it may be said that whereas it is proper for physicians to incorporate a patient's conception of her interests into their decision-making because medical care is fundamentally concerned with the interests of patients, it is not proper for IRBs to incorporate a research conception of his interests into its decision-making because the point of medical research is to create generalizable knowledge and not to advance the interests of subjects. I will consider this argument in more detail below. For present purposes, note that this reply effectively concedes that the standard view cannot be defended by reference to the interests and autonomy of research subjects. And that is the thesis for which I have been arguing

SUBJECT-ORIENTED OBJECTIONS

Assuming that I have sketched at least a plausible case for adopting the incorporation view, there are two lines of objection that might be raised against my argument. In this section, I consider arguments that work – or might claim to work – within the general framework of the interests and rights of subjects. In the following section, I consider arguments that are rooted in other considerations.

Abandoning risk/benefit assessment

In an important and under-appreciated article, Alex Rajczi argues that IRBs should not try to determine whether the benefits of research are greater than the risks -- what he calls "the improvement principle."[20] Rather, IRBs should adopt "the agreement principle," under which a protocol "has an acceptable combination of risks and benefits if it would be entered into by *competent and informed decision-makers.*"[21] Rather than explicitly incorporate monetary benefits into its own risk/benefit assessment, the agreement principle maintains that if competent decision-makers would agree to participate because they consider payment as a benefit, then that is sufficient to justify the protocol on risk/benefit grounds.

The incorporation view is close to being extensionally equivalent to Rajczi's agreement principle and rests on similar soft-paternalist foundations. Nonetheless, I think the incorporation view represents a more attractive approach to risk benefit assessment. First, by accepting the general framework of "the improvement principle," the incorporation view requires a less radical change by IRBs. Second, the incorporation view makes the critical change in perspective more transparent – it explicitly recommends that IRBs regard payment as a benefit.

Asymmetry

What might be called the *asymmetry* argument claims that IRBs should be concerned with limiting risks to subjects rather than promoting their all things considered interests. In colloquial terms, the defender of the standard view might say: "It's subject *protection,* not subject welfare." This objection takes the subject protection language too literally and presupposes precisely what is at issue. For we must ask why we should be concerned solely with protecting subjects from harm rather than advancing their all things considered interests, especially when the former desideratum is arguably derived from the latter. Moreover, on closer inspection, the standard view is not solely concerned with risks to the subject. It requires IRBs to balance those risks against the prospect of direct medical benefit to the subject.

Separate spheres

The critic could grant the latter point, but then maintain that "potential benefits should be of the same type as the risks they justify."[22] Call this the *separate spheres* principle. On this view, since subjects face risks to their health, these risks can only be offset by advances to their health or to the health of others, and "not by the potential increase in their bank accounts." I believe the objection fails. The separate spheres principle is superficially attractive and often invoked, but when one looks for an *argument* for that principle one is reminded of Gertrude Stein's famous remark about Oakland -- "there's no there there." Moreover, even if there are independent *moral* reasons to adopt the separate-spheres principle and not to allow such trade-offs, it cannot be justified by reference to the interests and autonomy of research subjects. And that is the argument under consideration.

Jacking-up

What might be called the "jacking-up" argument maintains that because inclusion benefits such as payment are largely within the investigator's control, they could tempt investigators to increase payment "when the "morally preferable course of action is … to minimize harms, to the maximum feasible extent."[23] But it is not obvious that even feasible risk-minimization is always morally preferable. If a taxi company could provide its drivers with ultra-safe Volvos and pay them $10 per hour or provide less-safe Fords and pay them $12 an hour, it is not obvious that the benefits of risk minimization are greater than the benefits of the foregone income and it is certainly not obvious that the drivers would prefer risk-minimization to greater salaries. And the same could be true in some contexts of medical research.

