

# BEYOND CONSENT

SEEKING JUSTICE  
IN RESEARCH

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## 1 EXAMINING JUSTICE IN RESEARCH

### AN INTRODUCTION AND OVERVIEW

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Claims about justice in research abound. Patients with life-threatening, devastating diseases demand access to experimental treatments.<sup>1-6</sup> Advocacy groups' lobbying for funding for research on particular diseases and conditions increasingly play a pivotal role in designing and conducting research.<sup>7,8</sup> Federal research policies require accounting for the gender, race, and ethnicity of those enrolled in research.<sup>9,10</sup> Sponsors and researchers more commonly consider their obligations to research participants and their communities when research concludes.<sup>11,12</sup>

Those claims all point to a series of critical questions related to justice: What does fairness demand in terms of selecting the types of research that are conducted, and with which participant populations? Ethically and practically, which individuals and groups should be included and which excluded? Who should decide, and pursuant to what criteria? How should fairness be interpreted in regards to the distribution of benefits to those participating in research, and to the relevance of that research for society? What are the impacts and implications of both real and perceived injustices in biomedical research on recruiting and retaining research participants? On public perception of research? And, on health care for the population generally? Such questions are both conceptually and practically difficult. Nonetheless, ethically acceptable research is contingent on answers to these questions.

This is not to say that the importance of justice is only recently recognized. Indeed, justice has long been a crucial part of the ethical analyses of research. For instance, in 1979 the National Commission



for the Protection of Human Subjects of Biomedical and Behavioral Research specified in the *Belmont Report* the need to consider the principle of justice as well as the principles of respect for persons and beneficence.<sup>13</sup> The National Commission found two senses of justice to be important:

Who ought to receive the benefits of research and bear its burdens? This is a question of justice in the sense of "fairness in distribution" or "what is deserved." An injustice occurs when some benefit to which a person is entitled is denied without good reason or when some burden is imposed unduly. Another way of conceiving the principle of justice is that equals ought to be treated equally. (p. 23194)<sup>13</sup>

In the context of research, the National Commission invoked the principle of justice in determining the fair selection of subjects. That selection was considered at the individual and societal levels:

Individual justice in the selection of subjects would require that researchers exhibit fairness: thus they should not offer potentially beneficial research only to some patients who are in their favor or select only "undesirable" persons for risky research. Social justice requires that distinction be drawn between classes of subjects that ought, and ought not, to participate in any particular kind of research, based on the ability of members of that class to bear burdens and on the appropriateness of placing further burdens on already burdened persons. (p. 23196)<sup>13</sup>

Holding that view of justice, the National Commission characterized certain populations ("racial minorities, the economically disadvantaged, the very sick, and the institutionalized") as "vulnerable," thereby requiring special protection (p. 23197).<sup>13</sup> The dominant interpretation of justice used by the National Commission, as well as by many others wrestling with issues related to research with human subjects at that time, emphasized approaches that would protect against potential harms of being included in research.

Although the principle of justice has long been an important part of research ethics, its interpretation and accompanying applications continue to evolve. For example, it is now not uncommon for patients to desire access to experimental interventions and to demand access to research.<sup>2-3,6</sup> Here, justice is viewed as fairness in access rather than protection from risk. As such, there need to be considerations that go well beyond simply obtaining consent to the risks and burdens of that research: they must include creating

opportunities for fair access to research and its potential benefits, while simultaneously developing mechanisms of protecting subjects from exploitation. That balancing is a critical challenge for research ethics.

In other instances claims may be made for compensatory justice. For example, a broad claim for compensatory justice might call for additional research efforts directed at understanding the problems faced by groups, or classes of persons that have not had access to research in the past.<sup>14-17</sup> At an individual level, a claim for compensatory justice might relate to developing a means of compensating those who were in some way injured or harmed in the context of research.<sup>18-21</sup> Thus, a comprehensive assessment of research with human subjects necessitates incorporating multiple considerations of justice.

## Chapter Previews

The chapters in this volume offer an opportunity for in-depth examination of the concept of justice in research. At times, that requires making implicit aspects of justice more explicit. At other times, it requires examining why a particular approach to justice dominated public discourse and policy development.

Chapter 2 begins the examination, with Eric Meslin and Charles McCarthy sketching a history of the federal policy stance toward justice in research that followed from, among other events, the revelation of scandals in research with human subjects. Punctuating this history is a series of cases that, when brought to public attention, greatly influenced attitudes and approaches toward research. Some of the most notorious cases involve violations of justice in research: African American men in the Tuskegee Syphilis Study from whom treatment was withheld even after effective antibiotic therapies became available; elderly patients in the Jewish Chronic Disease Hospital who were injected with live cancer cells without their consent; and intellectually disabled children in the Willowbrook State School who were deliberately exposed to hepatitis. In such cases research subjects seem to have been selected because of their relative lack of power compared to other potential, and less vulnerable, research subjects. In each of those cases, the risks or burdens of participation were borne by the subjects, yet there was very little prospect of direct benefit to them. Indeed, in light of such cases, it is not surprising that the regulatory stance adopted pursuant to the United States' landmark National Research Act of 1974 was a protectionist one.

