CLUSTER RANDOMIZATION AND POLITICAL PHILOSOPHY

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ABSTRACT
In this paper, I will argue that, while the ethical issues raised by cluster randomization can be challenging, they are not new. My thesis divides neatly into two parts. In the first, easier part I argue that many of the ethical challenges posed by cluster randomized human subjects research are clearly present in other types of human subjects research, and so are not novel. In the second, more difficult part I discuss the thorniest ethical challenge for cluster randomized research – cases where consent is genuinely impractical to obtain. I argue that once again these cases require no new analytic insight; instead, we should look to political philosophy for guidance. In other words, the most serious ethical problem that arises in cluster randomized research also arises in political philosophy.

INTRODUCTION

Suppose we want to determine whether a new hand-washing awareness program amongst intensive care unit ('ICU') staff will lead to fewer ICU infections than the status quo. Everyone in an entire ICU has to participate in the program, or none, because infections are easily communicable. In other words, to have only a portion of an ICU participating in the program might severely reduce or even eliminate its effectiveness, because some infections might creep over from the non-participating side. Therefore, the easiest way to measure whether the program is effective will assign the new program or status quo to entire ICUs rather than parts of a single ICU. Add to this the idea that random assignment makes for a better test than non-random, and we have *cluster-randomization*. A cluster-randomized study is one in which the unit of randomization is not the individual research subject, but rather a group of such subjects. In the case of our initial example, it is every patient in an entire ICU.

Cluster-randomization raises several thorny issues, many of a statistical nature.[1] However, it can also raise important ethical issues related to consent. Although bioethicists have recently begun to take note of the problem of consent in cluster-randomized trials, not enough attention has been devoted to the topic to be able to say that we have made genuine progress. Indeed, most papers that mention this topic do so in a perfunctory way, saying we need more and better analysis.[2] It would be nice if we could fill in this gap, but that is not my goal in this paper. Here, I will attempt to accomplish a methodologically prior goal. My main thesis is that, while the ethical issues raised by cluster randomization can be challenging, they are not new. My thesis divides neatly into two parts. In the first, easier part I argue that cluster randomized research need not raise any ethical issues at all, and that

[1] See, for example, N. Klar & A. Donner. Current and Future Challenges in the Design and Analysis of Cluster Randomization Trials. *Stat Med* 2001; 20(24): 3729–3740 and M. Campbell & J. Grimshaw. Cluster Randomised Trials: Time for Improvement. *Br Med J* 1998; 317(7167): 1171–1172.

[2] See, for example, M. Taljaard et al. Ethical and Policy Issues in Cluster Randomized Trials: Rationale and Design of a Mixed Methods Research Study. *Trials* 2009; 10: 61; D. Osrin et al. Ethical Challenges in Cluster Randomized Controlled Trials: Experiences from Public Health Interventions in Africa and Asia. *Bull World Health Organ* 2009; 87: 772–779; S. Mazor et al. Cluster Randomized Trials: Opportunities and Barriers Identified by Leaders of Eight Health Plans. *Med Care* 2007; 45(10): S29–S37; A. Donner & N. Klar. Pitfalls of and Controversies in Cluster Randomized Trials. *Public Health Matters* 2004; 94(3): 416–422; and J.L. Hutton. Are Distinctive Ethical Principles Required for Cluster Randomized Controlled Trials? *Stat Med* 2001; 20: 473–488. One of the very few pieces that gives a sustained (yet brief) analysis is also the first paper to note the need for ethical analysis in this domain: S.J.L. Edwards et al. Ethical Issues in the Design and Conduct of Cluster Randomised Trials. *Br Med J* 1999; 318: 1407–1409.

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many of the ethical challenges it can pose are clearly present in other types of human subjects research, and so are not novel. In the second, more difficult part I discuss the thorniest ethical challenge for cluster randomized research – cases where consent is genuinely impractical to obtain. I argue that once again these cases require no new analytic insight; instead, we should look to political philosophy for guidance. In other words, the most serious ethical problem that arises in cluster randomized research also arises in political philosophy. Thus, I intend not to supply the right answers to the ethical questions surrounding cluster randomized research so much as insist that the debate can be illuminated by an old, familiar, and analogous debate in political philosophy.