Moreover, what should IRBs do if researchers have minimized risk to the maximum feasible extent within the framework of the protocol, say in something like Case (3) in Table 1? If IRBs adopt the standard view, then investigators can do nothing to garner IRB approval because the risks to subjects is greater than the expected social value of the research. But if IRBs adopt the incorporation view, then IRBs could approve the protocol if investigators were to "jack up" the financial payment sufficiently high (as in (3a) and if subjects were paid even more (as in 3c), this would benefit subjects, investigators, and society.

A related but different version of the jacking-up argument maintains that investigators might "add weight to the benefit side of the balance, in ways that at best might *draw attention* away from minimizing the risks of harm and at worst could *unduly influence* potential participants in favor of participation despite the risks of harm."[24] (emphasis added) On this view, it's not (just) that researchers have an independent obligation to minimize risk, but that increasing payment might compromise the subject's consent by diverting attention away from or excessively discounting the risks of harm. There is an empirical question as to whether payment has this effect, and the evidence to date does not support it.[25] In any case, this version of the "jacking-up" worry concerns the validity of a subject's *consent* and is no objection to the incorporation of prospective subjects' *reasonable* and non-distorted judgments about risks and benefits in an IRB's risk/benefit assessment.

Objective interests

Still, it might be argued that the incorporation view reflects an excessively expansive and non-judgmental conception of a person's interests. A subject might think that having the money to purchase a big screen TV makes it sensible for him to accept certain medical risks, but he may be wrong on an "objective list" or moralized account of his "genuine" interests in which a person's interests are not reducible to her happiness or the satisfaction of her preferences or desires.[26] And, the argument goes, IRBs should not incorporate such impoverished conceptions of a person's interests into their decisions as to what opportunities should be made available to prospective subjects.

As a matter of moral theory, I am not averse to an "objective list" view, although I also think that attention to an individual's values and preferences must be a part of any plausible conception of a person's interests – it must be *on* the list. In any case, the reach of the view under consideration is potentially very large and very dangerous. It is possible that women who seek breast enlargements are making a mistake about their interests and that some men place excessive importance on avoiding impotence, but as a matter of social and political morality, I would be loathe to support a policy of not making surgery and impotence avoiding treatments available for that reason.

If the ethics of medical care should include a preference and value sensitive conception of a patient's interests, it would seem that the ethics of medical research should also reflect such a view. I grant that it is difficult to determine when a person's choices reflect reasonable judgments if not the "right" or "best" conceptions of the good and when they demonstrate genuine decisional impairments. But making that distinction cannot be avoided so long as we want to endorse a soft-paternalism that is prepared to override individual decisions based on cognitive mistakes while rejecting a hard-paternalism that would interfere with decisions that we think are erroneous on some objective account of a person's interests.

Now it may be argued that subjects are not actually likely to benefit, long term, from financial payment by reference to their own values and that we should therefore not regard payment as a benefit that can offset risk. If we were to compare two groups of subjects where half receive $500 and half receive nothing, the former group may be no better off in a year much less ten years. On the long-term view, however, almost nothing that we do or receive should be considered a benefit. And that would be silly. Many pleasures in life – including most consumption pleasures – are short term. In addition, much the same could be said for some of the risks of medical research. If transient aversive experiences such as pain and nausea are regarded as risks of research, then transient positive experiences should be regarded as benefits.

Epistemological objection

What may be called an *epistemological objection* to the incorporation view maintains that IRBs are not well positioned to determine how much weight to assign to the benefit of payment as compared to risk. Is the value of $500 to a person with a certain income equivalent to the risk and burden of a lumbar puncture? I do not doubt that these are difficult judgments to make. But there are two reasons for thinking that these cannot be compelling objections to the incorporation view.

First, it is difficult for IRBs to evaluate the entire range of risks and benefits. Although I concede that it is (by comparison) relatively easy to compare medical risks to subjects with the prospect of direct medical benefit to the same subjects, I see no reason to think that it is more difficult to compare medical risks to subjects with the benefit of financial payment to them than to compare risks to subjects with the benefits to *others* from generalizable knowledge -- particularly given the level of uncertainty involved in the latter comparison. So the epistemological objection to the incorporation view cuts too wide and too deep. It threatens the entire project of risk/benefit assessment.

