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**Context is needed when assessing fair subject selection**

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Mackay and Saylor provide a helpful taxonomy of different aspects of fair subject selection, dividing it up into four sub-principles: fair inclusion, fair burden sharing, fair opportunity, and fair distribution of third-party risks. (Mackay and Saylor 2019) These distinctions are worth highlighting because there will be tensions and conflicts between them, which investigators, research administrators, policymakers and others (hereafter, ‘practitioners’) must address in order to ensure human subjects research is conducted fairly. Mackay and Saylor, though, are not content to merely lay out a conceptual framework. They also offer a detailed account of how all the relevant conflicts should be resolved, resulting in a decision tree that in theory would be useful to practitioners, saving them the difficulty of engaging in complex moral reasoning on this issue.

However, Mackay and Saylor’s analysis of how to resolve conflicts between sub-principles is done without enough attention to how particular studies’ research questions, design, framing, and risk profile will affect the relative moral weight of fair inclusion, burden sharing, opportunity and third-party risk distribution in particular cases. The result is a ranking of relative moral importance of sub-principles that, in many cases, will result in all-things-considered unfair subject selection. We should prefer a context-sensitive approach that does not presuppose which sub-principles of fair subject selection will take priority in a given case. Such sensitivity will raise its own practical difficulties, but it is worth seeking systemic ways to ameliorate those difficulties in order to ensure that subject selection is as fair as possible.

**Inclusion above all?**

Fair inclusion, defined in terms of fairly benefitting members of society beyond just the study participants, is prioritised by Mackay and Saylor for most conflicts between sub-principles of fair subject selection. This is motivated by a well-taken point about scope: the value of fair inclusion is realized by study results that benefit a wide array of members of society, by generating generalizable knowledge that is salutary to the class of individuals. Fair inclusion is thus in line with the central reason research is conducted and (publicly) funded, namely, to produce socially valuable, clinically relevant research.

By contrast, the other three sub-principles affect a smaller subset of society (participants, or a limited group of third parties adversely affected by research), in ways ancillary to the primary purpose of research. Mackay and Saylor suggest that, in light of these differences, fair inclusion is more morally weighty, outside of exceptional circumstances where the burdens of research would be unacceptably high by threatening the basic interests of those burdened. (such studies that exceed the acceptable risk threshold would in any case be disallowed independent of any consideration of fairness, based on general considerations of risk minimization)

The difficulty with this analysis is that it presumes research generates a fixed, substantial social value that will in general outweigh competing, similarly fixed interests in fair access to research or fair distribution of its burdens. But both sides of the equation can and will vary considerably. Some studies may have weak study design, narrow research questions, lacking in clear implications for practice – in other words, have only marginal social value. Others could have the opposite, with robust designs, clear clinical translation pathways, addressing diseases of high priority, potentially being of very substantial social value.

Similarly for benefits and burdens to participants or third parties: there is much more at stake in ensuring fair access to a very promising drug for which there is no effective alternate treatment (as with antiretroviral treatments for HIV in the early days of the epidemic; see, e.g., Macklin and Friedland 1986) than ensuring fair access to a study’s $50 payment voucher. And even if we restrict analysis to those with ‘acceptable’ risks to participants and third parties, there will be considerable differences in burdens. For instance, while there may be some risk of re-identification when utilizing anonymized datasets (Henriksen-Bulmer and Jeary 2016), there will be much higher risks in using identifiable data.

These variabilities in turn affect how we should assess the relative moral importance of fairness sub-principles. For a high social value, low-personal benefit study, it may well be that the value of fair inclusion outweighs fair opportunity. But things are far less clear for a study with a very small social value but potentially very large personal benefits to participants. It could easily be in such cases that access needs to be prioritised over inclusion, given the relatively large moral weight of access in such a case compared with the social benefits of inclusion. The same applies to all the different types of sub-principle conflicts Mackay and Saylor described. We need to know a study’s details, evaluate its value, risks and benefits, before a determination about what fair subject selection sub-principles should take priority.

**Doing the hard work**

A pragmatic difficulty with the approach I suggest is that it requires substantial ethical deliberation and analysis on the part of practitioners, in contrast with Mackay and Saylor’s ready-to-use decision tree. Deliberation and analysis pose several problems.

Firstly, practitioners are not necessarily trained in the relevant ethical theories and methods of systematic analysis. A high degree of rigor is evident in, for example, Mackay and Saylor’s very thoroughgoing piece, but they are able to draw on years of dedicated bioethical study, training and reflection. While practitioners may have had some training in or experience with considered ethical analysis, it will often of necessity have been substantially more limited. Absent a clear rubric of analysis, they may not be able to reliably come to a well-reasoned determination on what constitutes fair subject selection in a given case.

Secondly, a proper ethical analysis may take substantial amount of time, as issues are raised, problems deliberated amongst colleagues, background literature is examined, and careful reflection occurs. While taking the time may produce value, it must be considered against how else the time may be spent. For researchers, it could be on improving study design and analysis, or on conducting more studies (both of which may contribute to the overall social value of their time spent).

Thirdly, leaving the analysis up to individual practitioners on a case-by-case may introduce substantial inconsistency into the adjudication process. Different practitioners will have different understandings of a study’s relative social value, of how much is at stake when access is denied, of how harmful a given burden really is, and so forth. Inconsistency is problematic insofar as it introduces an element of arbitrariness into the determination of whether a given study has fair subject selection, further undermining the reliability of such determinations.

**Coming together**

It is not all hopeless, though. Rather than adverting to a one-size-fits-all framework of sub-principle prioritization, we should look to systems that can mitigate the difficulties with case-by-case analysis. Indeed, one very useful system is already in place: ethics review. And while some have claimed research approval committees should eschew ethical analysis in favour of narrow enforcement of well-defined rules (Moore and Donnelly 2018), the present case of fair subject selection is an illustration of why ethics committees should go beyond the law and regulations: there are some issues that contextless general rules cannot adjudicate properly. (Schaefer 2018)

Addressing the first problem, ethics committees can bring relevant expertise to the table – not just in ethics, but in science, law, the humanities, as well as the lived experience of actual participants. And addressing the second, a dedicated committee can set aside time that busy researchers or policymakers may not have to adjudicate these issues – though the issue is not completely obviated, as researchers will still in the first instance need to propose reasonable selection criteria and recruitment methods.

The third problem, of inconsistency, remains an issue even for ethics committees, as there is evidence that different committees often come to very different determinations while reviewing the same protocol. (Trace and Kolstoe 2017) While some degree of inconsistency is inevitable and perhaps even desirable when ethics review takes place, (Friesen, Yusof, and Sheehan 2019) there may still be a need for greater inter-committee dialogue and adjudication. For example, members of different committees could convene to share actual case examples of subject selection dilemmas where two of the sub-principles conflict, and try to come to a consensus about the appropriate response. This could result in a case bank that serves as something like precedent to which future committees could refer when analysing new cases, promoting consistency without substantially sacrificing the importance of considered deliberation.

This is of course only suggestive, and there is not space in this brief commentary to delve further into appropriate mechanisms to promote robust ethical analysis. The main point is that preserving case-by-case analysis of the relative moral weight of sub-principles of fair selection is both desirable and, with the right level of systemic support, feasible. While Mackay and Saylor’s specification of the contours of fair subject selection is useful in this regard, a more context-sensitive approach is needed when actually adjudicating conflicts between sub-principles.

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