The Social Value of Research and Health Research Priority Setting
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Introduction

It has long been accepted within research ethics that clinical research involving human subjects is only ethical if it holds out the prospect of producing socially valuable knowledge. This tenet is codified across a wide range of guidance and regulatory documents governing human subjects research. For example, the 2016 revision of the Council for International Organizations of Medical Sciences (CIOMS) guidelines for international research begins by noting that, "the ethical justification for undertaking health-related research involving human subjects is its scientific and social value" and continues, "In order to be ethically permissible, health-related research with humans… must have social value" (Council for International Organizations of Medical Sciences (CIOMS) 2016). There is similar language present across a wide range of other documents, including the Declaration of Helsinki (World Medical Association 2013), the Belmont Report (The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research 1979), and stretching as far back as the Nuremburg Code (1949). The requirement also appears in research oversight documents of various nations.

The widespread acceptance and codification of this social value requirement ("SVR") by national regulatory agencies, global non-governmental entities, and research ethicists has established it firmly as a core precept of research ethics. But the proliferation of this standard

generates three important questions. First, what does it mean for research to have social value? Second, what is the basis for requiring research to have social value? Finally, what implications, if any, does the SVR have for the ethics of health research priority-setting?

In the following, I address each of these questions in turn. In section 1, I review the literature on the SVR to explore its possible meaning and the demands it might be thought to make on research sponsors and investigators. In section 2, I turn towards the question of justification, reviewing debates about the moral grounds for the SVR and implications for the scope of its application. I argue that justifications of the SVR grounded in features of research sponsors, researchers, research participants, and their interactions with one another are insufficient, and instead defend a view of clinical research as a basic structure institution, subject to demands of justice. In section 3, I briefly digress to consider how the SVR might be thought to apply to social science research. Finally, in section 4, I consider the implications of various accounts of the content of and justification for the SVR for the ethics of health research priority-setting.

1: Background & Meaning of the SVR

The origins of the SVR can be traced to the Nuremberg Code of permissible medical experiments, whose second point is that, "the experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random or unnecessary in nature" and which continues in point six, "the degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment" (1949). These two criteria for ethical research highlight two important facets of the SVR: first, that anticipated social value (or results for the good of

society) is a necessary precondition for ethical research with human subjects, and second, that the level of risk it is permissible to impose on research participants is determined at least in part by the value of the expected results.

These two facets of the SVR are reflected in the history of discussions surrounding the requirement. Importantly, some guidelines seem only to require the latter, that risks be proportionate to social value. The Declaration of Helsinki, for example, states that, "the primary purpose of medical research is to generate new knowledge," but makes reference to the value of that knowledge only in discussing risks to research participants (World Medical Association 2013). This distinction might be made another way, as between those interpretations of SVR that require scientific validity as a baseline plus social value as indexed to risk (with perhaps no need for any social value at the no or minimal risk limit); and those interpretations that require both validity (which is necessary to generate new knowledge) and some minimal threshold of social value as a requirement for ethical research (Freedman 1987).

Whether set as a minimal threshold or used to regulate risk levels, the SVR requires an account of what constitutes research-generated social value. One early account suggested that we should understand the social value of research via its clinical value: clinical research should be conducted with the goal of contributing to clinical practice, and this goal is what grounds the ethical conduct of research. On this view, research results are clinically valuable insofar as the knowledge generated is generalizable – which requires not only study validity but also eligibility criteria that result in an appropriately representative study population and primary endpoints that reflect clinically significant benefits. A useful way to assess a study's value on this account is to ask, "if this research is successful as you planned it, would its results change your clinical

practice or would further research be needed?" (Karlawish 1999, 261). If further research would be needed, it "suggests strongly" that the research is not clinically valuable.

One seeming limitation of this view is that in indexing social value to clinical value, it under-values research that does not lead directly to the approval of new interventions or changes in clinical practice, such as early-phase or first-in-human research; often simultaneously the riskiest research with the lowest prospects for direct benefit to participants. This observation may have partially motivated the broader definition of social value offered by Emanuel and colleagues. The notion of social value they espoused encompasses not only research which "evaluates a diagnostic or therapeutic intervention that could lead to improvements in health or well-being" but also research that "is a preliminary etiological, pathophysiological, or epidemiological study to develop such an intervention; or tests a hypothesis that can generate important knowledge about structure or function of human biological systems, even if that knowledge does not have immediate practical ramifications" (Emanuel et al. 2000, 2703). On this account, early-phase research can be construed as socially valuable in the relevant sense, but research with non-generalizable results, research with substantial overlap with existing bodies of research, research the results of which will not be disseminated, and research into interventions that could not be practically implemented will fail the test.