Second, IRBs *cannot* refuse to make judgments about the value of financial benefits relative to risk on epistemological grounds if they are concerned to ensure that financial payments not constitute *undue inducements* – as they are held responsible for doing by all the relevant policies and laws. For to say that a financial payment constitutes an undue inducement is precisely to say that a subject's consideration of the risks of research has been distorted by the offer of financial payment. In effect, the incorporation view merely asks IRBs to transfer judgments they are (or should be) already making from the assessment of undue inducements to the assessment of risks and benefits.

To elaborate on the previous point, we must consider how IRBs should understand their undue inducement mandate. When one examines the various documents and policy statements, one finds two interpretations of undue inducement: a *no difference* view and a *distortion* view. An OHRP document appears to adopt the no difference view when it says that "The level of remuneration should not be so high as to cause a prospective subject to accept risks that he or she would not accept in the absence of the remuneration."[27] Despite its impressive institutional pedigree and all too widespread popularity, the no difference view is a non-starter. It surely makes no sense to insist that remuneration offered as an incentive for participation should make *no* difference to the risks one would accept any more than it makes sense to think that remuneration should make no difference to one's willingness to work. It borders on the incoherent to say that financial incentives offered to a healthy volunteer are unacceptable if they cause him to agree to blood draws or to FMRIs to which he would not agree in the absence of remuneration. So we should set the no difference view aside.

Interestingly, the just mentioned OHRP document implicitly adopts the distortion view when it goes on to say that "IRBs should be cautious that payments are not so high that they "could compromise a prospective subject's examination and evaluation of the risks … "[28] On this – and I think correct – view, payment constitutes an undue inducement only it triggers irrational decision-making given the agent's own settled (and reasonable) values and aims. As *The Official IRB Guidebook* puts it, an offer is troublesome if it is so "attractive that [it can] *blind* prospective subjects to potential risks or impair their ability to exercise *proper judgment* about the risks of participation."[29]

On the distortion view, payment does not constitute morally problematic undue inducement if a prospective subject weighs the value of the payment against the risks in a reasonable way and decides that the benefit of the payment exceeds the risks, just as it is reasonable for

a patient to conclude that the expected benefit of chemotherapy exceeds the predictable harms. Although there is some evidence that increased amounts of payment do *not* show decreased sensitivity to risk, an agent's decision-making could be distorted by *tunnel vision* if the lure of the payment causes her to ignore or give inadequate consideration to other relevant interests or *decisional myopia* if she is aware of her other interests, but the lure of the inducement causes her to overweight the short-term benefits and underestimate or underweight the long-term costs of accepting the proposal. In any case, it is an empirical question as to whether offers of payment compromise a subject's judgment. If and when such offers are likely to do so, that is a reason to regard a subject's consent as not valid. But the possibility of such distortions give us no reason not to incorporate a subject's reasonable and non-distorted evaluation of the benefits of financial payment in risk/benefit assessment.

Building a fence

Another objection to the incorporation view is similar to the Talmudic notion of a "fence around the Torah." Just as the Talmud adds laws to those found in the Torah as a fence to protect Jews from inadvertently violating the law of the Torah, it might be argued that IRBs should adopt the standard view as a way to provide extra insurance that payment does not constitute an undue inducement rather than as an independent principle of risk/benefit assessment. Although I have not encountered this (or, for that matter, any other) argument for the standard view, it is a coherent argument. But it does not work. First, this argument does nothing to protect subjects against undue inducement in those cases where the risk/benefit assessment is acceptable on the standard view. Second, this argument does not take seriously the way in which the standard view fails to show respect for the non-distorted judgment of prospective subjects. It's fine to provide extra protection against an unwanted phenomenon when doing so is relatively costless, but, as I have argued, the standard view has the potential to prevent research that benefits investigators, society and participants as well.