1 CLUSTER RANDOMIZED COMPARED TO REGULAR RESEARCH

Recall my initial example of a cluster-randomized study, wherein two hand-washing programs are being compared in different ICUs. How does one guarantee that all the ICU patients will consent to participate? The problem is not that it is conceptually impossible to obtain consent in cluster-randomized studies, only that it might be so improbable or costly as to be close enough to impossible for all practical purposes. As another example, consider a hypothetical cluster-randomized study in which Cincinnati gets sprayed with an insecticide and Cleveland with placebo. Now, it is theoretically possible that everyone in those cities consents to being in this study, in which case everything is fine. The problem, though, is that it is overwhelmingly likely that at least some residents of those cities will not want to participate, and it is prohibitively costly to relocate and/or compensate the dissenters.

Still, some cases of cluster-randomized research pose no ethical problem at all. Suppose I want to test the effectiveness of two different 'please be quiet' movie trailers. It might be that the easiest way – and, if my budget is limited, maybe also the only feasible way – to do this research would be to randomize each trailer to play in a different theater, so that the unit of randomization is the theater rather than individual viewers. Still, obtaining individual consent for this study may pose no problem at all: I can still ask individual movie-goers if they would like to participate in my study. If yes, they can attend either of my controlled showings, and if no then they cannot. (Suppose it is opening weekend for a very popular movie at a very large theater, so that several screens are showing it nearly simultaneously.)

Note that this is a genuine instance of cluster-randomization, not one of individual-randomization masquerading as such. That is because the study did not randomly assigned various individuals to attend one or the other showing. Rather, it allows patrons to choose

whichever showing they please, and then the researcher assigns at-random – the particular trailer to different screenings. The patrons (subjects) choose which of the two study-theaters they want to sit in. Then, after everyone is seated, the researcher randomly assign trailers to each theater. An example of an individual randomization would be: each patron shows up and consents, after which the researcher flips a coin and assign her to one or another theater based on the outcome. No, in the cluster-randomized study, the thing being randomized is the trailer, and the unit of randomization is the showing.

The first point I want to emphasize, then, is that there can be cases of cluster randomization where obtaining consent is not a problem. Contrary to what is sometimes suggested, there is no necessary connection between cluster randomization and thorny ethical issues involving obtaining consent.[3]

My second point is related: sometimes obtaining consent for a cluster-randomized study is no *more* a problem than it is for individually randomized studies, in the sense that problems which arise for cluster randomized research also arise for other types of research. For example, there may be an ethical problem with *Zelen consent*, where an experimental arm is being compared to status quo but only those in the experimental arm are asked for consent (after they are enrolled in the experiment).[4] Though Zelen consent is sometimes used for individual randomization, it is perhaps more likely to be used for cluster-randomized experiments. Still, even if so that is no special worry for the legitimacy of cluster-randomization in particular. In that case what we need to do is to focus our ethical attention on Zelen consent, not on cluster randomization.

Here is another example of a cluster-randomized trial where the ethical issue of consent is one we already face in other kinds of research. Suppose Nevada and Utah use slightly different fluoridation programs for their tap water, and California wants to test which is better. They propose to use Nevada's program in northern California and Utah's in southern California and then measure and compare various outcomes of effectiveness. It is practically impossible to obtain consent from every resident in the state, so is California's proposed study ethical? Well, assuming that it was ethical for Utah and Nevada to implement their different fluoridation programs without the benefit of research, then maybe it is likewise ethical for the state of California to assign one such program to the north, the other to the south, and then collect data on the differences. (Assume no relevant differences between any of these places.) In other words, if it is permissible to

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[3] See, e.g. Hutton *op. cit.* note 2.
[4] See, e.g. J.S. Hawkins. The Ethics of Zelen Consent. *J Thromb Haemos* 2004; 2: 882–883 and R. Schellings et al. Indications and Requirements for the Use of Prerandomization' *J Clin Epidemiol* 2009; 62: 393–399.

do something outside the context of research – such as implement either of the fluoridation programs – then it is permissible to do those things within the context of research, i.e. to conduct a study where we do those things and then take data on the effects.

Objection: in the last case, the residents of California still have a legitimate complaint. Unlike people in Utah and Nevada, California residents had their water supply changed *and were forced to participate in research* (without their consent).