This account of social value appears to offer a threshold of value: a study without the prospect of producing socially valuable results is not ethical to conduct. But it doesn't supply a means of balancing social value with risk level once a study is assumed to have social and scientific value (Emanuel et al. 2000, 2705). In service of this latter task, Nancy King helpfully

distinguished between three types of research benefits: direct benefits to subjects (those benefits that are due to receiving the study intervention), collateral benefits to subjects (benefits that subjects receive from being in the study that are not due to receiving the study intervention – for example, better follow-up care), and aspirational benefits, which are benefits to science and society from the results of the study. Additionally, King highlighted that any consideration of benefits must account not only for the nature of the benefit, but also its magnitude and likelihood (King 2000).

This latter consideration is especially important when considering social benefit, or what King calls "aspirational benefits". Clinical research is conducted precisely because we lack definitive knowledge of what works, how, and how well. A significant proportion of studies generate negative results, and only about 16% of investigational new drugs result in successful marketing applications (DiMasi et al. 2010). If risks to subjects are to be balanced against a set of benefits that include social benefits, there must be some way to take the uncertainty of outcomes into account. One attempt to provide such an account distinguishes between immediate and future health value, where immediate health value refers to the belief of experts that a trial's results can be immediately used to improve health and well-being (what Karlawish called "clinical value"), and future health value might improve our knowledge or understanding of a disease or condition but not immediately improve health. This distinction is intended to largely track the distinction between late-phase interventional trials and health policy studies, on the one hand, and earlier phase trials and studies of human physiology, for example, on the other. According to this view, immediate health value will generally be more certain than future health value, but the distinction between near- and long-term is orthogonal

to the magnitude of value expected from a study (Casarett et al. 2002). This means that although future health value may be quite significant, the greater uncertainty of that value should cause us to discount it in our risk/benefit assessments.

As a metric for assigning value, we might worry about two limitations of this approach. First, the framework is likely to underestimate the value of negative trial results, whose downstream impacts may be particularly uncertain. Yet failure is essential for efficient clinical translation for at least two reasons: It allows for expansive exploratory research with the corresponding trade-off that much confirmatory research will fail to substantiate benefit. And it is necessary for the refinement of what Kimmelman and London refer to as "intervention ensembles" – that set of physical materials, clinical practices, and constraints that together make up a therapeutic or preventive intervention (London and Kimmelman 2015, Kimmelman and London 2015).[1]

The second important limitation of this framework is that given the uncertainty of the future benefits of early-phase research, this model will be biased in favor of late-phase research. This is especially the case given that the causal chain between first-in-human and early-phase studies and ultimate interventional outputs is fairly muddy (Resnik 2008). Early-phase studies are often used not only to assess safety and dosing toxicity, but also to investigate novel pathways and mechanisms, to assess the feasibility of delivery models, to highlight gaps in existing knowledge, and to inform additional pre-clinical and early-phase research (Kimmelman 2010, 92-94). Each of these represents important social value that a framework which discounts future benefits will risk under-valuing.

[1] For the distinction between exploratory and confirmatory research, see (Kimmelman et al. 2014).

Moreover, such an account, like that which locates social value in clinical value, implies a tension between the role of social value in offsetting risks to participants and the generally much higher risks associated with early-phase research. Both seem to entail that earlier-phase research will be of less social value, but since there is typically no direct benefit to participants in early-phase research, and typically significantly higher risks, much early-phase research seems on these views harder to justify (Habets et al. 2014).

Later work seeks to fill the lacuna regarding early-phase research by assessing three dimensions of social value: the anticipated social value of any eventual intervention developed; the translational prospect of the trial itself, understood as the likelihood of the trial's success in further progressing the intervention towards clinical deployment; and the validity of the study design in terms of its ability to answer the research question(s) of interest (Habets et al. 2014). Yet ultimately this view stops short of identifying what constitutes sufficient social value for a study to proceed. Recognizing that measures of social value may draw on the severity of the disease or condition under study, the number of patients likely to benefit from an intervention, improvements in quality of life, or distribution of health over the course of a life, social value is construed as a measure of how *society* values new interventions, and thus a political matter that should be determined not by funding agencies or scientists, but rather society at large. This political orientation reflects the idea that disagreements over fundamental moral or political values may influence how individuals would assign value to various research outputs (Resnik 2008).

A more concrete account indexes the value of research to its ability to alter the decision-making of various health system and research stakeholders. On this view, the

knowledge generated by research is valuable when it can alter the expected social utility assigned to various policy options sufficiently to change which policy is ultimately selected. "Policy" is used loosely here to encompass decisions made not only by government policy-makers, but also decisions made by, for example, NGOs working to address local health deficits and decisions made by research funders and researchers regarding future research priorities (Wenner 2017). This account acknowledges the political nature of value judgments emphasized by the previous approach, but recognizes that research can only be valuable to a society if the relevant actors within that society are prepared to use the information generated to inform their decisions. Assessments of a study's instrumental value for the purposes of satisfying the SVR should be made by reference to existing priorities as determined by those empowered to make the relevant decisions. The political nature of such decisions is manifest in the expectation that health policy decision-making at local, state, and national levels is informed by popular will via democratic political processes.