Exploitation

A final subject-oriented objection to the incorporation view maintains that it is likely to lead to the exploitation of research subjects because it will allow IRBs to approve risky research with economically vulnerable populations so long as investigators are prepared to pay subjects enough to counterbalance those risks. And this is especially so with respect to research in developing societies. Here I would make two points. First, and as I argued above, if offers of payment are likely to induce economically vulnerable subjects to make unreasonable decisions about their interests, then IRBs are well advised not to approve such research on grounds of undue inducement. Second, the incorporation view does *not* entail that researchers and investigators should be left alone to negotiate the relevant level of risk minimization or the proper level of payment

Consider the case for minimum wage laws. Left to fend for themselves, it may be perfectly rational for many workers to agree to employment at very low wages rather than remain unemployed. At the same time, if the state requires employers to pay a higher wage than they would otherwise offer, then employers may offer employees the higher wage rather than not hiring them at all. Minimum wage laws are a strategic intervention by the state to help workers solve a collective action problem and overcome the inequality of bargaining power with potential employers. Such laws can force employers and employees to reach what is a better deal for employees without setting the wage so high so as to deter a significant number of employment opportunities. Similarly, if investigators will reduce risks and/or offer greater compensation to subjects if IRBs refuse to approve what are barely minimally beneficial arrangements on the incorporation view, then we have a perfectly serviceable argument for refusing to endorse those unfair arrangements. But so far as I can

see, this sort of intervention has precisely nothing to do with whether IRBs should regard payment to subjects as a benefit in its risk/benefit assessment. After all, we don't deny that workers benefit from being employed at sub-minimum wages. We just want them to benefit more.

NON-SUBJECT ORIENTED OBJECTIONS

I have argued that it is difficult to defend the standard view if the point of risk/benefit assessment is to protect the interests and autonomy of research subjects. It is possible, however, that the standard view can be defended on grounds not normally associated with the purview of IRBs and subject protection. It is difficult to evaluate such arguments because no one has produced or seen the need to produce them. Putting my limited imaginative abilities to work, there are at least three non-subject protection arguments that might be advanced in its defense: (1) an appeal to role morality; (2) an appeal to legal moralism; (3) an appeal to trust.

Role morality

The first line of argument refers to the special mission or aims of medicine and clinical research. To put this argument in a broader context, we often distinguish between the permissions and obligations of common-sense morality which apply to all of us and the permissions and demands of professional roles. For example, a criminal defense lawyer may justifiably seek the acquittal of her client as if she were indifferent to society's interest in putting a dangerous person in prison. A doctor may refuse to divulge to a patient's wife that her husband is HIV positive. A breast cancer lobbyist is legitimately concerned with securing funding for research on breast cancer even if this means that fewer and perhaps insufficient resources will be devoted to other diseases. And so on.

Along these lines, it is arguable that the medical profession is concerned with the promotion of health and has no special interest in advancing what others may regard as legitimate ends. Suppose, for example, that a physician believes that participation in a trial is not optimal for his patient from a *medical* perspective, but knows that the patient needs money. It could be argued that even if participation is entirely reasonable from the *patient's* perspective, this is not a choice that a *physician* should invite or encourage a patient to make. The physician's role is to advance the patient's *medical* interests, and not her interests, writ large. And perhaps much the same could be said for the relationship between IRBs and subjects.

A full assessment of this line of argument is clearly beyond the scope of this paper. Here I want to make a general point about role morality before considering its relevance to the defense of the standard view. Roughly speaking, there are two approaches to justifying the special aims and restrictions on professionals. On a "top-down" or "essentialist" view, the shape and content of professional roles and obligations are thought to be intrinsic to the character of the relevant profession. Some will argue, for example, that physicians should not assist in executions even if capital punishment is otherwise justifiable or even morally required. Why? Because it's inconsistent with the values that underlie the practice of medicine. On a "bottom-up" view, the shape and content of professional roles and obligations are ultimately based on general moral considerations such as the interests of the parties to a professional relationship and the wider interests of society.