Reply: First, one might think that such dissent is unreasonable and therefore need not be respected, especially if the data would be used only in anonymous form. Second, one can evade this objection by keeping track of dissenters and then collecting and publishing data only on consenters. But third, and most importantly, even if the mere fact that you are participating in research without consent is objectionable, again, this problem is not unique to cluster randomization. It arises in other areas too, for example in cases of randomized controlled trials between two agents which are thought to be equally efficacious.[5] Many of the moral difficulties posed by cluster randomized studies, then, are in fact present in other areas.

2 CLUSTER RANDOMIZED RESEARCH COMPARED TO POLITICAL PHILOSOPHY

I have suggested both that sometimes it is easy to obtain consent to a cluster-randomized study and that some of the ethical challenges posed by cluster-randomized research are in fact familiar to research ethicists, but I have purposely neglected the most difficult sort of case, where (a) the intervention involved would not be permissible outside the context of research and (b) it is genuinely impractical to obtain consent from all participants. Call cases where (a) and (b) hold *hard cases* of cluster-randomized research. Think again of the hypothetical example of spraying Cincinnati with pesticide, Cleveland with placebo. A less fanciful example of hard case cluster randomized research might be cluster-randomizing an experimental vaccine versus an only moderately efficacious standard, where the disease is sufficiently virulent that the most effective trial must randomize between different population clusters. It is now time to address this hard problem. I will argue that even the hard problem is not novel – its general contours appear in the debate over distributive justice in political philosophy.

A natural way to rephrase our hard problem is to ask under what conditions it might be ethical to waive consent requirements for research. Thus, for example, we might ask under what conditions we think it is ethical to test the experimental vaccine even knowing full well that we cannot get unanimous consent from everyone in the relevant clusters. And a natural place to look for an answer to this problem is the Common Rule, which, in addressing the issue of when one may permissibly waive consent requirements for research, cites such factors as practicability and minimal risk.[6] We might then to go about refining what is meant by each of the criteria in those regulations, such as what is meant by 'practicability' and 'minimal risk'.

However, this strategy is sub-optimal. Or perhaps more cautiously, it may be useful in the short run, because it will permit quick decisions about cases where we need answers imminently. But in the long run, there is a much better strategy, one that is more likely to approach the truth of the matter. To get a sense of what this strategy might be, let us step back and reflect on the general contour of the problem. The problem starts with our need for research results, which would benefit society. In order to get those results, we need to subject a group of people to an intervention which carries some risk of harm. Although we would like to be able to assign the intervention only to people who consent, particular details of the study make that impractical. And although we would like to ensure that the intervention is something we are permitted to implement outside the context of research, that too is for whatever reason impossible. So we are left wondering under what conditions we can proceed anyway, thereby potentially harming a sub-group in order to benefit the super-group, without the (unanimous) consent of everyone in the sub-group.

This last question – when we can potentially harm a sub-group in order to benefit the super-group, without the consent of everyone in the sub-group – is quite difficult, but I hope it sounds familiar. It is, in essence, the exact question with which political philosophers have grappled in debates over principles of distributive justice. For example, we need principles that tell us when and to what extent it is permissible to take a portion of a worker's salary, thereby harming that worker, in order to fund public schools. This is a clear example of the more general problem of when it is appropriate to harm some citizens (the workers, via taxation) in order to benefit society (with a public school system).

Now, one might think that taxation is not a harm, especially if the tax is being used to fund public goods

[5] See, e.g. R.D. Truog et al. Is Informed Consent Always Necessary for Randomized Controlled Trials? *N Engl J Med* 1999; 340: 804–807; J.L. Hutton et al. Ethical Issues in Implementation Research: a Discussion of the Problems in Achieving Informed Consent. *Implement Sci* 2008; 3: 52; and E. Chwang. A Puzzle about Consent in Research and in Practice. *J Appl Philos* 2010; 27(3): 258–272.