On the heels of the *Final Report of the Tuskegee Syphilis Study Ad Hoc Advisory Panel*, the National Commission for the Protection of Human



Subjects invoked two primary notions of justice: fairness in distribution of burdens and benefits, and equals ought to be treated equally.<sup>13</sup> Those notions provided conceptual support for the largely protectionist federal policy toward research. Nearly twenty years later, in response to a variety of forces and influences, research policies began to emphasize inclusion of research subjects—not only in terms of actual participation in research but also in terms of research design—in setting research priorities and making funding decisions. The shift in emphasis toward inclusion of research subjects has focused considerations of justice in somewhat different ways, with effects on not only who is included in research but how research is performed, reviewed, and overseen. Meslin and McCarthy examine those issues through the lenses of distributive, compensatory, and procedural justice, and the various relevant actors for each.

Following that historical overview are a series of chapters, each examining how the concept of justice has been either ignored or applied in the selection of particular groups of research subjects, with suggestions about how the concept should be applied today and in the future. The groups examined include patients, persons with cognitive impairment, children, women, racial groups, captive and convenient groups, communities, and global populations. Of course, those groupings overlap, sometimes substantially, challenging the ability to characterize every relevant consideration of justice for any particular grouping. The text's overall examination does not capture the full range of relevant considerations that must be given to other important populations, such as people with disabilities, the elderly, and LGBT (lesbian, gay, bisexual, and transgendered persons)—groups that have largely eluded special attention regarding inclusion in research, despite their unique concerns. In addition, the claims and uses of the concept of justice vary across the chapters, demonstrating the complexity—and utility—of the concept. This should not be terribly surprising, since such divergent claims have long been part of conceptual work on justice. In the *Nicomachean Ethics*, Aristotle used two definitions for justice: (1) "the whole of virtue" and (2) "fairness in distribution."<sup>22</sup> The remaining chapters in this volume examine and apply each or both definitions in their focus on particular populations.

In Chapter 3, Baruch Brody and Neal Dickert examine questions of justice from the perspective of the vulnerable sick. In this context, they touch on some competing values of justice: the social need for research, potential benefit to subjects, and their protection from exploitation and harm. In actual cases none of those values is controlling on its own. Rather, Brody and Dickert

argue that a "balancing" conception of those values, and of the competing claims of protection and access, must be employed.

The authors use the balancing conception in examining three cases, engaging policies that reflect this conception of justice. First, they consider the conduct of research on acute, emergent illnesses, such as heart attacks and strokes, where clinical circumstances may preclude obtaining informed consent. Despite a strong moral obligation to obtain informed consent for research, the competing values of access to experimental treatments that may benefit the subject and the social need to conduct this research must also be considered, and in so doing, highlight the complexities of that context. Second, in describing the push for effective treatments for HIV infection and cancer at times when prognoses are poor, Brody and Dickert demonstrate how the balancing conception of justice accommodates the desperate claims of those patients for whom there is not an established effective treatment with the social need for sound scientific data so that other persons are not exposed to the risk of experimental treatments that have not been adequately tested. Third, Brody and Dickert examine Phase I oncology trials, using the balancing conception of justice to suggest alternative trial designs that may be more commensurate with the concerns of patient-subjects than those that employ traditional designs.

In Chapter 4, Scott Kim examines and analyzes questions about when and under what criteria research participation by individuals with progressive loss of cognitive function could be ethically acceptable, focusing on patients with Alzheimer disease (AD). Kim first examines the history of research involving human subjects with decisional impairment, focusing on the injustices experienced by them, and the longstanding absence of policy directed at the inclusion of decisionally impaired individuals in research. Until relatively recently, those abuses took place in research that was unrelated to participants' primary condition of cognitive impairment. Those injustices are now being addressed by ensuring that those with decisional impairment are excluded from research when the research can instead be performed with participants capable of consent.

Kim notes, however, that there remains an unprecedented need for more research on diseases, ailments, and treatments related to decisional impairment, and therefore a need to create ethically acceptable (including more equitable) approaches for research participation by those with AD and other decisional impairments. He examines the merits and practical considerations of using families and intimates as surrogate decision-makers, followed by important policy recommendations to prevent unjust exclusion of individuals with decisional impairment from research participation.



