PART I

DOES RESEARCH ETHICS REST ON A MISTAKE?

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Introduction

1.1 Neglected Foundations

The philosophical foundations of research ethics are underdeveloped and riven with fault lines that create uncertainty, ambiguity, and disagreement. The goal of this book is to rethink these foundations and to articulate an alternative in which research is recognized as a collaborative social activity between free and equal persons for the purpose of producing an important social good. Research is a collaborative activity, in part, because it requires the cooperation of a wide range of stakeholders, often extended over time, and often mediated and facilitated by basic social institutions. These institutions impact the rights and welfare of community members and employ a range of scarce social resources. The information that research produces is a social and a public good because it constitutes the evidence base on which a range of stakeholders rely to make decisions that impact the rights and welfare of individuals and that influence the capacity of basic social institutions to safeguard the health, welfare, and rights of persons. It is my contention that research with human participants is thus connected to social purposes of sufficient moral weight that they ground a moral imperative with two aims. The first is to promote a research enterprise that produces information that bridges important gaps between what I refer to as the basic interests of community members and the capacity of the basic social institutions in their community to safeguard and advance those interests. The second is to ensure that, as a voluntary scheme of social cooperation, the research enterprise is organized on terms that respect the status of its many stakeholders, especially study participants, as free and equal.

Defending every aspect of this vision is a larger project than I can complete here. As a result, my main constructive goal is to show that the conception of research ethics articulated here is coherent, that it dissolves or addresses deep tensions at the foundation of orthodox research ethics, and that it places many existing norms and practices on a firmer foundation while fruitfully expanding the purview of the field. It accomplishes these goals, in part,

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by understanding the research enterprise as a voluntary scheme of social cooperation that both calls into action the basic social structures of a community and generates the information on which elements within these social structures rely to advance the basic interests of the community members whose life prospects they shape and influence. As a result, this framework foregrounds issues of justice and fairness that have been neglected within orthodox research ethics.

To establish the need for this constructive project, the main critical goal of this book is to highlight flaws in the conceptual foundations of contemporary research ethics and to illustrate how they threaten to undermine some of the hard-won progress the field has achieved in only a few decades. These flaws are powerfully illustrated in chapter 3 by a series of arguments that are forged out of the foundational values and principles of research ethics, but which effectively undermine a wide range of common requirements that those foundational values are seen as grounding. These arguments reveal a conceptual instability that calls into question the coherence of current requirements and practices. Examining these tensions also reveals arbitrary and often unhelpful limits on the scope of issues that are seen as falling within the purview of the field and on the set of conceptual resources that are used to address them.

In §1.2 I briefly outline eight problematic commitments that shape the conceptual ecosystem of orthodox research ethics and that are discussed at greater length in chapter 2. By the "conceptual ecosystem" I mean the interconnected set of often tacit assumptions that structure the field in the sense that they determine the scope and limits of its purview, the stakeholders whose conduct warrants assessment and oversight, and the terms in which core problems are framed and out of which possible solutions can be crafted. It is against this background set of assumptions that certain ways of formulating problems appear salient or intuitive, certain values appear relevant, and certain strategies for resolving problems appear promising and appealing or irrelevant and inauspicious. Whether they are explicitly stated or tacitly assumed, these eight commitments often reinforce one another and make certain views seem natural and intuitive. Their influence in orthodox research ethics is a recurring theme throughout the book, and it is my contention that we should reject all of them.

Starting in §1.3, the rest of the chapter provides a detailed summary of the core components of the positive program I defend in subsequent chapters. My hope is that this introduction will highlight some of the key respects in which the positive program that I defend here departs from orthodox research ethics and that it will provide a useful roadmap to the main contributions in subsequent chapters of the book.

1.2 Eight Problematic Commitments

1.2.1 An Inherent Dilemma

In this section I outline eight problematic commitments that shape the conceptual ecosystem of orthodox research ethics. One goal of this section is to make these commitments explicit so that it is easier to identify when they emerge in subsequent chapters and to track their influence on a range of issues. Another goal is to bring the outlines of my positive program into sharper relief by explicitly stating some of the often tacitly held positions that it rejects.