[6] Code of Federal Regulations. 2009. *Title 45, Public Welfare, Department of Health and Human Services, National Institutes of Health, Office for Protection from Research Risks, Part 46 Protection of Human Subjects 116(d).* Bethesda, MD. Available at: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.116 [Accessed 26 Sep 2010].

such as schools or roads. However, this is incorrect. Forcibly reducing the amount of money I have harms me, even if that harm is compensated with goods or services I may receive in trade. And the distinction between monetary and other kinds of harms (e.g., to body or property) is morally irrelevant. One way to see that it is morally irrelevant is to note that people are willing to trade off one type of harm against the other. For example, we pay for helmets (give up money to protect our bodies), and we also work in risky professions (incur risk of harm to our bodies in order to make money). And in any case, there are clear non-monetary examples of the same idea, that we need principles to tell us when states are permitted to perpetrate a harm on some of its citizens in order to benefit society. Eminent domain is such an example, where the harm to me occurs via appropriation of my property. The state may even, in some circumstances, risk harm to my body for the good of society, as when it issues a mandatory draft or decides where to place a toxic waste dump.

Now, cluster-randomized research shares many of its morally significant properties with political philosophy.[7] In both cases, we have a group of people being asked to sacrifice for the greater good. The sacrificing group may be harmed from the sacrifice, as in phase 1 drug toxicity research, but the larger population (society in general or the population of patients the research targets) benefits (one benefits even from knowledge that an experimental drug is ineffective). And presumably there is some natural metric by which the expected benefit to the larger population as a whole is greater than the expected cost to the sacrificing sub-group. Still, the ethical issues are distinct in an important way. Political philosophy concerns itself with the welfare of everyone in the state, whereas cluster-randomized research need not be so all-encompassing. For example, a medical researcher may care only about the welfare of people with type I diabetes. That means that the hard problem in cluster-randomized research is at best analogous to the issue of distributive justice in political philosophy, not really a species of it.

The next point I want to make may seem so obvious that it need not be stated, but I want to state it anyway, so that the logic of my argument is clear. Unlike for cluster randomized research, there is an enormous, rich, and detailed literature in political philosophy discussing precisely the question that interests us: when it is legitimate to infringe upon some in order to benefit others. I suggest, then, that we can gain insight on how to proceed in hard cases of cluster randomized research by examining this literature, indeed by incorporating it. In other words, the

reasons why and when we should allow cluster randomized research without consent should be the same as, or at least very similar to, the reasons why and when we should allow political bodies to infringe upon some of its citizens, for the sake of the larger political community.

The logic of this point is that bioethicists interested in ethical issues surrounding cluster-randomized research can stand to gain a lot more by studying political philosophy than political philosophers can stand to gain by studying what has been published so far on hard case cluster-randomized research. There are two (related) reasons for this. First, political philosophy has been studied a lot longer than has research ethics. Indeed, randomization was recognized as a useful research technique only in the middle of the 20th century, long after, say, Plato wrote *The Republic*. Second the problem of distributive justice is also more important than research ethics. (These two answers are related in that the second answer partly explains the first answer.) Thus, we should expect more and therefore higher quality work on political philosophy than on research ethics. Of course, I am also presupposing that in examining questions of political philosophy and ethics we can make genuine progress, and that said progress is more likely the longer we examine a question and the more minds are bent to the task. And, of course, I am open to the possibility that a lone genius working in isolation from the received paradigm may have a fresh perspective and therefore usher in a revolutionary answer to very challenging problems.[8] So, yes, it is *possible* that we will make more and better progress in research ethics – and especially on the hard problem of cluster randomized research – by ignoring the received wisdom of political philosophy, even on the assumption that there is an illuminating analogy between those two topics. But that is very unlikely. The converse hypothesis – that we can make a lot of rapid progress in research ethics (and especially on the hard question of cluster-randomized research) by looking to political philosophy – is much more likely.

Of course, there are many rival theories on the issue of distributive justice, and it is safe to say that a consensus has not been reached as to what the right answers are. After all, the question is very hard. In that spirit, let us begin by considering a hypothetical proposal which gives the following four criteria as defining when it is permissible to waive the consent requirement in infringing against some citizens in order to benefit the larger political community:

1. The infringement involves no more than minimal risk to the citizens.
2. The waiver will not adversely affect the rights and welfare of the citizens.

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[7] In what follows I will simplify my discussion by referring to the analogy to 'political philosophy', as if the entire concern of that discipline were the single question of when it is permissible to harm some citizens (without consent) in order to benefit society. But, of course, that simplification is false.

[8] See T. Kuhn. 1962. *The Structure of Scientific Revolution*. Chicago, IL: University of Chicago Press.

3. The benefit could not practicably be carried out without a waiver.
4. Whenever appropriate, the citizens will be provided with additional pertinent information after the infringement.