Another approach abstracts away from political decision-making and instead asks whether any net risks from a study – that is, risks that are not justified by potential direct or indirect benefits to subjects – would be viewed as justifiable to an objective party. On this view, whether a study has sufficient social value to meet the SVR should be determined by asking if "a fully informed and impartial social arbiter would recommend the study in question" after giving fair consideration to all perspectives (Rid and Wendler 2011, 166). The natural limitation of this approach is that it requires some specification of what it means to give fair consideration to all claims. A procedural interpretation of fair consideration might seek to give

equal weight to all perspectives, while a more substantive view of fairness might assign greater weight to the perspectives of those who are worst off, for example.

The latter is the approach taken by Barsdorf and Millum, who argue that social value should be construed as a function of both the expected health benefits of interventions and the relative well-being of those who are expected to benefit. Other things equal, those who are worse off should be given greater priority, so research expected to benefit the disadvantaged has greater social value than research that will primarily benefit those who are better off (Barsdorf and Millum 2017). This prioritarian view appears consistent in most cases with how alternative substantive views about just distribution – such as utilitarianism or egalitarianism – would assign value in the case of health research, so this understanding of the SVR is pluralistic with respect to moral theories and may be seen to sidestep the political questions of other approaches.

2: Foundation for SVR

In addition to unpacking the substantive content of the SVR, a more fundamental question relates to why the requirement should be thought to apply at all, and in particular, why it should be considered to have wide applicability in a research context dominated by private entities. Early discussions of the SVR sought to ground it primarily in the scarcity of research resources and the desire to avoid exploiting research subjects (e.g., Emanuel et al. 2000), with some additional attention to the distribution of the value generated (Casarett et al. 2002, Resnik 2008, Rid and Wendler 2011).

However, it's not immediately clear how or why a principle of non-exploitation or the scarcity of research resources would warrant a broadly applicable SVR. First, consider what is

required to protect research participants from exploitation. While there are competing accounts of what constitutes exploitation, a key component seems to relate to the distribution of benefits from an interaction: one party receives a disproportionate share of the social surplus, relative either to the amount of surplus created or to the needs of the other party (Wertheimer 1996, Sample 2003, Valdman 2009). Insofar as distributive concerns are essential to exploitation, that a study produce social value seems neither necessary nor sufficient to ensure non-exploitation. If a study produces great social value but none of that value devolves to study participants, worries about exploitation persist. And conversely, if research participants were well-compensated then it would be hard to sustain a claim of exploitation, even in the absence of social value (Wertheimer 2015, Resnik 2016).

Second, consider the claim that research resources are scarce and so ought to be used responsibly. This seems clearly relevant to publicly-funded research. But private entities are generally thought to have no responsibility (at least not to science or society) to use their resources in any particular manner. Rather, private entities are free (subject perhaps to constraints imposed by shareholders) to pursue their interests in the manner they see fit so long as they are not violating some particular moral obligation (Wertheimer 2015).

Other attempts to justify the SVR have sought to ground it in other features of either the researcher/participant dyad or the sponsor/researcher/participant triad. On one account, while there is no universally-applicable justification for the SVR, a patchwork of justifications explains its applicability to a wide range of clinical research, including research funded by private, for-profit sponsors. So, for example, although only about one third of clinical research is publicly funded, even private research relies heavily on public resources, whether by drawing

on conceptual, first-in-human, and early-phase testing that was publicly-funded or by drawing on social investments in health care infrastructure, the training of medical personnel, and research and development oversight. This suggests that society has a valid claim to such research producing social value. Net risk research with patients who can't consent must be justified by virtue of the expected social value of the research, regardless of funding. Similarly, high risk research – even with competent adults – requires sufficient social value to justify the imposition of higher risks on research participants. And given empirical evidence that many participants enroll in clinical trials because they believe they are contributing to valuable science that will help future patients, conducting research that is not sufficiently valuable may actually be deceptive in the absence of clear statements that research lacks that value. The authors go on to worry that a policy expecting researchers to make such clear statements in the relevant instances is unlikely to be adopted (Wendler and Rid 2017).