I shall mostly assert and not defend at length the proposition that the second – bottom-up – view is a more compelling strategy for defending the role defined obligations and permissions of various professions or institutions. I believe that one cannot defend role obligations of physicians simply by saying "physicians don't do that." Rather, the role obligations and permissions of physicians are justified by showing that ascribing those

obligations and permissions to physicians serves important social goals and interests more effectively than alternative conceptions of those obligations and permissions. Consider the principle of physician/patient confidentiality. As a general rule, physicians have an obligation to respect the confidentiality of their patients even when doing so is likely to adversely affect others or the patient herself. On a bottom-up view, the obligation to respect confidentiality may be justified by its role in facilitating openness between patients and physicians and perhaps because patients might otherwise refuse to seek medical care in some circumstances. But this principle is not sacrosanct. Although physicians may once have thought that they had a professional obligation *not* to report suspected child abuse out of respect for the confidentiality of their patients, many states now *require* physicians to do so because society has decided that its members will be better served if it makes this exception to the confidentiality principle – even though it might deter some parents from seeking medical care for their children. Professions and institutions may well have special obligations and permissions that allow or require them to deviate from what common sense morality would seem to prescribe. But the shape of a profession's ethical responsibilities is not for the profession to decide.

On the assumption that a profession may have role-specific obligations and permissions, it may be argued that the enterprise of clinical research has role obligations that are rooted in the advancement of health and generalizable knowledge. From that perspective, subject protection acts as a *constraint* on the pursuit of those ends but not as an aim or goal. And it may be argued that to regard financial payment as a benefit that can offset the risks of participation would violate the integrity or be untrue to the special aims of the research enterprise. From this perspective, it is perfectly reasonable for research institutions to refuse to be associated with what it would be perfectly permissible and reasonable for individual subjects to do.

Consider this analogy. Seana Shiffrin has argued that one may refuse to buy cigarettes for a friend not because one paternalistically seeks to advance one's friend's health, but because one does not want to be complicit with or lend one's support to her habit.[30] One refuses for one's *own* reasons, not to promote one's friend's interests. Perhaps for similar reasons, IRBs may refuse to regard financial payment as a benefit not in order to protect subjects, but precisely because research is not primarily concerned to advance the interests of subjects. IRBs need not integrate a subject's values – even her reasonable values -- into its own decision-making.

This is a coherent argument, but it is not clear that it can be sustained in this context. First, it is not at all clear that the special social aims of research would be better protected or reflected by a decision to reject the incorporation view if, as I have argued, the standard view is a barrier to research that has genuine social value. Second, this argument might have limited application to private or commercial research in which the institutions are more sympathetic to viewing science and research as an economic enterprise. Third, and as I argued above, one can't simply assert the essentialist view that research has certain values. As with other professions, the shape and content of the obligations, permissions, and aims of medical research must be justified from the ground-up. I believe it is possible but not likely that that an appeal to institutional or professional integrity will support the standard view in the face of the considerations that tell against it.

Legal moralism

The standard view might be defended on perfectionist grounds or by something like *legal moralism*.[31] Consider the practice of "dwarf tossing."[32] Dwarf tossing is a pub "game" in which participants compete to throw dwarfs, who wear special padded clothing or Velcro costumes, onto mattresses or at Velcro-coated walls. The dwarfs are paid to be thrown. It is

difficult to object to dwarf-tossing on paternalistic grounds. There is no reason to doubt that the dwarfs are giving informed consent to be tossed and that they reasonably think that they benefit – all things considered – from allowing themselves to be tossed for a fee. In signing New York State legislation that banned the practice, former Governor Mario Cuomo did not take the paternalistic tack. He stated that "Any activity that dehumanizes and humiliates these people is degrading to us all."[33] On this view, society has its own reasons for not wanting people to take certain risks or be treated in certain ways even if they would prefer to take such risks or be so treated. Along similar lines, society may prefer that research not be viewed as an economic transaction and it may symbolize its commitments by not allowing such values to intrude on the assessment of risks and benefits.