Of course, such a proposal raises a host of questions. On 1, what is meant by 'minimal risk'? On 2, is the state not already adversely affecting their rights and welfare by the very act of infringing? On 3, what is meant by 'practicably'? And on 4, why is additional information after the fact important enough to be required (when appropriate), whereas for example compensation (when appropriate) is not? These questions and many others like them should lead us to suspect that this proposal is not well thought out. For example, the thought that political harms must be at most 'minimal' is not part of any well-received theory in political philosophy.[9] It may turn out that, when confronted with a political theory like this, the appropriate response of a thoughtful political philosopher should be to reject it and continue searching, rather than to try to shore it up by answering the multiple objections that come to mind. That is because it is more likely that the right answer to the very hard political question will appeal to some part of the enormous and mature received canon in political philosophy, rather than the above four criteria, which seem to be an unprincipled hodge-podge of various ideas, each of which alone already seems on shaky ground.

Of course, as is probably already clear, the above proposal – constraints 1, 2, 3, and 4 – is the political analog to the four constraints that actually appear in the current US federal regulations for when it is permissible to experiment without consent.[10] Just replace every occurrence of 'infringement' with 'research' and 'citizen' with 'subject'. The point is that those criteria would be unacceptable as an answer to the very hard political question, so they should likewise be unpalatable as an answer to our question about hard cases in cluster-randomized research. The right answer, to both questions, is much more likely to refer to or rely on one or another of the received contenders in political philosophy. For example, maybe the right answer is consequentialist, so that whether we should infringe on some citizens depends (only?) on the net effect of the infringement's consequences. Or maybe the right answer is roughly libertarian in nature, in which case infringing on some citizens is never justified merely by benefits to the community. Or maybe the right answer is more Rawlsian, that what is

permitted depends on what would be agreed to under a veil of ignorance. Or maybe it is communitarian, so that what is permitted depends on the effect that various policies would have on the community, rather than focusing on individualistic and atomistic rights.

The pros and cons of actual specific proposals are not my main concern here. Mainly I want to suggest that the question of when it is permissible to conduct hard-case cluster randomized research has an instructive analog, where extensive scholarly work has already been done. Yes, there is no consensus yet in that extensive scholarly work, but then we should likewise expect no adequate consensus for this smaller problem, of hard cases of cluster randomization research. Or, if we do reach a simple consensus on the smaller problem any time in the very near future, I suggest that it is likely a sham, too facile to be accurate, as I take it the current US federal regulations are.

To re-emphasize the main point: whatever the right answer to the very hard political question, the answer to our small, humble (yet still difficult) question on cluster randomization should be the same. The same considerations come in to play, so we should expect isomorphic answers. Thus, if you favor consequentialist reasoning for the very hard political question, you should be drawn to consequentialist reasoning for our small humble question about cluster randomization. If you are a libertarian at heart, that should not change just because the topic is now cluster randomization rather than the state. And Rawlsian principles are just as defensible for determining when cluster randomization is appropriate as they are for determining who gets which and how many of the primary goods.

3 POLITICAL PHILOSOPHY ALL THE WAY DOWN?

I have suggested that there is an important analogy between hard cases of cluster randomized research and the very hard political question of when it is permissible to infringe on some citizens in order to benefit society. But I want to note that the analogy could be said to hold even for other kinds of research, specifically for research which is randomized by individuals, for cluster randomized research where consent is easy to obtain, and for research where the intervention in question can be implemented even outside the research context. In other words, there is a loose analogy between the legitimacy of (human subjects) research *generally* and the very hard political question: both distill down to the same basic question of when it is permissible to infringe on some for the good of others, and the qualifications that the research be randomized by cluster, that consent is difficult to obtain, and

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[9] To say that harms must be at most minimal is not to say merely that they should be made as small as possible. Even in the research case, the 'minimal risk' constraint is intended to rule out research which imposes a significant risk of harm, even if that significant risk of harm is as small as is feasibly possible.