One common thread across these different accounts is a focus on the interests of those we might construe as parties to research interactions. Early emphasis on avoiding exploitation sought to ensure that all parties received a fair share of the benefits of cooperation. The idea that society has a claim to valuable research due to the scarcity of public resources casts "society" as one party to the research transaction. Attempts to apply this reasoning to privately-funded research via the observation that even industry sponsored research draws on publicly-funded physical, human, and conceptual resources function similarly to try and expand our understanding of who counts as a party to the research transaction and why. And viewing social value as a requirement to ensure participants are adequately consenting or as means of

justifying risk imposition similarly makes the requirement about ensuring that the entitlements of those who are party to the research interaction are met.

The limitation of these inward-facing (or "transactional") justifications is that they fail to locate the clinical research enterprise within the context of the social role that it plays. Clinical research is conducted with the explicit intention of impacting health systems. Researchers and research sponsors seek to publish the results of clinical trials in medical journals whose target audiences are practicing physicians and other researchers, successful trials are leveraged to support marketing applications to oversight bodies and to inform ongoing research, and private pharmaceutical companies participate in these activities to no less extent than public research funders. The former may actually engage in more extensive efforts to impact health systems with their research, by investing in lobbying efforts, direct-to-consumer advertising, and continuing medical education, while also embedding sales representatives in clinical settings where free samples and meals function to increase uptake of new interventions into clinical practice (Lieb and Scheurich 2014, Yeh et al. 2016, DeJong et al. 2016).

A different approach grounds the SVR in the interests of investigators and sponsors of maintaining the public's trust in the research enterprise. On this view, adhering to ethical standards for research is one way to ensure the public's ongoing support of clinical research as a system via investment in basic research, enrollment in clinical trials, and the general social esteem that adheres to researchers and research institutions. However, adherence to ethical and methodological constraints on research is costly, such that if unenforced each individual researcher and research sponsor would have rational, self-interested reason to abstain from self-constraint and to allow the costs of maintaining the public trust to be borne by other

stakeholders. Ultimately, in such an environment, each individual actor behaving in a self-interested way would result in large-scale failure to adhere to the ethical and methodological standards in question, and undermine the public trust that all stakeholders rely on. Insofar as belief that the research enterprise is contributing something of value to society is one plank upon which the public's trust is built, the SVR should apply broadly to all clinical research (London 2012, Holzer 2017).

Framing the SVR in terms of the maintenance of the public trust encourages a broader understanding of research as a social institution in itself rather than merely a series of individual transactions. On this view, the SVR can be seen as one means of protecting the integrity of a health information economy whose validity and credibility have impacts on stakeholders well beyond those who can meaningfully be construed as parties to research transactions. Given these externalities, the research enterprise should plausibly be constrained to be used in pursuit of social value.

Another view takes this line of reasoning further, arguing that these externalities are in fact fundamental to a research enterprise that ultimately functions as a basic social institution. The dissemination of new research into the academic literature and new interventions into clinical practice has lasting impacts on health systems that devolve to individual patients. Importantly, these impacts are characterized by three, related, features: First, individuals cannot in general opt out of the health systems they participate in being impacted by the results of clinical research. If a new intervention has replaced an old one in a physician's go-to armory, chances are low that the patient will even realize it, much less understand the reasons for it or have the knowledge and will to advocate for the older intervention if it were for some

reason better for her. She will have no say in whether older, potentially cheaper interventions continue to be manufactured. And whether she participates in a publicly-funded health system or a private, insurance-based model, in one way or another she will be impacted not only in her health outcomes but will also bear some of the financial burden of decisions about how health resources are prioritized – whether via out of pocket costs or taxation and allocation schemes.

Second, the kinds of impacts that clinical research is intended to have on health systems will also have deep, lasting, and unavoidable impacts on the life chances of those who participate in those health systems as patients (or who do not because of various problems of access, bias, etc in clinical medicine). The access that individuals have to health and health care, and the nature of the care available to them, impact virtually every aspect of their lives, as health deficits are not only direct threats to well-being but also contribute to missed school and work, lost income, and increased costs and personal burdens related to care.

Finally, third, a just distribution of access to the fruits of the research enterprise cannot be secured by the application of only principles regulating individual interactions. Permitting research priority-setting decisions to be driven primarily by unconstrained market incentives has led to dramatic inequality in health outcomes, both within and across states, as decisions about what to research and develop are driven primarily by pursuit of interventions that can be marketed at high prices to wealthy populations, with little incentive for biomedical progress that would address the most pressing health needs (Evans et al. 2014). This profit-driven model has resulted in a large share of research resources being devoted to the development and marketing of new innovations that are neither particularly innovative nor particularly valuable in terms of therapeutic gain over existing interventions (Trouiller et al. 2002, Chambers et al.

2017). In the absence of structural constraints, pharmaceutical companies will continue to effectively dictate the direction of biomedical progress via their research and development investment decisions, and drastic inequalities in access to health and health care will not only persist but most likely worsen.

