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Christopher Robertson
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The Ethics of Research That May Disadvantage Others

Christopher T. Robertson
The University of Arizona
James E. Rogers College of Law

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The Ethics of Research That May Disadvantage Others

Christopher Robertson, JD, PhD
robertson@arizona.edu

Abstract

In prospective interventional research, a treatment may provide an advantage for the recipient over other humans not receiving it. If the intervention proves successful, the treated are better able to compete for a scarce ventilator, a class grade, or a litigation outcome, potentially risking the deaths, jobs, or incomes of non-treated persons. The concerns for “bystanders” have typically focused on direct harms (e.g. infecting them with a virus), unlike the mere competition for rivalrous goods at issue here.

After broadly scoping this problem, analysis reveals several reasons that such research is typically permissible, notwithstanding the potential setbacks to the interests of non-participants. After considering the almost-dispositive concept of clinical equipoise, insights are gleaned from the harm principle, status quo bias, the levelling-down problem, and a potential bias against prospective interventional research versus program interventions with retrospective study. Consideration of institutional relationships also does not change the analysis that such research is permissible.

Introduction

Scientific research routinely seeks to determine whether an intervention will provide an absolute benefit for those who receive it, but there are important cases where the hypothesized benefit would also provide a relative advantage over others not receiving the intervention. In such cases where the intervention proves successful, the treated are better able to compete against non-treated persons for a good that is in limited supply. To illustrate, consider the following scenarios.

- 1) A research team has a new investigational therapy for the worst-off patients suffering the most severe forms of an infectious disease (such as COVID-19). During the raging pandemic when this therapy will be tested, ventilators are in such short supply that the patients suffering such severe forms of the disease are typically given only palliative care, as the ventilators are instead allocated to those who are more likely to recover. If the investigational therapy is effective, however, those patients receiving it will then become eligible for ventilators, and thereby compete against other marginal patients, who might be denied a ventilator and die as a result.
- 2) A research team has a new educational program that may improve student learning in a given domain. The students' school grades "on the curve," such that only the highest-scoring students receive a limited number of A grades. If the intervention is effective, then the recipients will be more likely to get the top grades, which are key determinants of securing jobs upon graduation.
- 3) A research team has a new informational intervention (a letter and pamphlet) that may help patients facing collections for large medical bills understand their legal rights and thereby avoid having a default judgment that garnishes their wages. If the intervention is

effective, the patients may have less stress and improved access to subsequent healthcare, but the doctors and hospitals who hold the medical debt will recover less money.

Across any of these domains (and others), if such research is allowed to proceed, it risks the deaths or unemployment or revenues of other persons, who do not participate in the research but who may be affected by its success. Local ethics regulators have raised precisely such concerns in real cases.¹ As distinct from laboratory research or observational/archival research, the problems are likely to grow sharper as interventional field research becomes more commonplace to rigorously study programs in real-world settings.

Concerns for non-participants (aka “bystanders”) have been mentioned in the literature,² and in recent years have received more sustained attention.³ However, these concerns focus on direct harm to the non-participants (e.g. infecting them with a virus), unlike the mere competition for rivalrous goods at issue here. There are some analogous ethical issues outside the research context, e.g., how legal services should be rationed considering divergent effects on adversaries⁴ and whether parents should be allowed to use genetic engineering to give their children relative advantages over others.⁵ Yet, there seems to be no systematic scholarly treatment of this particular problem (if it is a problem).

This article undertakes that study, to clarify the issues and produce generalizable knowledge about the appropriate ethical and regulatory approach to such problems. Just as importantly, with primers on basic ethical and regulatory concepts, along with graphics to illustrate the issues, this article also seeks to be a resource for ethics regulators and field partners who raise concerns.

After showing the broad scope of this problem for research ethics and regulation, analysis reveals several key reasons that such research is typically permissible. After considering the

almost-dispositive concept of clinical equipoise, additional insights are gleaned from the harm principle, status quo bias, the levelling-down problem, and a potential bias against prospective interventional research. Ultimately we also see that consideration of special institutional relationships does not change the analysis that such research is permissible.

Scoping the Potential Problem

From the outset, let's distinguish an orthogonal concern that certain populations (e.g., children, non-Whites, women, and the elderly) have been systematically, and often intentionally, excluded from scientific research.⁶ Although there has been some interest in access to investigational treatments, the primary concern has been epistemic – that exclusion of these populations has undermined the generalizability of research for those subpopulations. Let us presume fair inclusion of the relevant populations. The concern for risks to others exists even if there is no discrimination or disparities, and even aside from any epistemic value.

Within the scope of this paper, I will use the three focal examples where individuals compete for ventilators, for A-grades, and for medical bills, but there are innumerable other such interventions in a world of scarcity. Here, individuals compete for goods that are “rivalrous” to use the economic term,⁷ or “adversarial” in the legal literature.⁸ In this vein, Cohen & Greiner describe the peculiar ethical problems of potential randomized control trials (RCTs) in the legal context, where there is a single winner or loser for each case.⁹