Chapter 5, authored by Lainie Friedman Ross and Robert Nelson, raises some of the challenging aspects of justice in research involving children. On the one hand, our intuitions may weigh on the side of protection since children are not able to provide meaningful informed consent to participate in research. On the other, such a stance would preclude children from the potential benefit of research, both as individuals and as a group. Just as in the case of emergency research with adults who are not capable of giving consent, at an individual level certain children would be deprived of the possibility of benefiting from new therapies if research is not permitted. Moreover, if research with children is not conducted, children, as a group, will subsequently not have access to safe and effective treatments.

Despite those real concerns, the history of research with children, along with our intuitions that children ought to be protected, suggest a need for a balanced and considered approach. Ross and Nelson begin the chapter with an account of some of the most notorious cases in research ethics involving institutionalized children: the aforementioned Willowbrook study, where subjects were infected with hepatitis, and studies at the Fernald School where subjects were fed radioactive oatmeal. Given cases such as these, it is not surprising that federal regulatory policy historically leaned toward protection, delineating the limited situations in which research with children would be acceptable. Considerable controversy surrounds this approach since other standards may be more responsive to claims about justice that support increased access and greater inclusion of children in research. Other standards might set the level of acceptable risk differently, such as at the level of risks encountered in daily life, the level of risk determined by individual parents to be acceptable, or simply at whatever risk is assented to when a child reaches a specific age. Controversies surrounding the determination of whether it is acceptable to conduct clinical research in a range of pediatric populations, and with a range of therapies or therapeutic approaches, make it clear that understanding those competing methods of determining risk is critical. Even with more recent policy pronouncements promoting the inclusion of children in research, the extent to which children are both given access to, or are protected from, research hinges upon such an assessment of risks.

Chapter 6, authored by Nancy Kass and Anne Drapkin Lyerly, shifts the focus to women. As in the case of children, until relatively recently, many women had not been included in research. One explanation is founded in notions of fetal protection—a presumption that every woman could become pregnant during a research study, potentially subjecting a future child to an otherwise avoidable risk of harm. Such a stance might not seem terribly surprising in the wake of the tragedy of the early 1960s in which women who had

received thalidomide outside of the clinical trial context while they were pregnant later gave birth to infants with severe malformations. Other explanations for excluding women from research focus on cultural factors (such as the assumption that male functioning is the “normal”), liability concerns of research sponsors related to potential fetal harm, and a lack of female leadership in science and medicine.

Historical justifications aside, as in the case of children, such an exclusion may affect women as individuals and as part of a group when it comes to their ability to receive safe and effective medical care. Kass and Lyerly use three case examples to demonstrate a range of important considerations regarding justice and women in research. Those examples are derived from research in cardiovascular disease, HIV disease, and pregnancy. In the aggregate, the examples suggest the ongoing need to attend to the appropriate inclusion of women in research. As in the case of the vulnerable sick and with children, this conceptual move from protection to access is mirrored in regulatory and policy statements that should continue to have an influence on the conduct of clinical research.

In parallel with initiatives to include more women in research has been the promulgation of policies to enhance the representation of members of racial and ethnic groups in research. Such is the focus of Chapter 7, authored by Patricia King, which considers issues of race and justice in research, with an emphasis on African Americans. She argues persuasively that implementing justice in that context requires an understanding of African Americans’ experiences not only in research but also in society and health care. Her examination of three research cases underscores the pervasiveness of racism present in society—in research practices, institutions, decision-making, and protections. King illuminates the legacy of degrading and exploitative experimentation and research in the African American community, most notably the Tuskegee Syphilis Study but also the saga of the HeLa cell line derived from Henrietta Lacks’ cervical cancer and the more recent lead paint study conducted by the Kennedy Krieger Institute in Baltimore. She notes that the African American community’s distrust of the research infrastructure is not surprising.

King, who participated in the drafting of the *Belmont Report*,<sup>13</sup> argues for a reexamination of the report’s articulation of distributive justice. That ethical calculus hinges on the fair distribution of risk. In that calculus, the need to protect those who are deemed to be vulnerable, in terms of their prior education, socioeconomic status, or relative lack of power, deserves special attention. While concerns about vulnerability are essential, overprotection combined with a lack of trust in the research community may result in



a failure to properly address the health needs of those in racial and ethnic groups—clearly another relevant concern about justice. More guidance is needed to attend to inherent power differentials in the researcher-participant relationship and to counter the prevalence of implicit racial bias in research, including the tendency to rely on biological explanations for differences.

Examining issues such as race and racism in research and attending to the important moral claims of those who face other forms of stigma and discrimination make clear the need to consider justice in regards to communities as well as individuals. In Chapter 8, Katherine King and James Lavery review the growing recognition of the roles of communities in research. The power of communities to shape the research enterprise and address concerns related to justice is exemplified by HIV/AIDS activism, which contributed to accelerated pathways for drug approvals and the formal engagement of communities in the research process. On the other hand, the lack of community engagement has contributed to harms in settings such as research with aboriginal populations and genetic research.