The substantial impact that the research enterprise has on individual life chances, the non-voluntary manner in which that impact is imposed, and the extent to which the enterprise contributes to inequalities when left unconstrained combined entail that it be treated as one component of what John Rawls referred to as "the basic structure of society". By this he meant the major social institutions that together determine the rights accorded to individuals and the division of advantages and burdens that arise as a result of social cooperation (Rawls 1971, 7). Rawls argued that basic structure institutions should be first and foremost subject to considerations of justice because of the importance of their role in preserving the background conditions necessary for free and fair interactions, and because of the deep and inescapable effects such structures have on the lives of those who live within them. On a view of the research enterprise as basic structure, the primary justification for the SVR is not located in the interests of the parties to research transactions but rather in the goals of the research enterprise and the role that it plays in circumscribing the opportunities available to members of society much as other major social institutions do (Wenner 2018b).

There are at least two important ways that the shift in grounds for the SVR away from a transactional and towards a social institution or basic structure model impacts the content and scope of that requirement. First, as we saw in section 1, because the social value of research is frequently taken to justify the imposition of risks on trial participants, on some accounts of the

SVR the requirement is weaker when risks to participants are lower. However, on accounts that justify the SVR by appeal to its broader social impacts, the requirement does not become less demanding simply because risks are minimal. Within the basic structure model, for example, this is because regardless of risks to research participants, research is nevertheless conducted with the intention of impacting health systems and the health interventions that are available within healthcare markets. Thus the grounding of the SVR – the impacts that research has on the kinds of health systems that individuals can access – does not vary along with risk levels.

Second, while the SVR grounded in what I above called "transactional" accounts seems only capable of assigning obligations to produce social value to public research funders (when "society" or the public can be construed as parties to the research transaction) or to trials with specific risk:benefit ratios or with participants who hold certain beliefs about the value of research, models of research as fundamentally social in nature like the basic structure model ground such obligations regardless of the public or private nature of the funder. This is because the obligation is not grounded in the ethics of individual transactions, but rather in the impacts that clinical research has, as its primary purpose, on health systems. Privately funded research, like that funded by public research sponsors, is fundamentally about changing health systems and the healthcare options that are available to participants in those systems.

Ultimately, these different views about the content and justification of the SVR will have different implications for the ethics of health research priority-setting. I explore these implications below in Section 4. First, however, a brief digression on the SVR and its application to other kinds of human subjects research.

3: SVR and Social Science Research

Before continuing to explore the implications of different views about the SVR and its grounding for the ethics of health research priority-setting, it is worth pausing to ask whether the arguments above generalize to research outside of the biomedical setting. In particular, do social science researchers have obligations to conduct research of "social value", and if so, on what basis?

There is a large body of literature bemoaning the attempt to generalize ethical norms from biomedical research to other research with human subjects. One important strain of reasoning within these discussions is that the bases for asserting strong participant protections in biomedical research are not present in social scientific research. The need for robust participant protections in biomedical research is often seen as arising from a constellation of factors including the position of dependency of patients on medical professionals for their own well-being, the knowledge gap between physicians and their patients with respect to factors that could contribute to or detract from that well-being, and the potential for significant harms from exposure to unproven medical interventions. Yet much social scientific research does not share these features. Social science research subjects are generally not dependent on researchers for access to well-being or for knowledge directly relevant to their well-being. And although there can be harms from social scientific research, those harms are rarely as severe as can be caused by unproven medical interventions.

Whether some version of the SVR can be justified in social scientific settings will depend significantly on the types of research being conducted and the relationships between researchers and research subjects. Below, I'll briefly discuss how something like the SVR might

be thought to apply to political science research, but research in other social sciences will differ in important ways. Although some other fields may share relevant features (economics, for example), other areas of research such as education or psychology may differ substantially and therefore require altogether different frameworks for ethical analysis.

Within political science, some have argued that it is not merely that models of participant protection that dominate clinical research ethics do not generalize. Rather, for researchers to meet their responsibility to inform the public about the structure of their social institutions, there needs be a presumption in favor of prioritizing the social interest *over* the potential harms that could come to some research subjects. Specifically, those whose interests are deeply intertwined with the maintenance of unjust social structures should not have high-priority claims to protection from harms due to research on those social structures. To give high priority to protecting such participants from harm would be in "considerable tension with the social sciences' moral responsibility to (amongst other things) explore prejudicial practices, uncover injustices and scrutinize prevailing power relationships" (Sleat 2017, 41). Given this tension, the traditional grounding of something like the SVR in the balancing of risks to participants and benefits to science and society may not be appropriate.