Beyond such direct, institutional adversarialism, there are a range of other such cases. In the medical context, even outside of pandemics, there are competitions for scarce goods. For example, a research team has a new therapy for tuberculosis (TB), a contraindication for lung transplantation. There is a shortage of lungs that could be transplanted, and they are allocated

largely to those who have the best prognosis. If the TB therapy is effective, those receiving it will be more likely to qualify for and receive a lung transplant compared to others not receiving the therapy, who might die for lack of a transplant. Beyond healthcare there are a range of cases including research projects studying a mentoring program for disadvantaged medical residents to improve chances of securing a fellowship, a training course to help veterans secure a job, a mentoring program for inner-city youth to matriculate at highly selective colleges, an agricultural technique to increase crop yields in a competitive market with other growers, a fitness regimen for athletes seeking to win an upcoming competition, a canvassing technique to support a political candidate in a contested race, a tax waiver program for businesses effectively lowering the cost of production of widgets in an opportunity zone, financial counseling to homebuyers competing against others who seek a given house, distribution of self-help materials or attorneys to individuals facing eviction, or an outreach program delivering vaccines that are in limited supply. In all these cases, if the intervention is successful, it will advantage participants, relative to those competing to get the very same transplanted organs, fellowships, jobs, college admissions, commodity sales, race trophies, elected positions, business opportunities, home purchases, home repossessions, or vaccines.

Even beyond these cases, there are ubiquitous situations where a relative advantage is foreseeable, even if not so directly intended. As Eyal and Wikler explain in the context of an HIV treatment, “participants may emerge from the study as powerful economic rivals to others who ply their trades, leading to predictable small financial losses to identified rivals.”¹⁰

Whenever a clinician treats a patient’s disease (whether inside a research trial or otherwise), she makes him a more competitive candidate for whatever race he might run, class he may enroll in, or job he may seek. (It is hard to compete for any of these rivalrous goods, if you are flat on

your back in a hospital, or even worse, dead.) So if the problem of relative advantage is real, it could be profound in its implications for the regulation of research (and the ethics of clinical care).

One can imagine variations of these cases, where the intervention is tested on some but not others. Suppose that Adam and Bert are potential ventilator candidates or students in the same curved class, or that Adam is the medical debtor and Bert the creditor (e.g., doctor). In one version, Adam meets inclusion criteria for the study (e.g., having a severe infectious disease needing treatment, or being part of a historically disadvantaged group the program seeks to benefit, or being medical debtor), while Bert does not. (Or vice-versa: Bert may have an exclusion factor, such as a comorbidity, preventing him from participating.) In another variation of the ventilator or school studies, suppose that Adam and Bert were both recruited into the study, but Bert was randomly assigned to the control group. Or, the investigators randomized first and thereby assigned Adam to be invited to participate, and he agreed, but Bert was not selected for recruitment. In yet another variation, Adam and Bert were both invited to participate, but with full information, Bert declined or started but then dropped out (perhaps feeling that it was just too inconvenient or onerous to comply with the regimen). In a final variation, the researchers tried to recruit broadly, and happened to reach Adam and recruit him, but not Bert, before the study was full and the budget for the intervention was exhausted. For simplicity, in all these cases let's call Bert a "non-recipient" of the intervention.

Regardless of the variation, the key feature of the problem is that if Adam does receive the intervention (and it is successful) then it will reduce Bert's chances to receive the ventilator or get an A grade or recover the full value of the claimed debt. Of course, having an advantage does not guarantee a favorable outcome, since there are many other drivers of outcomes, but it

helps Adam on the margin. So in each case, Bert would prefer that Adam *not* receive the intervention.

In research and clinical contexts, informed consent is often a way to resolve ambiguous ethical situations. In this context, consent is unhelpful – if asked, Bert will withhold consent, but if that preference is respected it will have the effect of overriding Adam’s interest in receiving the treatment. Accordingly, this mechanism would be better conceived as something more like a *veto* than consent.¹¹

From an ethical and regulatory perspective, these sorts of objections are interesting in part because, in several of the variations (e.g., he was not recruited at all, or he declined to participate), Bert is arguably not actually a human subject in the scientific research.¹² If his identifiable, non-public data are not being used, and researchers are not manipulating *his* treatment, then to what degree should his interests even be considered by those whose mission is to protect human subjects? Arguably, from a regulatory point of view, Bert’s interests are irrelevant as a non-subject.¹³ The Federal Common Rule, which empowers Institutional Review Boards (IRBs), is titled, “Federal Policy for the Protection of Human Subjects,”¹⁴ and the operative section¹⁵ directs that the “IRB shall determine that ... risks *to subjects* are minimized ... and are reasonable...” (emphasis added).

Thus, it is not clear that these entities have any obligation, jurisdiction, or authority to assert the interests of non-recipients, who are not recruited for a research study.¹⁶ The problem thus implicates the literature on IRB “mission creep”.¹⁷

On the other hand, the Common Rule could be read expansively to include anyone affected by research as a human subject. The Common Rule defines a human research subject as: “a

living individual about whom an investigator ... conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information.” The Rule then defines “interaction” as including “both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s *environment* that are performed for research purposes” (emphasis added). If a competitor for a rivalrous good receiving an intervention can be considered a manipulation to the “environment” then virtually everyone is a human subject.¹⁸ Some have suggested that even if not human subjects, these persons may be considered “indirect” or “collateral” research participants.¹⁹ Such an expansive conception threatens, however, to make ethical review untenably broad.²⁰

As matter of fact, in some versions of the focal cases, Bert may have been recruited as a human subject but assigned to a control group, or researchers may seek to use his identified, non-public information for comparison purposes, making him a human subject, even without referring to a capacious definition of “environment.” Moreover even if outside the ambit of human subjects protection, a fulsome ethical analysis might consider all affected persons. If there is an ethical problem here, *somebody* should have responsibility to resolve it, whether through a broader IRB mission or supplementation by another entity.²¹ Some have called for “Comprehensive Ethics Review Committees” to consider non-subjects’ interests.²² In many cases, the institutional context (e.g., the school where the educational intervention would be provided) may themselves raise such objections. Accordingly, I refer herein to the “ethics regulator,” and argue whether the present sort of cases should fall into even their capacious purview.