King and Lavery present alternative approaches to community engagement, including participatory research, community advisory boards, and direct engagement. As an ethical matter, community engagement serves to extend respect beyond the individual. As a pragmatic matter, those forms of community engagement can help identify risks and benefits that might otherwise be overlooked, thus prompting attention to their mitigation or enhancement, as appropriate, and ultimately furthering research integrity.

In Chapter 9, Jonathan Moreno reflects on the ethical tensions that implicate justice considerations when research includes captive and convenient populations. Prisoners are the paradigmatic example. Prior to the 1970s, prisoners participated in a large number of clinical studies, and were compensated for that participation. Thereafter, when regulatory amendments addressed ethical concerns about exploitation, with particular focus on prisoners' ability to freely consent to participation in a potentially coercive and hierarchical environment, research involving prisoners plummeted. The characteristics of research involving prisoners are relevant for research with other convenient and captive populations as well, including other institutionalized persons, military personnel, and those in status relationships involving power differentials and hierarchical authority, such as students and employees. Decision-making challenges of some institutionalized persons may be further compounded by the condition that prompted their institutionalization, such as profound intellectual disability or debilitating psychiatric illness. Moreno stresses the contribution of historical perspective in his examination of justice in each of those convenient or captive populations. He

includes condemnation of recently revealed studies conducted by the United States in Guatemala, which spanned populations that qualify as convenient or captive: prisoners, soldiers, and institutionalized psychiatric patients and Hansen disease patients.

Questions raised by research with convenient and captive populations not only involve distributive justice (i.e., the fair distribution of the burdens and the benefits of research) but also implicate procedural justice, in which the abilities of those to make decisions may be compromised due to their circumstances. While concerns about appropriate protection of such populations are obvious and, to Moreno, rise to the level of a presumption of protectionism, he acknowledges that justice may require research in those populations in limited circumstances to ensure that benefits accrue to them, both to individuals and to the group as a whole. As has been demonstrated in other populations that have been excluded from research studies, without clinical research little will be known about conditions that are unique to these groups.

In Chapter 10, Ruth Macklin delineates some of the vexing justice issues associated with global health research, including the challenges of balancing protection and access, and risks and benefits. The chapter dissects the ethical acceptability of "double standards" in research—whether it is appropriate, for example, for a risk-benefit calculus to vary based on the wealth status of a study site, employing different standards for resource-poor countries versus industrialized countries. Using this lens, Macklin highlights the difficulties inherent in determining whether research is just or unjust. Using three cases, she examines whether there are there circumstances in low- and middle-income countries that are distinctive enough from those in industrialized countries to justify the applications of different ethical standards in research.

The chapter also examines the controversial topic of post-trial responsibilities. When products are ultimately successful, what obligations do sponsors from industrialized countries have to the individuals and communities in which the research was conducted? Perspectives differ, and critics raise competing allegations of paternalism and exploitation. Macklin next focuses on procedural justice considerations, providing examples of when slavish attention to procedural review requirements mandated by the United States may unjustly fail to account for cultural differences internationally.

Armed with those rich descriptions of how justice has been and might be applied in particular populations, in Chapter 11 Yashar Saghai addresses some of the conceptual aspects of justice that seem most relevant to its application in the context of research with human subjects generally. He starts by assessing the usefulness and applicability of principles of justice to examples



of research ethics discussed in the other chapters, and highlights aspects he believes will be most salient for more general application. Saghai then lays out the case for a different and complementary approach, which is to examine theories of justice and their applicability to justice issues in health research from both US and global perspectives. He makes the argument that this latter move has the value of applicability to a wider range of topics to be considered within the scope of health research, from basic biomedical sciences to clinical research, public health and health policy, research on health systems, and health-related social and behavioral sciences.

With this conceptual scheme before us, in Chapter 12 we suggest how to pursue and implement justice in the context of research. Such decisions need to be made explicitly at each stage of the research process, ranging from the decisions about research priorities and formulation of research questions, to the design and conduct of research, and the dissemination and use of research findings. Moreover, this effort must involve a wide range of participants in the research enterprise, including researchers, research subjects, IRB members, institutional administrators, policy makers, public and private funders, and pharmaceutical companies. The realization of justice in research will only be achieved through its consideration at every point in the process by all relevant actors.

The chapters in this edition continue, we hope, to advance the discussion of justice in research. Only through such ongoing reflection and related policy action can issues be appropriately addressed, whether they are longstanding and tied to history or newly confronted and resulting from advances in biomedicine, technology, globalization, and other future challenges arising in research.

## Notes

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