Other means of grounding the SVR also seem inappropriate in the context of political science research. While researchers often gain professional standing from the conduct of their research, there is rarely the kind of profitability that could ground claims of exploitation on the part of research subjects if exploitation is construed as a distributive wrong. While transparency with research participants is in many cases valuable in itself, it seems less relevant to attracting research participants than in the setting of health research, where participants

want to be assured that the (potentially large) risks they undertake are justified by the expected results. And while research on political and economic systems is arguably about our basic social institutions and how to improve them, it is not clear that as an enterprise it can be construed as *part of* that basic structure in the way that health research might be. The link between such research and the maintenance of the conditions for free and fair transactions, for example, is at best far more tenuous.

We might have better luck grounding an SVR for political research in the obligation of researchers to responsibly steward scarce research resources. Some substantial portion of such research is publicly funded, and it might be argued that the public therefore has a claim to research being responsive to the public good. But even accepting this, there is the further problem of unpacking the meaning of an SVR in social scientific research.

The notion of clinical value may be subsumed by something like the view that research is valuable if it informs public decision-making in some way, at least for research in politics or economics (Wenner 2017). But this understanding quickly runs into two problems. First, much research that is policy-relevant is going to impact citizens in different ways. Conflicting interests among social groups or between political ideologies will make the value of any impact both harder to measure and also more politically contestable. To the extent that the value of research becomes politicized, the scientific community will be highly vulnerable to shifting majorities and political landscapes.

Second, a focus on policy impact as a surrogate for social value is likely to significantly constrain research in ways that are in tension with the goals of promoting social welfare or justice. In order for social scientific research to be taken up by policy-makers, it has to answer

the questions that policy-makers are interested in. But policy-makers tend to do things incrementally, in ways that take the dominant social and political forces for granted. Moreover, policy-makers themselves often benefit from the perpetuation of existing social structures and are likely to be oriented towards policy proposals that work within existing paradigms rather than changing systems themselves. If the need to inform policy directly were to dictate social science research priorities, it seems that much important critical social theory would be stymied (Green 1971, Seidman 1986).

While the concern about conflicting interests could potentially be addressed by taking up a view of social value that places greater weight on benefits to those who are worst off (Barsdorf and Millum 2017), concerns about the fundamental orientation of policy-makers are less tractable and therefore more troublesome for any proposed requirement of social value for social scientific research.

4: Social Value and Health Research Priority-Setting

In this section, my goal is to explore the implications of different interpretations of the nature and ground of the SVR for the ethics of health research priority-setting. There are two dimensions along which the SVR might have implications for priority-setting. First, we might think that all things being equal, research with the potential to generate more social value should be prioritized over that with the potential to generate less. If this is the case, then some manner of comparing the social value of different trials is necessary over and above the ability to assess a trial's potential for generating social value with respect to its risk levels. That said, many of the accounts discussed in the first section don't appear to be so demanding as to require that a research agenda maximize social value. In at least some of the accounts

discussed, the potential for social value appears to operate as a threshold condition: once a study is deemed to have it, the requirement has been met.

Second, several theorists have recognized that social value as a desideratum is insufficiently attentive to the distribution of that value, and that in assessing clinical trials we need to consider how benefits are distributed and not merely how they stack up against potential risks (Rid and Wendler 2011, Barsdorf and Millum 2017). Many of the approaches canvassed above will ultimately prove silent on the question of distribution of value generated, while others will have concrete implications for distributional questions. Some have argued that any plausible account of social value would track distribution insofar as attempting to maximize the benefits from research, increase equality in health outcomes, and prioritizing the worst off will each converge on a weakly prioritarian view that ascribes more social value to research likely to benefit those who are worst off (Barsdorf and Millum 2017). If this view is correct, then the gap between maximizing social value creation and distributional concerns would seem to have been bridged. But in some cases, an approach that recommends maximizing overall social value may come apart from distributional considerations grounded in other ethical commitments such as egalitarianism or a concern for the worst off. We can well imagine that some on some measures such as QALYs or DALYs, a greater overall improvement might come from an intervention that makes a small contribution to quality of life for a very large number of people, while interventions that might make much larger differences to worse off individuals would be overall less impactful. In either case, we should ask what different views about the nature and justification of the SVR entail for the ethics of health research priority-setting.

Consider, first, the SVR construed as a means of justifying the imposition of research risks on participants. Such approaches to the SVR suggests that low-risk research or research which is of net benefit to participants need not have social value. Similarly, this basis for the SVR doesn't have obvious distributive consequences. At most, such approaches can contribute to questions of priority-setting by indicating whether a particular research endeavor is likely to be valuable enough to offset the risks involved. But this does not provide a mechanism for comparing studies or research portfolios with one another to determine which lines of investigation should be prioritized in a scenario of limited material and human resources, where any investigation has opportunity costs with respect to what other research can be conducted.