However, I will ultimately argue that the purported ethical problem is illusory. The basic bioethical principle of equipoise goes a long way. Even more, Bert is not, strictly speaking,

harmful by the study going forward (even if the treatment turns out to be effective for Adam). Even worse, as we will see, if the ethics regulator blocks the study that would benefit Adam (the potential human subject), it harms him in order to satisfy Bert's preferences. This would be a fascinating situation of an ethics regulator doing harm, the opposite of what IRBs are supposed to do. Yet, at least some ethics regulators may see it as their duty, which motivates this analysis.

Clinical Equipoise

Clinical equipoise is a fundamental principle of bioethics.²³ The idea, simply put, is that we should not do research on human subjects when we already know the answer to the research question. This principle is satisfied, and research is allowed, when there is genuine uncertainty in the expert medical community over whether a treatment will be beneficial.

To elaborate this point, consider that for research that seeks to determine causation, such as the efficacy (or risks) of a treatment, it is necessary to compare people with and without the treatment. The latter group is typically referred to as the "control" group. But if we already know that the treatment is the best one, then it would be unethical to have a control group – everyone should get the good stuff. In the real-world practice of bioethics, clinical equipoise is rarely an issue at the outset of a study, since investigators (and the funders of research) are rarely motivated to embark on research projects for which they already know the answer. Sometimes, however, a research project starts with clinical equipoise, but early data show that one treatment is so obviously better (or worse) that ethics requires a premature end to the research, so that all participants can be shifted to the better treatment.²⁴

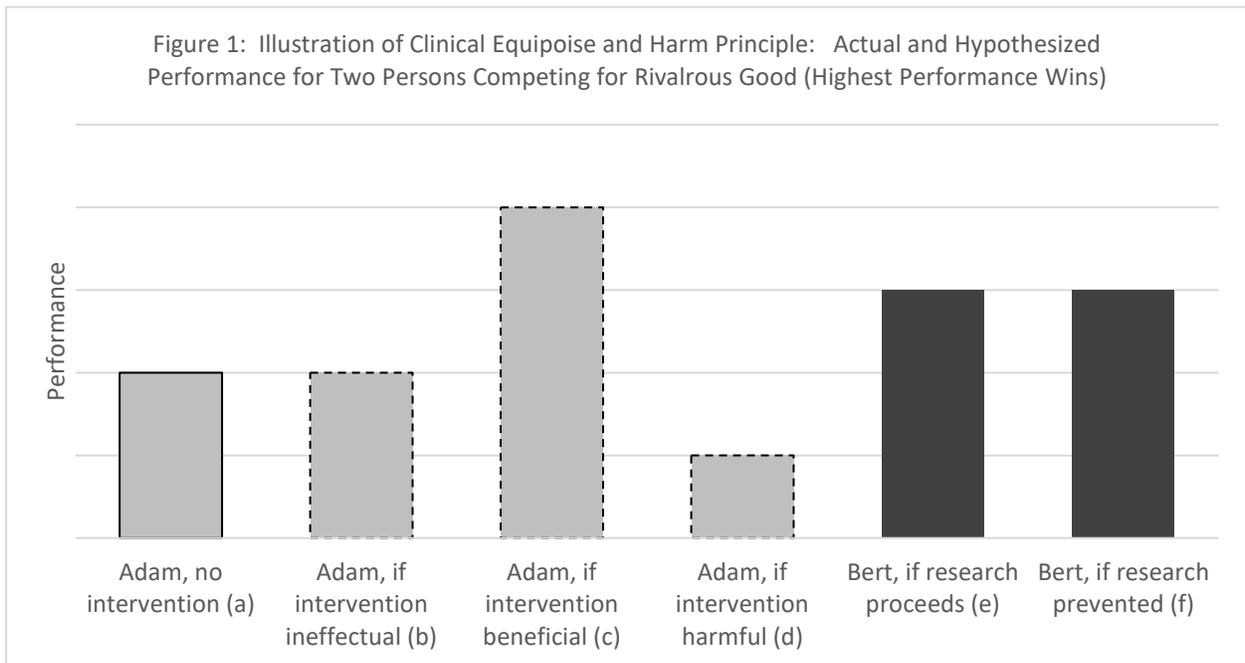
Figure 1 illustrates this point. From the *ex ante* perspective of an ethics regulator, we do not know whether compared to no intervention (a), Adam will do the same (b), better (c), or worse

(d) with the intervention. And for that same reason we do not know whether the intervention will make him perform better or worse than Bert.

Contrary to equipoise, human subjects often suffer from a “therapeutic misconception” that the purpose of clinical research is to provide them with a treatment benefit, and they overestimate the likelihood of the intervention doing so.²⁵ Ethics regulators (e.g., IRBs) should not fall into the same fallacy, and thereby push to include others in a study (or veto a study from proceeding for fear of relative disadvantage to others), unless they actually know that an intervention will in fact be successful. To the contrary, it is possible that the drug treatment or educational program or pamphlets will be harmful to Adam and the other participants (at the very least wasting their time or money, if not outright hurting their performance). Or the interventions might not have discernible effects at all, which also negates the prior assumption of efficacy.