[10] Code of Federal Regulations, *op. cit.* note 6.

that the intervention cannot be implemented outside the context of research are inessential.[11]

One way to appreciate this more general yet tenuous analogy is to contrast it to a clearly inapt analogy, that between political philosophy and research on non-human animals. In particular, there is very little, if any, fruitful interaction between literature on political philosophy and literature about ethical obligations in research on non-human animals. Of course consequentialists may have well-worked-out ideas on both distributive justice between citizens of a state and on how one should interact with sentient non-human animals, but besides that family of theories I do not expect the bioethicist grappling with questions about animal welfare in research to gain much by learning the canon in political philosophy. That is mainly because non-human animals are typically not thought of as citizens of the political community (though perhaps that is a mistake). In contrast, the permissibility of various forms of human subjects research may be more analogous to the permissibility of various forms of state intervention on some citizens in order to benefit the entire community.

The difference between the more tenuous analogy (to all of human subjects research generally) and the clearer analogy (to hard cases of cluster-randomized research) turns on the presence versus absence of consent. Note that the political question – when we can harm some citizens in order to benefit society – is actually quite easy to answer when there are enough consenting citizens. If enough citizens consent to, say, donating a portion of their money to public schools, then the question of whether the state is permitted to use that money to fund public schools is easy: of course it is! And if that is all the money the school needs (suppose the point is to buy one new chalkboard), of course it would be inappropriate to take more. That should be derivable from any plausible political theory.

Now, most cases of (human subjects) research are just like that: there are plenty of potential research subjects willing to consent, so the question of whether it is permissible to proceed with the research using these consenting subjects is easy – of course! And the related question of whether it is permissible to proceed with the research instead using different or extra *dissenting* subjects is also easy – of course not. Obviously, this has all been slightly over-simplified. For example, one might argue that we should forbid exploitative research even if it is also mutually consensual. But, of course, the political thesis was also over-simplified in the same way: one might argue that we should forbid political exploitation of some citizens, even if it is also mutually consensual. So, even cor-

recting for over-simplifications, the tenuous analogy between political philosophy and research ethics still holds.

The political question becomes very hard only when there is a group of citizens, all of whom need to contribute in order to benefit the society as a whole, but where it cannot be guaranteed that everyone in this group will agree (consent) to make this contribution. For example, when is it legitimate for the government to *enforce* taxation for public schools, when some of its citizens dissent (or would dissent if asked)? This is a very hard question, a test where rival political theories may yield different results. And it also perfectly describes a cluster-randomized research study where you cannot distinguish or separate those who are willing to participate from those who are not. That is why the analogy between political philosophy and the hard problem of cluster-randomized research is tighter than is the analogy between political philosophy and human subjects research generally: in each domain the absence or (practical) impossibility of obtaining consent is what makes the problem hard. Otherwise the 'problem' is so easy it is essentially not worth thinking about.[12]

This brings me to a second point for which the initial observation – that the analogy to political philosophy holds (tenuously) for all kinds of human subjects research, not just hard cases of cluster randomized research – is relevant. Even if I am right that we should switch to thinking about political philosophy in very hard cases, I have still been unhelpful, in two ways. First I am unhelpful because I have not said what the right political philosophy is. I have no remorse for continuing to be unhelpful in this way. But second, I am unhelpful because I have not specified exactly when cases are hard enough that we should switch to so thinking. A researcher looking for practical guidance has so far come away from my paper with no useful guidelines. The reason I have not tried to specify what we might call the burden of consent is that it too depends on the correct answer to the very hard question in political philosophy. That is because the answer to the question of the lengths to which one must proceed in order to obtain consent is also internal to political theory.

Call our favored political theory 'X-ism'. X-ism could be, for example, utilitarianism, egalitarianism, libertarianism, or communitarianism. Then it is not as if researchers trichotomize their thinking:

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[11] See, for comparison, D. Marquis. Leaving Therapy to Chance. *Hastings Cent Rep* 1983;13(4): 40–47.

[12] Another family of very hard cases where I expect the analogy to political philosophy to be particularly helpful is research in emergency medicine. It may also apply to trials where at least one of the arms is known to be inferior to the other, i.e., non-equipoise research (most dramatically illustrated by the use of placebo control when there is already a clearly efficacious standard treatment).

I. When consent is easy to obtain, ignore political theory and obtain it.
II. When consent is genuinely impractical to obtain, look to X-ism.
III. When it is not clear whether consent is sufficiently impractical, cast about for a guide to dictate whether it should be obtained or whether we should look to X-ism.