Appeal to participant altruism and a desire for transparency is likewise indecisive with respect to the distribution of research benefits, and thus for priority-setting. This approach to justifying the SVR may have distributive implications were participant altruism shown to be indexed to a particular population subgroup, but absent such evidence it's not clear why participants' desires to contribute to advancing biomedical knowledge for the benefit of future patients would entail any particular research priorities. In fact, as Wendler and Rid note, simply informing participants of the extent of value expected from a study, and perhaps who is expected to benefit from it, seems to satisfy any obligation grounded in transparency and worries about fully informed consent (Wendler and Rid 2017).

Locating the force of the SVR in the maintenance of public trust may have implications for priority-setting insofar as the public's willingness to trust and invest in the research enterprise is positively correlated with some measure of social value. With that said, whether

public trust in the research enterprise is truly indexed to social value is an empirical question, and one to which the answer may not necessarily depend on the social value of individual trials. Perhaps public trust in the research enterprise is not sufficiently informed about the array of different studies being conducted and their overall contribution to biomedical progress to be impacted much by research without social value. Equally plausible is that public trust in the research enterprise can be maintained by the existence of some research that is of social value, even while large swaths of research are not. For this defense of the SVR to have significant impacts on health research priority setting, however, it would seem a much stronger claim would need to be substantiated: that public trust is conditional on a research enterprise that is largely or entirely comprised of studies with social value, or conditional on the nonexistence or low likelihood of research of minimal value. Yet this stronger claim seems clearly false: there is much research conducted today (consider the rampant proliferation of me-too drugs, for example) that generates little, and sometimes even negative, social value (Chambers et al. 2017). And yet, the public's trust in biomedical research as an enterprise does not appear to be appreciably undermined if levels of participation and ongoing investment in research are any indication.

The implications of the public trust model for the distribution of health research priorities are likewise unclear. It might be the case that groups who have historically been the victims of research misconduct or denied the benefits of biomedical progress (or both) would be more trusting of researchers and of research as an enterprise if greater attention was seen to be given to addressing their health needs. Similarly, potential host communities in low-income settings may be more trusting of foreign researchers were international research seen

to prioritize the diseases and conditions that are most prolific in the global south. These are empirical questions, however, such that any connection between the social value and distribution of research benefits and the trust of the public will be a contingent one.

Other accounts of the SVR seem to have more direct implications for the ethics of priority-setting. For instance, if the SVR is grounded in the responsible stewardship of research resources, this lends itself naturally to a view of health research priority-setting that ties sponsor obligations to the source of research funding. Research that is publicly funded should presumably be responsive to the public's values within prioritization schemes, which might require procedural constraints on priority-setting to ensure that it is informed by public deliberation and principles of public reason such as relevance, publicity, revisability, and enforcement (Daniels and Sabin 1997, Daniels 2008). The responsible stewardship argument also seems to lend itself naturally to views which limit such obligations to public funders, and which assign priority-setting obligations to other kinds of research sponsors based on their social roles. This view is consistent with the idea that there may be some underlying principle or principles of justice that should inform priority-setting, but that obligations grounded in those principles can be overridden by other obligations that research funders have based on the kinds of institutions they are and what kinds of public commitments they have made with respect to addressing the health needs of different populations (Nayak and Shah 2017). So, for instance, non-profit research sponsors may have obligations to support the kinds of research they have run fundraising campaigns on (otherwise they will have deceived donors), and for-profit sponsors obligations to their shareholders to engage in profit-making activities (Pierson

and Millum 2018). Such obligations will override duties of justice that might demand prioritization of the needs of the worst off, for example.

Similarly, a grounding of the SVR in exploitation avoidance seems to have at least some distributive implications for priority-setting. Insofar as the justification of research with human subjects is grounded in its generation of social value, then recognizing that specific knowledge has differential practical value in different contexts, we should expect different research questions to be valuable enough to satisfy the SVR in different social contexts (Wenner 2015, 2017). This approach to health research priority-setting asks whether the same population that is burdened by research is benefiting from its results via affordable access to a health system that is improved as a result.

Note, however, that there is a tension in such views. Consider exploitation as construed in Section 2, as a concern about the distribution of benefits from an interaction. There, the worry is that research participants don't receive a fair share of the benefits from the cooperative endeavor of a clinical trial. On this view, approaches that seek to minimize exploitation by ensuring that research is valuable to the communities from which participants are drawn will not directly serve this purpose since there can be no guarantee that individual research participants will benefit directly from the results of research. At best, such constraints can address worries about exploitation indirectly, by ensuring that the health systems which research participants are likely to access in the future benefit from advances in biomedical knowledge (Wenner 2018a).