Greiner and Matthews detail several instances in which randomized field trials were prevented, interfered with, or prematurely cancelled due to unfounded beliefs that an intervention would be successful, obviating the need for a rigorous study with a control group.²⁶ This is a simple violation of clinical equipoise. Here although there is a chance of benefit, the principle of clinical equipoise invokes the epistemic value of scientific research, and the need for a control group. In short: *We will override your mere chance of benefit and exclude you from the intervention as a means to generate scientific knowledge about which treatment is ultimately effective.*

The case here is slightly more subtle, as the valence is flipped. Rather than claiming that he will not get a presumed benefit from participation in the study, Bert instead claims that his interests may be set back, if Adam participates and the intervention turns out to be successful. Bert would rather get the ventilator or the A-grade or the debt value, than for Adam to get it. Thus, even if we are not sure that the intervention will be effective for Adam, Bert views that as a “risk” to himself, a risk to which Bert prefers that he not be exposed. Because ethics is asymmetric – requiring consideration of risks to people, even if we do not have an affirmative obligation to benefit them – we arguably need additional analysis to resolve this question.



The Harm Principle

Let us now address this concern that normal principles of equipoise do not apply to special cases where the research project may actually impose a relative disadvantage on those not treated. It is not just that Bert does not receive the treatment he wants, but when other people

receive it they make him worse off (reducing his chances of getting the ventilator or the grade of A or the full claimed value of the debt). The answer is that Bert is not actually harmed. Without alleging harm, Bert has no basis to object to Adam or the scientists pursuing their own agendas.

It is true that Adam's participation sets back Bert's interests. However, there is a key distinction between a harm and a mere setback to interests. Building on a concept developed by John Stuart Mill, philosopher Joel Feinberg has clarified this relationship.^{27, 28} A "harm" is a "*wrongful* setback to interests" (emphasis added). Generally, harms (not mere setbacks) are the proper focus of regulation that would restrict liberties.

After all, setbacks to interest are ubiquitous. If I prefer that Charlie win the election, but you vote for Davis, then you set back my interests. If I am hoping to get a coveted job, but you submit your stellar resume, then you set back my interests. If am hoping to get an A in a curved school class, but you spend extra time studying, you set back my interests. If I need a ventilator, but you get an investigational drug that gives you a better prognosis, you set back my interests. If I am wanting to collect \$10,000 for the debt, but you go to court and get a judgment allowing me to recover only \$1,000, then you set back my interests.

The rule is reciprocal. Just as Adam may participate in the research intervention, Bert may pursue other means, such as an off-label drug or a special study regimen of his own. Or he can hire an attorney or go to court himself to collect his debt. Adam has no right to object to those efforts either, because they do not harm him even if they do setback his interests.

Importantly, none of these examples constitute a harm because none of them is wrongful. Adult persons have the right to vote, apply for jobs, etc. All this presumes, of course, that the infectious disease treatment or educational program or legal procedure must be otherwise

permissible. If the treatment is illegal or if the educational program is prohibited by the school as a form of cheating, or the legal filing is frivolous, then of course it would be impermissible to provide those interventions. That’s true, regardless of whether they are provided in the context of research.

Similarly, it bears emphasis that the hypothesized competitions are “fair,” but it is in the minimal sense of facial fairness, relevant to the institutional context. Courts presume that a legal proceeding is minimally fair, even if one party has retained a better attorney than the other, or makes a competent but ill-advised decision to represent herself. Running a clinical trial that recruits among patients who present to a hospital with a given illness is minimally fair, even if it is true that other persons lack economic wherewithal to present themselves to the hospital in the first place. We wrestle with broader notions of fairness, social justice, and equity below. For now, it is enough to say that Bert being a loser in a facially fair competition does not constitute a harm to him.

Because there are no real harms at issue here, the present inquiry is thus distinct from other research settings where third-parties (aka “bystanders”) may actually be harmed by research. “For example, subjects involved in a vaccine study might infect [others] with some ailment, and children born to research participants exposed to mutagens might have birth defects. Not treating the syphilis of the men observed in the Tuskegee study put their sexual partners at risk of being infected.”²⁹ The latter concern has arisen again, in the context of HIV-remission studies³⁰ and in proposed studies of Zika virus through intentional infection of volunteers.³¹ These are real harms to non-participants, which may well make the research unethical.

In contrast, for the types of research considered here, Figure 1 also illustrates this point. Bert’s performance is unchanged, regardless of whether the research proceeds (e) or is prevented

(f). It's not as if Adam's intervention involves poisoning Bert, so that he suffers a comorbidity or fails to remember the material taught in class (a decrement to his welfare, not shown on Figure 1).

In the focal cases here, however, since there is no harm to Bert, ultimately, Bert has no more right to demand that the ethics regulator cancel the research study than he does to *request* that Adam not study for the exam or get healthcare treatments or forgo his legal rights. If asked, Adam would be free to decline. Similarly, if Bert asked the scientific researchers to sacrifice their careers and scientific research agendas to help him win the ventilator or the grade, we would normally expect them to exercise their academic freedom to decline.³² With regard to strangers, we typically only have the duty not to harm them; we have no obligation to avoid fair competitions with them or to choose one side in a fair competition with others.