No, option III is bogus: X-ism should itself dictate the point at which the consent requirement should be jettisoned. For example, if utilitarianism is your favored political philosophy, then you should be thinking like a utilitarian all along, in all cases, including for calculating the precise disutility of waiving consent.

As before, the reason it looks as if you should ignore X-ism in cases of type I and use it in type II and therefore have a serious problem in cases of type III is that all the best contenders in the political philosophy realm give roughly the same answer in type I cases. Thus, because all the most serious theoretical rivals converge in their answers to type I cases, the false impression that you do not need political theory at all is created. But you do, and that is shown by type II *and type III* cases: coming off the political theory fence may not be needed to solve type I questions, but it is needed to resolve the other two types of cases: not just cases where consent is clearly impractical (type II) but also cases where it is unclear whether consent is impractical (type III).

Philosophers of a certain stripe may now begin to worry about type IV cases, where it is unclear whether it is unclear whether consent is impractical. And then there are also type V cases, in which it is unclear whether it is unclear whether it is unclear whether . . . And so on. The right way to break this cycle is that political theory can be safely ignored only in those cases where all the serious contenders give the same answer; otherwise, the path to truth lies through political theory. The relevant marker is not how burdensome consent is (how easy it is to obtain), which admits of degrees such that it is vague whether the relevant degree of burden passes some threshold. Rather, the marker is what all serious contenders would dictate we do (which of course may also be vague!). Indeed, this suggests an interesting methodology for obtaining a quick and dirty and potentially useful *sufficient* condition for research without consent, if that is desirable: all the most serious political contenders must dictate in the political analog that it is permissible to infringe without consent.[13]

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[13] I say only *potentially* useful because I view the libertarian option as dictating that, at least for certain important rights, it is never permissible to infringe without consent, and I take libertarianism to be a serious contender. Of course, both counts are controversial.

4 OBJECTIONS

In this section I respond to two objections to my alleged analogy between hard case cluster randomized studies and political philosophy. Both objections take the form of allegedly important disanalogies between research ethics and political philosophy.

The first objection is that there is a disanalogy between research and political philosophy in that in the political case you are sure to be harming the citizens in the sub-group, e.g., via income tax. In contrast, in a well-designed research case there is an expected benefit even within the experimental arm. If this is right, then we might expect the political question to be quite a bit more difficult than the corresponding research question, for it is much harder to figure out when one may harm some citizens in order to benefit society than it is to figure out when one may benefit some subjects in order also to benefit others. Or, perhaps equivalently, we might expect much tighter restrictions on political action than on research. There are two responses to this objection. First, not all research carries with it expected benefit – an example is phase 1 toxicity studies. Second, even when there is an expected benefit, the risk of harm may outweigh it, such that there is an expected net harm. These are exactly the sorts of cases I had in mind in specifying hard cases to be those where some people will dissent and it is not permissible to implement the intervention outside the context of research. In other words, I insist that we need to be able to determine when we can conduct (hard-case cluster randomized) research we expect to *harm* subjects, and the ethical principles we need to illuminate this debate will correspond to analogous political principles.

The second objection alleges that there is a disanalogy between political philosophy and research in that the typical target of political intervention is well-off, whereas the typical beneficiary is badly-off. Think of redistributive taxation, for example. In contrast, it seems we intentionally target the sick in our research in order to benefit everyone. Here I respond that both suppositions are open to dispute. First, the contention that political interventions always infringe on the better-off in order to benefit the worse-off is in fact internal to and disputed by various rival political views. A prioritarian political theory makes that contention a basic axiom, whereas it is repudiated in a libertarian system. And in yet other systems (say egalitarian or utilitarian) the contention that we should infringe on the better-off to benefit the worse-off will be derivable as a general rule of thumb that admits of exceptions. Thus, if one is already inclined to believe that, in the political realm, one ought to redistribute (without consent) only by taking from the better-off and giving to the worse-off, then one should also believe the same in hard case cluster-randomized trials. Second, while it is often true that research subjects are sick, this is of course

not always true. Often we need to conduct research on healthy people. Third, even in cases where the subjects are sick it is typically true that the research is intended to benefit others with the same illness; for example, we test anti-retrovirals on subjects with HIV, in order to benefit others with HIV. In that case it is false that we are harming the worse off to benefit the better off.

