

## **Risk limits in fair subject selection**

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### **1. Introduction**

In this welcome contribution, MacKay and Saylor break down the widely accepted principle of fair subject selection into several sub-principles. Because these subprinciples can conflict, there are cases where some type of unfairness seems inevitable. They suggest we address such cases (roughly) according to the relative moral seriousness of each type of unfairness.

This commentary addresses the specific claim that a “fair burden sharing” principle limits the amount of net risk to which participants can be exposed. MacKay and Saylor take the unfairness of excessive net risks to be serious enough to defeat any other conflicting principle: “participants should not be exposed to unacceptably high risk for any reason.” (MacKay and Saylor 2019). This implies, for instance, that it would be better to allow moderate risk research that would produce unfair racial and class disparities than to allow very high risk research that would not produce such disparities.

MacKay and Saylor defend the priority of risk limits in part by arguing that justice requires them for the sake of protecting participants’ basic interests, citing both Rawls and Alex John London’s Rawls-inspired work on equipoise (Rawls 1999, London 2007). Here I raise doubts about that defense.<sup>1</sup> I give reasons to believe the opposite: that taking account of participants’ basic interests does not require, but rather contradicts, the imposition of absolute net risk limits.

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<sup>1</sup> They also separately draw on (Rid and Wendler 2011), but addressing that line is beyond the scope of this commentary.

## **2. Basic interests and moral powers**

MacKay and Saylor begin by signalling their acceptance of a Rawlsian picture on which society, including clinical research, is best conceived of as a system of fair cooperation whose terms are governed by justice.

On a Rawlsian conception, justice requires respect for each individual's possession of the two moral powers: the power to form and pursue one's own conception of the good, and the power to regulate that pursuit in light of mutually recognized demands of justice (Rawls 1999). Possessing these powers entails having a "basic interest" in securing the continuing conditions under which to exercise them. To illustrate, perhaps one finds fulfilment in the arts and loves the symphony. Another values life in nature and prefers to hike the woods. Regardless of these differences, both share the same basic interest in maintaining the personal freedom, disposable income, and other conditions that enable them to go through life deciding for themselves what to value and pursue. Justice requires cooperating under terms that secure this shared basic interest in the free exercise of our moral powers.

What does this picture imply for health? Morbidity and mortality can compromise a person's ability exercise their moral powers by forming, revising, and pursuing their individual life plans. Hence when participation in clinical research imposes risks of morbidity and mortality, it also threatens participants' basic interests. Of course, it may promote other people's basic interests at the same time, as current and future patients stand to gain from new medical knowledge. Still, MacKay, Saylor, London—and, for that matter, Rawls—all hold that equal regard for each person prohibits sacrificing some for the sake of others. MacKay, Saylor, and London additionally take this constraint to limit the extent to which individuals can justly be offered participation in risky clinical research.

What should we make of this argument? It is relatively clear how illness-related morbidity and mortality could threaten our basic interests (Daniels 2007). It is also relatively clear how an injunction against sacrificing the basic interests of some for the sake of others could make it impermissible to *force* anyone to participate in risky research. But, by contrast, it is not at all clear what that has to do with *allowing* people participate. To the contrary, it seems that maintaining the option of voluntary participation promotes our basic interests, insofar as the option itself affords us an important opportunity to exercise our moral powers, should we see fit. To see how, consider an example.

### **3. Choosing risks: HIV research**

The medical prospect associated with HIV cure research is often quite poor (Eyal 2017), yet there is support from people living with HIV for such research and interest in participation (Simmons et al. 2017). Why? One reason is identification with the goal of the research. Consider this description of being diagnosed with HIV and later deciding to participate in HIV cure research (Evans 2017):

*“It was so devastating when this happened to me... But now I think there's a reason. I'm supposed to do these studies... In a sense it's kind of a blessing... I figure if I'm going to have this then I'm going to do whatever I can to help someone, the next generation or the one after that. It would make something good out of something bad.”*

Taken at face value, this participant describes a moving exercise of Rawls' first moral power: in response to his changed circumstances, he revised his conception of the good to include being a man with HIV who participates in cure research.

Or consider these quotes, from hospice patients living with HIV who were unable to participate in HIV cure research due to their frail health (Gianella et al. 2017): *“I feel like these last few weeks are wasted;” “I wish I could do something else to help;” “At least I could be doing something.”*

Again, taken at face value, they appear to judge that participation in HIV-related research is the most meaningful thing they could be doing, and they appear frustrated by their exclusion. These judgments also look like an exercise of the capacity to reflect on, revise, and apply a conception of the good to their personal circumstances.

It appears that it is sometimes precisely the free exercise of their moral powers that explains why some potential participants might seek to undergo research-related risks. If so, restraining them from participation appears contrary to their basic interests: the restraint frustrates, rather than furthers, their ability to define and pursue their own conceptions of the good.

#### **4. The possibility of error**

Even if some people genuinely do value the opportunity to participate in high net risk research, not everyone does. Single quotes do not decisively diagnose anyone’s values. And general expressions of altruism are not equivalent to willingness to participate in any specific protocol with its array of serious risks. One might naturally worry, then, that regardless of whether high degrees of altruism are perfectly understandable in the abstract, the recruitment and consent processes of any given high net risk study will still struggle to pick out suitable individuals sufficiently reliably.

One might further conclude on these grounds that under realistic conditions, high risk research will inevitably end up with at least some people being enrolled by mistake. When mistaken, participation could not be explained as an exercise of anyone’s moral powers. Hence this objection could provide the missing connection between, on the one

hand, a Rawlsian commitment to protecting people's abilities to pursue the good as they see it, and, on the other, the practice of forbidding participation in high risk research *even for those who appear to take participation to be good as they see it.*

This worry contains an important grain of truth. Indeed, I have argued elsewhere that we ought to research risk in terms of how successful we think the research will be at recruiting *only* those participants for whom participation genuinely makes sense given their values and interests (Steel 2019). I even allow that concerns about the reliability of the recruitment process may *de facto* make some categories of high risk research impossible. But nonetheless, it will always remain open that the appropriate way to proceed is just to insist on sufficiently robust practices ensuring that participants appropriately value their participation. Sometimes those safeguards may be adequate, even for extremely risky research.

Hence, even once the possibility of error in identifying genuine exercises of the moral powers is taken into account, it remains unclear how the protection of participants' basic interests supports an absolute risk limit.

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