Having his entreaties rejected by Adam and the researchers, suppose that Bert exerts some power over Adam to extract such a concession. Suppose Bert locked Adam in a room in the library to ensure that he could not participate in the prep course, or threatened his doctor so he would not provide the infectious disease treatment. Note the principled asymmetry here – in these cases, it is clear that Bert is harming Adam, not merely setting back his interests, but doing so wrongfully, since Adam has a right to compete fairly. And that is true regardless of whether Adam was participating in the context of research or otherwise. Even if neither Bert nor Adam has a right to *win* the ventilator or the A-grade, they both have the right to compete for it, using whatever permissible regimen they may choose.

In this regard the ethics regulator is in no different position. In these real-world competitions for rival goods, the ethics regulator has no authority to pick the winners and the losers, nor stop scientific research about the efficacy of methods for improving the chances of winning. If the

ethics regulator exerts its position to ensure that Adam does not get the hypothesized benefit he and the scientists are freely pursuing, it harms Adam and the scientists.

And this is the height of irony, since the IRB's reason for existence is the protection of prospective human subjects, like Adam.³³ As the Belmont Report provides, “To show lack of respect for an autonomous agent is to repudiate that person's considered judgments [or] to deny an individual the freedom to act on those considered judgments,” and of course research participants and scientists are autonomous agents.³⁴ By harming Adam to protect Bert from a mere setback to his interests, the IRB would itself perpetrate an injustice and pervert its own mission.

A particular provision in the Common Rule reflects this insight. “The IRB should not consider possible long-range effects of applying knowledge gained in the research ... as among those research risks that fall within the purview of its responsibility”.³⁵ Accordingly, Hausman explains that the IRB must focus on the risks of the research process itself, not “outcome-related risks.”³⁶ The fact that Adam may go on to get a ventilator or win an A-grade or discharge a debt is precisely this sort of downstream consequence that is beyond the purview of ethical gatekeeping, even if the regulator had a preference as to that outcome.

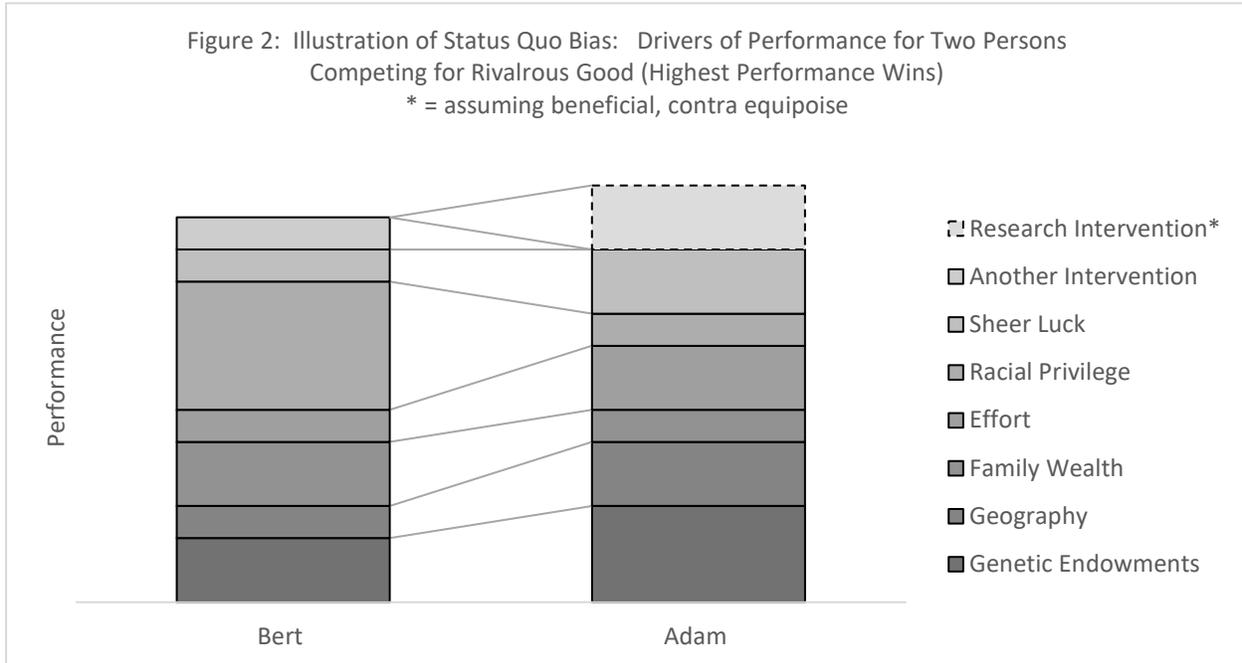
Status Quo Bias and Background Advantages

This conclusion may seem premature. Even if it does not harm Bert, one must concede that in the marginal case, if the intervention is successful, then the research project will cause Bert to lose the position he might have otherwise won. This sort of disruption may seem somehow impermissible as a “harm to the ‘social fabric’”³⁷ or “violation of wider social values”,³⁸ and worthy of the ethics regulator's attention. After all, Bert's welfare will be impacted if the study

proceeds; in the infectious disease case he may well die for lack of a ventilator he would have otherwise received. That redistribution caused by the research project seems unfair to Bert. The Belmont Report does include concern for “justice” and “fairness”, which can be capacious concepts in the hands of an ambitious ethics regulator.³⁹

However, this issue of justice or fairness requires a theory about the distribution of the sorts of rival goods at issue here. Generally, the ethics regulator will lack a reasonable basis to prefer the default distribution of outcomes in a world *without* the research project compared to the distribution of outcomes *with* the research project (or any other distribution of outcomes). Without a justice/fairness-based reason to prefer the *status quo*, disrupting the status quo cannot be unjust or unfair.