5 A TENTATIVE POSITIVE PROPOSAL

So far I have given no practical recommendations, besides the negative suggestion that the Common Rule's four criteria for permissible research without consent are unsalvageable. In this section I give a very brief and very tentative positive proposal consistent with my methodological thesis that we would do well to borrow from political philosophy.

The proposal starts with a further, tentative extension of my primary idea, that hard cases of cluster-randomized research are analogous to hard questions in political philosophy, so that political theory should be informative for hard cases of cluster-randomized research. The extension is that actual political systems in the real world, not just political *theories*, should likewise be informative for our humble yet difficult research question. That is because we can treat the real world (or maybe, 'the history of the real world') as an experimental crucible for political theories, to see which ones are viable and which not. Now, obviously this suggestion raises an enormous host of issues that fall outside the scope of this paper but that worry me enough to label this entire section 'tentative'. (For example, why suppose that evolutionary fitness of a political system is at all related to moral fitness?) Still, in this last section I will run with this idea and explore its consequences briefly.

Simplifying greatly, in the United States we use representative democracy for many questions of distributive justice. Why not do the same for ((hard cases of) cluster-randomized) research?[14] In other words, why not use our political system to answer our research question too?

A natural negative answer to this is that it is too much of a hassle to employ the full power of our political machinery just for this small issue. But this leads to a natural response. The whole point of having a representative democracy rather than a pure democracy is to reduce the cost of having to (educate ourselves on and)

vote all the time on a lot of detailed issues – instead, we vote on leaders, who then dictate the details. We could just include ((hard cases of) cluster-randomized) research in the responsibilities of our political leaders.[15] A natural objection to this last even more tentative proposal is that our leaders are completely ignorant of the relevant issues in research. This is of course true, but no more true than it is for ignorance in any other areas where we relinquish responsibility to them, e.g., economics, foreign policy, military strategy, or the law. And this is why our leaders take on expert advisors.

This section has been both very brief and very tentative, but I include it to illustrate that my methodological thesis – that work in political philosophy can help illuminate ethical issues in hard cases of cluster randomized research – can have practical import too.

6 CONCLUSION

Let me end with a qualification. I have said that those asking when it is permissible to conduct (human subjects cluster-randomized) research (without consent and where the intervention would not be permissible outside the context of research) would do well to look to political philosophy for illumination. In saying this, I do not mean to imply that research ethicists working in isolation always get things wrong, whereas political philosophers (working in isolation) always get things right. Nor do I mean to imply that the best way to answer practical questions is first to hammer out the theory and then apply it blindly, never allowing for the possibility that counter-intuitive practical applications should affect what we think of the theory. No, everything I say here is consistent with respect for the method of reflective equilibrium.

My main point is modest, and more pragmatic: why reinvent the wheel? We have stumbled upon a rather difficult question in research ethics, and we are not sure how to resolve it. I am merely pointing out that a very similar difficult question has been asked in political philosophy, and a lot of people, including some of reasonable talent, have tried to chip away at an answer to it. Instead of starting from scratch on our research question, we can and should stand on the shoulders of giants and therefore make genuine progress, rather than re-treading along no-longer-productive ground. Thus, for example, instead of tinkering with the four constraints from the Common Rule meant to cover situations where we need to experiment without consent, we may do better to reject those constraints entirely and instead import our favored political principles.

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[14] The nested parentheses indicate my ambivalence about and hence ambiguity over whether the proposal is to use representative democracy for all forms of research, versus only cluster-randomized research, versus only hard cases of cluster-randomized research. And even if this question is decided, I also intend to leave open-ended just what in particular is meant by 'representative democracy'. To peek ever so slightly into this can of worms, one might wonder whether research questions should be decided at the local, state, or federal level.

[15] See Edwards et al., *op. cit.* note 2 and Osrin et al., *op. cit.* note 2 for a related suggestion, that consent for the cluster be given by an appropriate guardian who looks out for the cluster's best interest.

Indeed, my concern has not been primarily discovering the right answers at all, but rather the prior methodological question of how best to discover them. Consider this final analogy, to mathematics. One way to make progress in math is to solve a previously intractable problem. But another legitimate way to make progress in that domain is show how one intractable problem reduces to another, such that we can solve the first one if we solve the second. I am trying to do something of the latter sort in this paper, except my domain is bioethics rather than math.

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