Perhaps more importantly, this view's implications for priority-setting function primarily as constraints on the kinds of research it is permissible to conduct in particular settings. What it

does not do is motivate positive obligations to conduct research that will benefit particular communities or populations. For example, we might think that pregnant women have justice-based claims to research being conducted on pregnant women so that they can access evidence-based care while pregnant (Lyerly et al. 2008, Krubiner and Faden 2017), or that the global poor have justice-based claims to research being conducted that focuses on the diseases and conditions of the poor (Nayak and Shah 2017). Yet exploitation-avoidance approaches to the SVR will be unable to ground such justice-based claims for priority.

When justice-based claims are taken as central, on the other hand, there will be a close relationship between the SVR and priority-setting. For example, priority-setting obligations can be seen to stem from the preexisting social, political, and economic relationships that provide the context of clinical research. Two features of this background context are of particular relevance. First, the roles that research sponsors have played in supporting or upholding particular policies that have contributed to disparities in health outcomes generate duties of rectification that attach to both sponsors as well as researchers who work for or are funded by such entities in their research. And second, when the basic legal, political, and economic institutions of a community are insufficient to ensure that members of that community have the opportunity to develop their basic human capacities, the demands of justice ground strong claims of entitlement to have such deficiencies addressed. Where local social structures fail to address these deficiencies, this should limit the range of permissible research that can be conducted within such populations to that which will aid in the development of such opportunities (London 2005).

Like views grounded in exploitation avoidance, this argument might seem only to constrain that research which may permissibly be conducted in particular settings, rather than providing a basis for positive claims to justice-based priority. But in fact this account can be seen as far more demanding on the grounds of both of the aforementioned considerations. Duties of rectification, if they adhere to researchers and research sponsors by virtue of their contribution to an unjust social and economic scheme that predictably leaves large swathes of the global population without access to basic health needs, would not merely limit the kinds of research that can be conducted in or on underprivileged populations, but would ground positive obligations to conduct research that addresses unmet needs attributable to that scheme. Similarly, recognition that many do not have access to the opportunity to develop their basic human capacities due to the failure of local social structures to meet basic demands of justice generate strong obligations to promote the development of such opportunities (Rawls 1971, 99). Each of these considerations grounds positive obligations to ensure that research priorities are set in a manner strongly informed by principles of justice and that research oversight in general "move away from an over-reliance on the largely reactive IRB review mechanism toward a more proactive model in which issues of justice are considered much earlier in the research process" (London 2005, 34).

Finally, on the basic structure view of clinical research there will necessarily be a close relationship between the SVR and priority-setting. Not only does the basic structure account suggest that research participants or the groups of which they are members have claims to benefit from research; it also suggests that groups may have preexisting justice-based claims to research being conducted that will benefit them, regardless of whether they are already

engaged in research as participants or host communities. This is because all individuals who live within basic structure institutions are entitled to fair consideration in the design and operation of those institutions. Insofar as health research and related health outcomes impact individuals' abilities to form and pursue a conception of the good life, the research enterprise as a basic structure institution should be organized so as to distribute access to health and health interventions in a manner that is directed by considerations of justice.

One of the fundamental upshots of the basic structure model is thus that the direction of the health research enterprise should be dictated in large part by considerations of justice, and that these considerations should feature prominently in determinations of which diseases and conditions to study. Once clinical research ceases to be considered as primarily comprised of transactions between researchers, research sponsors, and individual research participants, we can better understand how and why even private, for-profit research entities have ethical obligations to science and society that should inform not only health research priority-setting but also how the knowledge gained in health research should go on to be leveraged. And because these obligations are grounded in the impacts of health research on health systems and not on the obligations of research transactors to one another, these considerations of justice should impact health research priority-setting regardless of funder type.

Conclusion

The SVR plays an important role in both constraining and directing the health research enterprise. However, different interpretations of the content of and justification for the SVR entail different obligations related to health research priority-setting. These implications can be seen to vary along two dimensions: one dimension concerns the amount of social value

required to justify research, and whether a particular interpretation of the requirement entails an obligation to prioritize research with the greatest social value, or requires only that some threshold of social value be met. The second dimension relates to the distribution of any social value generated, and whether particular interpretations of the social value requirement entail considerations of distribution when making research priority decisions. While many interpretations of the requirement seem to entail at a minimum a threshold of social value to justify clinical research, most of them are silent with respect to the ethical distribution of that value.

However, the strongest defense of the SVR – that which locates its force not in the ethics of free and fair transactions but rather in the role that the research enterprise plays in conditioning the life chances of individual members of society – has significant implications for the ethics of health research priority-setting. Not only does social value function as a threshold of permissibility, the distribution of that value is subject to substantive considerations of justice. This approach to the SVR has direct implications not only for the ethics of health research priority-setting, but ultimately, for how the benefits of research, both interventional and epistemic, should go on to be leveraged.

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