If an IRB or other ethics regulator were to nonetheless insist that the research not proceed for fear of disrupting the default distribution of outcomes, it would seem to be succumbing to a status quo bias,⁴⁰ a phenomenon that has been widely confirmed empirically.⁴¹ In this body of research, it is shown that humans tend to unreflectively prefer extant policies and extant distributions, even when progress and efficiency suggest better approaches to achieve agreed goals.



As figure 2 illustrates, in any situation, including the exemplar cases, the default distribution is subject to all sorts of contingencies, which are either ethically irrelevant or are themselves unjust. In the world without the research project's intervention, perhaps Bert is a better student because his parents were wealthy and paid for a private prep course. This background advantage is at best ethically irrelevant, but worse it may be an affirmative form of injustice, if for example Adam's family, as the victim of systemic racism, could not afford the private prep course. Similarly, perhaps Bert is a better ventilator candidate because of lucky genetics, or because he grew up in a neighborhood with fewer environmental toxins, compared to Adam's neighborhood near a polluting factory. In reality, we know that education and healthcare both suffer from severe racial and class disparities, with whites and the wealthy enjoying both better access and better outcomes on average.⁴²

Some proposed research interventions may affirmatively target disadvantaged populations. For example, suppose that the treatment in the infectious disease case is a precision medicine for

a gene variant carried by African Americans or suppose that it treats one of the diseases of poverty. Either way, it can help this disadvantaged population claim their fair share of ventilators, which are otherwise disproportionately consumed by the privileged. Or suppose the educational intervention is designed to level the playing field for disadvantaged students, who are shown to have less background knowledge, less confidence, and narrower support networks in the grade-curved environment. In these cases, the research intervention arguably “de-privileges” Bert rather than disadvantaging him.

Even if Bert’s advantaged position is not itself an injustice, it is at the very best unjustified and contingent. Even if he would have secured the A or the ventilator or the debt out of sheer luck or hard effort, it does not give him or the ethics regulator a right to prevent Adam from competing, and that’s true regardless of the research context. In short, the research intervention may mitigate unjust disparities or neutralize/override irrelevant advantages, but neither provides a reason to proscribe it.

These considerations illustrate the difficulty of an ethics regulator looking through the ethical pinhole of a particular research study, and considering whether to veto it as an attempt to resolve a nebulous “fairness” concern. Even assuming that the particular research intervention is beneficial (*contra* clinical equipoise), the concern for justice, fairness, or equality cannot turn on the distribution of any such particular benefit in isolation (just deleting one block from Figure 2). Instead, the ethics of a particular intervention would have to be assessed in terms of the background welfare of each person (in terms of health, wealth, and other determinants of welfare), information not typically available to an IRB nor within their capacity to assess. How could the IRB know if the intervention is likely to give Adam too little of an advantage or too much of an advantage, to rectify whatever inequity may be at issue?

As a legal proposition, it seems doubtful that American IRBs have the mandate to undertake such a breathtakingly ambitious task of reallocating social resources, which raises much broader policy questions.⁴³ But to be sure, the IRB, or any subsequent ethics regulator, is not in a better position to optimize the allocation of social resources than everyone else in the society acting on their own legally-constructed incentives and information.⁴⁴

Equity and the Levelling Down Problem

Let us look more closely at the concern for justice or fairness. It may simply seem wrong that the research project allows one person to perform better than the other, and thus an ethics regulator may see fit to veto the project out of a sheer sense of equality.

Here again, the principle of clinical equipoise does not allow us to assume the effectiveness of the intervention, but setting that aside, it is important to note that the hypothesized benefit of the intervention is typically not *merely* a relative advantage in a zero-sum game. If it works, the educational program causes Adam to learn more – that is how he secures the A grade; the average (or total) learning in the class is higher if Adam participates in the educational program. The infectious disease therapy improves Adam’s prognosis, so that he is objectively a better candidate for the ventilator, meaning that whomever receives the ventilator (in this case, Adam) is less likely to die. The story is somewhat less obvious for the medical debt collection example, but one can similarly say that access to justice, and achieving whatever outcomes the law specifies, is a *prima facie* good, one that the pamphlet intervention expands.⁴⁵ In these cases, a veto of the research study would undermine overall learning and health and procedural justice – key components of social welfare.

In political philosophy and bioethics, this is known as a “levelling down” problem – one reduces an inequality by reducing the welfare of the advantaged person.⁴⁶ It is one thing to tax the wealthy to provide social infrastructure or programs for poorer individuals who can extract greater value from the funds; quite another to simply smite the wealthy (destroying their wealth), simply reducing their welfare to that of the median person.

The problem with any levelling-down approach is that it harms some, without benefiting others, and thereby actually reduces aggregate social welfare, making the world worse off overall. Many philosophers, including most famously John Rawls, have explained why society does and should tolerate some inequalities, which plausibly make the world better off.⁴⁷ (For example, we tolerate inventors getting wealthy from patent royalties as a way to incentivize the production of new technologies for society generally.) Accordingly, hardly anyone defends rote equality as the singular goal of social policy, above all other goals such as aggregate welfare.