It is a large question as to whether *any* sort of legal moralism can be defended. Although the ban on dwarf-tossing might seem unobjectionable, we do well to recall that legal moralism has an important dark side – as evidenced by our long tradition of restrictions on homosexuality. But even if some forms of legal moralism can be defended, it is another question as to whether the incorporation view violates deeply held values in a way that justifies interfering with consensual transactions from which society, investigators, and subjects all gain – save the alleged harmful symbolic effects of adopting that view.

Public Trust

Finally, given the history of research scandals, it is crucial that the public believe that research subjects are not abused or exploited. Given that the incorporation view will allow IRBs to approve high risk research that would be rejected on the standard view, it may be argued that adoption of the standard view is more likely to sustain *public trust* in the research enterprise than the incorporation view. Whereas society accepts with a relative yawn the fact that people incur job related injuries or deaths as coal miners, fishermen, and off-shore oil service workers, society seems to react with great intensity to research related injuries and deaths as evidenced by the public concern with the Jesse Gelsinger case.[34] Moreover, given that the public is likely to react more intensely to the injuries and deaths that do occur if the incorporation view is adopted than to the foregone beneficial opportunities that do not occur because the standard view is adopted, it is arguable that the standard view is likely to generate a higher level of public trust. So even if the public is mistaken to react more intensely to research related harms than to normal occupational harms, and even if the public is mistaken in thinking that the standard view serves better to advance the all things considered *interests* of prospective research subjects than the incorporation view, the public trust argument maintains that their beliefs are a fact that must be accommodated.

I have two responses to this argument. First, I think the general form of the public trust argument is sound, although some think that it would be a moral mistake to accommodate or respond to erroneous beliefs. Second, if sustaining public trust requires that IRBs refuse to approve research that exceeds a certain level of risk, then that is an argument in favor of such a policy, although the weight of that reason would have to be balanced against the advantages of allowing higher risk research. In any case, the need for a limit on allowable risk is separable from and does not entail that IRBs should adopt the standard view. After all, the standard view also allows IRBs to approve high risk research if the expected social benefits are sufficient.

CONCLUSION

I have not sought to defend the incorporation view, *tout court*. I have argued that insofar as risk/benefit assessment is designed to protect the interests and autonomy of research subjects, we should reject the standard view that IRBs should not regard financial payment

to subjects as a benefit for the purpose of risk/benefit assessment. Since the standard view is surely *thought* to be defensible on subject-oriented grounds, my argument should go some way towards supporting the adoption of the incorporation view. Of course, my argument may be wrong or incomplete. Despite what I have said, a critic might show that the standard view can be successfully defended by appeal to the interests and autonomy of research subjects. In addition, even if the standard view cannot be defended on subject-oriented grounds, a critic might show that it can be defended on other grounds. In either case, we will have then made progress. My argument will have indirectly produced what we now lack -- a defense of the standard view.

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Table 1

	Medical Benefit	Financial Benefit	Overall Personal Benefit	Social Benefit	Overall Benefit
	$$ exclusive		**$$ inclusive**		
1 (*SV*)	−	NA	NA	++	+
1a (*IV*)	−	+	0	++	++
1b *(IV)*	−	++	+	++	+++
2 (*SV*)	−	NA	NA	+	0
2a *(IV)*	−	+	0	+	+
2b *(IV)*	−	++	+	+	++
3 (*SV*)	−−	NA	NA	++	0
3a *(IV)*	−−	+	−	++	+
3b *(IV)*	−−	++	0	++	++
3c *(IV)*	−−	+++	+	++	+++