Suppose, however, that the ethics regulator is more clever. Instead of merely vetoing the research study, it insists on a revision of the protocol to include Bert (on threat of vetoing it). Here, it tries to “level up” (still assuming the intervention is beneficial, *contra equivoque*). This solution is likely to harm aggregate social welfare also, but it does so in much more complicated ways that may be harder for the ethics regulator to observe.

First, in some variations of the cases, Bert was allocated to a control group. As noted, in order to support causal inference, scientific researchers need to be able to observe cases both with and without the intervention, and ideally randomize patients between those conditions. A policy that prohibited control groups would undermine the production of generalizable knowledge.

Second, in some variations of the cases, Bert was invited to participate but declined to do so. Or, the intervention simply isn't applicable to him (e.g., because he does not have the comorbidity that it treats, or is not a medical debtor). In these versions, Bert's only request is to demand levelling-down.

Third and more generally, there are innumerable other reasons why the research study may have been designed in a way that excludes Bert. First, is sheer resource scarcity. There may be only so many spots in the educational program class, or so many doses of the new biologic drug for ventilator candidates. Rarely is it just Bert, by the way – behind him are Caleb, David, Edward, and others also hoping to get some of the presumed-effective treatment.

A given sample size balances the cost of recruiting and treating each subject, with the risk that each subject faces if the treatment turns out to be harmful (or merely wasteful), versus the statistical power necessary to produce generalizable knowledge.⁴⁸ Aside from risk to subjects, adding additional subjects beyond that point has diminishing returns from a statistical point of view, suggesting that resources might be better allocated elsewhere. Rather than trying to expand trials with unknown risks and benefit profiles, normally, an IRB should be focused on ensuring that such trials are as small as possible consistent with the production of knowledge, to reduce risks to participants.⁴⁹ The same minimization rule applies to studies using non-human animals.⁵⁰

Ultimately then, even if the “inequity” of Adam receiving a relative advantage were a valid basis for concern, the ethics regulator has no mechanism for systematically resolving such concerns, without undermining social welfare. Here any such remedy is worse than the purported disease.

Bias Against Prospective Interventional Research

It is important to note the double standard that would arise from an ethics regulator proscribing a prospective interventional research study like those described here, while nonetheless allowing retrospective study of the same sorts of programmatic interventions. Such a double-standard cannot be justified by ethical principles.

Outside the research context, health, justice, and educational interventions are themselves not objectionable. Indeed, they are ubiquitous. In the hospital context, a physician may try innumerable treatments for a patient, any of which may improve her health and prognosis for a ventilator. In the competitive school environment, there are innumerable extant programs, products, and services designed to help students learn. These interventions range from proprietary or nonprofit prep programs and private tutors, to supplemental books that can be purchased by individuals or borrowed from the library, and faculty office hours, review sessions, tutors, mentors, and study guides. And likewise for justice, there are already books and professionals and service providers able to help people with their legal problems.

Scholars have noted a “research exceptionalism”,⁵¹ where ethical regulators hold research activities to a different standard than non-research activities that raise exactly the same risks. Here, however, the exceptionalism is more peculiar, since it is clear that nobody could object to a retrospective study of any of the health, educational, or justice interventions. For example, suppose a social scientist (Sue) sought to determine what proportion of the students in the competitive school environment completed a prep program before attending, and whether those students in fact performed better, as measured by their first-semester grades, in a school that grades on the curve. Sue selects a particular school with a prep program, and proposes to survey

students to find out whether they participated and their grades (or alternatively proposes to achieve the same through review of records). Assuming other routine human subjects protections (e.g., privacy and/or consent, as may be applicable) are met, no ethics regulator would object to this study merely because the prep program itself may have successfully provided an advantage to its participants. Indeed that is the research question Sue seeks to answer.

Strikingly then, it is clear that neither the interventions themselves nor retrospective study of the interventions is objectionable. If one nonetheless objects to a prospective study of the very same sort of intervention, it would seem to be a sheer bias against prospective interventional research.⁵²

This bias (if it exists) is quite unfortunate, because it flips rational management, the ethics of social welfare, and the rules of human subjects protection on their head. It can be terribly wasteful, and in some cases harmful, to launch interventions without studying them prospectively. This is why the Food and Drug Administration *requires* prospective studies of new drugs and devices – it’s better to know whether they are minimally safe and effective before disseminating them broadly, and similarly why we are trying to incorporate evidence into routine practice.⁵³ In contrast, if an ethics regulator rejects the prospective study, it might increase the risk of waste and harm, without necessarily securing any benefits.

Oddly, in this domain, it is clear that even if an ethics regulator were to veto the prospective study, the researchers can proceed to launch the very same program as non-research. Similarly, physicians can often try off-label or surgical interventions, outside the context of a formal research study. They can even do so with the intention of studying their effectiveness, as a form of “quality improvement”.⁵⁴ And the Federal Common Rule allows such work because, “if we

want our health care system to engage in data-guided improvement activities that prevent deaths, reduce pain and suffering, and save money, we shouldn't make it so difficult to do so".⁵⁵

Here the ethics regulator's only point is to insist that the very same information cannot be used to produce generalizable knowledge. The ethics regulator thus can be the force for societal ignorance, in these high stakes domains, where knowledge of safety and efficacy is key to social welfare.

Special Institutional Relationships

Recall that the analysis of harm turned on the notion that Adam and the scientific researchers do not owe Bert, a stranger, any duty to consider his preferences or try to prevent permissible setbacks to his interests. In law, this insight that individuals do not have to affirmatively help others is known as the “nonfeasance” rule, but it is subject to certain exceptions.⁵⁶ Suppose that Bert and Adam have a special relationship with an institution that employs the research scientists, or perhaps a relationship with a particular physician or a teacher. Or maybe the court in which Bert's collections lawsuit is pending is considering whether to itself send to Adam the pamphlet that may improve his chances of showing up and defending his case. Would such a relationship with the parties create a special duty for the institution to consider Bert's interests? Would it violate the nature of the relationship if Adam received an investigational treatment that benefited him, in his competition with Bert? These are potentially distinct questions from the foregoing concerns.

The easiest cases are where the institution (whether hospital or school) offers the intervention to all of the relevant members (including Adam and Bert), but only some of those members (Adam) accepted the offer. Although self-selection undermines the rigor of scientific research, if

that is the study's mechanism, then it is hard for one client (Bert) to object simply because others (Adam) took advantage of an opportunity that was equally open to all.⁵⁷ A contrary suggestion would be utterly unworkable, given the ubiquity of different clients exerting different levels of interest and effort to take advantage of various programmatic offerings. For example in the school setting, some students attend more office hours, go to more review sessions, or check out more books in the library. Nobody would suppose that this differential uptake in a realm of equal opportunity is ethically problematic.

This is not to say that the institution or professional must always offer all its clients the same services. Academic hospitals routinely recruit patients into a study until it is full, and then stop recruiting (excluding others). If it is a randomized study, they then allocate some to treatment and control. This practice suggests that the mere hospital-patient relationship does not implicate a duty that all similarly situated patients receive exactly the same care. Instead, they each receive care that that they have contracted to receive, or which would be reasonable under the circumstances. (And this observation recurs on the foregoing point that the physicians are in clinical equipoise, and the non-recipients are not harmed by their exclusion.)

Institutions have all sorts of reasons why some of its clients may have a different experience than other clients. A very common one is sheer scarcity.⁵⁸ In a competitive school, for example, some courses may be very popular, perhaps because they give students an advantage in a future course or on the job market. But the school may cap the size of the class at a given point, and then allocate the seats on various bases, including either by first-come-first-served (not unlike recruitment into a research study) or lottery (not unlike randomization in an experiment). An institution may even use discretion, for example, requiring an application for enrollment in a particular class, or targeting a particular population of students (e.g., Hispanic women) where

they hypothesize that the population will receive the greatest benefit or to rectify a prior injustice to that particular population. Similar targeting is appropriate in the research setting.

Finally, of course, institutions can employ fees for services provided in the course of research, just as most of them charge fees for their primary services. For example, a competitive school charges tuition, and may charge a supplemental fee for the prep course. An ethics regulator may be concerned that the fee is a barrier for others who will then not participate, but for all the same reasons explained above (e.g., lack of harm to non-recipients and the levelling down problem), this is a question for program design and social policy, not a basis for the ethics regulator to prohibit the research itself.⁵⁹ Scientific study of either the paid education program itself, or the paid prep course, are both valid, even if the costs may exclude some potential participants. The research does not somehow create a risk or a harm beyond that of merely existing in a world of scarcity. Nonetheless, there are broader distributional questions that should be addressed by social policy (e.g., Congress creating an insurance coverage mandate to cover access to investigational medicines⁶⁰). But human subjects research need not await for those broader issues of social policy to be resolved.

These considerations suggest that mere invocation of a relationship or institutional setting does not change the primary analysis of this article. Non-recipients have no valid claim to stop research or demand their inclusion.

To the extent that these special relationships do create special duties, it is not vis-à-vis the research relationship. As Smalley and colleagues explain, the “responsible party for protecting the rights and welfare of indirect participants [non-human subjects affected by the research] is not an IRB, because IRBs do not generally control routine operations in the relevant institutional environments.” Instead, “facility administrators should be systematically involved in the design,

planning, and conduct” of programs, regardless of whether they are in the research context.⁶¹

This point recurs on the foregoing section, which shows why the ethics regulator should not impose a bias against prospective interventional research in a context where the program administrators have discretion to undertake the intervention regardless.

We can apply these insights to the medical debt justice research. If the investigators are working independently to contact medical debtors facing collection (perhaps using public records and private grant funding), then there is no relevant institutional relationship that requires consideration. But suppose instead the local court is asked to facilitate the intervention (e.g., mailing the pamphlets to the debtors), and it must determine the appropriateness of doing so. Here the difficult questions are about the programmatic intervention itself, not the proposed research to evaluate the effects thereof. The court should consider whether medical creditors will be harmed by the intervention, or whether it will merely redistribute outcomes that medical creditors enjoy in the status quo (default judgments against ignorant debtors), but for which the medical creditors have no right. The court should also consider whether participating somehow erodes its own role as a fair tribunal for both parties. If there is no harm or role erosion, then the intervention is appropriate and research on the effects of this very same intervention is also not particularly problematic.

Conclusion

Ultimately, in a world of rivalry for scarce goods, the concern for equity between recipients and non-recipients raises a range of provocative questions. But the answers to these questions are as clear as any ethical analysis can be. The possibility that an intervention may produce a relative advantage for recipients over non-recipients is not a basis for proscribing the research.

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