First, research ethics has been shaped both practically and conceptually by the widespread perception that there is a fundamental moral dilemma inherent in research involving human participants. This dilemma is expressed in various terms in different contexts. During formative debates that shaped the foundations of the field—discussed in chapters 2 and 4—it was framed as a conflict between the good of the individual versus the common good. In the discussion of high-profile cases of abuse or in guidance documents—discussed in chapters 2 and 5—it is cast as a conflict between respect for the sanctity of the individual versus concern for humanity and the science that will improve the lives of large numbers of future people. In conversations about the reasonableness of research risks—discussed in chapters 5 and 6—it is framed as a conflict between the clinician's duty of personal care and the utilitarianism of the research enterprise.

The idea that research with humans involves a deep moral dilemma helped to shape the origins of the field because it structured the way that both proponents and critics of research oversight framed what was at stake. Early critics of research oversight often treated medical research as an activity with a larger social purpose and argued that this larger social purpose created an imperative to promote research in order to advance the common good. However, because they saw the relationship between the common good and the good of individuals as one of direct conflict—in which efforts to advance one good necessarily required compromising the other—the early critics of research oversight often asserted that the research imperative grounded, if not a duty to override the rights and welfare of individuals, then at least a moral permission to do so. As Walsh McDermott notoriously claimed, "When the needs of society come into headlong conflict with the rights of an individual, someone has to play God" (1967, 39).

In chapter 2 I show that proponents of research oversight and regulation tended to accept this way of framing the problem at least to the extent that they shared the assumption that if appeals to the common good grounded a moral imperative to carry out research with humans, then this imperative would license the abrogation of individual rights and interests. Whereas researchers like McDermott regarded playing God as a part of their rightful social responsibility, proponents of research oversight sought to erect formidable deontological bulwarks around the rights and interests of study participants to protect them from overreach.

The most influential of the early proponents of research oversight, Hans Jonas (1969), went the furthest. He too accepted the claim that if there is a social imperative to conduct research with humans grounded in its ability to advance the common good then it would have sufficient moral force to override the rights and interests of study participants. But Jonas made the bold claim that the antecedent of the conditional is false. In other words, Jonas rejected the claim that research advances the common good and argued that there is thus no social imperative to conduct research with humans. Making this move severed the connection between research with humans and morally weighty purposes that might ground a moral imperative of sufficient weight to override the rights and interests of individuals.

1.2.2 From Social Imperative to Private Transaction

The second commitment that shapes the conceptual ecosystem of orthodox research ethics is that it tends to treat the research enterprise as a morally optional activity of private parties. In chapter 2 I argue that, to some degree, this attitude reflects the success of Jonas's argumentative strategy—if research is not tied to the common good and a moral imperative in the public sphere, then it must be an undertaking in the private sphere that advances more parochial ends. But this attitude likely also reflects the highly pragmatic nature of research ethics and the fact that in the United States it emerged as a distinctive field of inquiry in response to revelations of scandal and abuse at places like Tuskegee, Willowbrook, or the Jewish Chronic Disease Hospital.

Chapter 2 provides a brief introduction to some of the institutions, policies, and regulations created in the wake of these revelations of abuse and suggests that they have contributed to what I refer to as the parochialism of the field. This includes a relatively narrow conception of who the key stakeholders in research are, of the purview of research ethics, and of the terms in which problems in this space are formulated and in which their resolutions are to be crafted.

1.2.3 Two Main Stakeholders

A third aspect of the conceptual ecosystem of orthodox research ethics reinforces the parochialism of the field by framing the moral epicenter of research as falling within what I call the *IRB triangle*, namely, the discrete interactions of researchers and participants that are reflected in study protocols; informed consent forms; and that are evaluated by an Institutional Review Board (IRB), sometimes referred to as a Research Ethics Board (REB) or a Research Ethics Committee (REC). If research has a deep moral connection to a network of social purposes that constitute the common good, then the boundaries of the field cannot be so narrowly constrained. If nothing else, there would have to be some consideration of whether the initiatives and programs that are funded are aligned with and likely to advance these larger social purposes, and such considerations would be likely to implicate the activities of a much wider range of stakeholders. Severing research from these larger social purposes and treating the IRB as the primary focus for moral evaluation limits the focus of the field to issues that arise from the review of individual study protocols and that revolve around the discrete interactions of researchers and study participants.

Treating the IRB triangle as the moral epicenter of research ethics has a number of consequences. In chapters 4 and 7 I show how it treats the activities of a range of stakeholders as falling outside the purview of the field. This includes stakeholders who exert influence on research prior to the formulation of individual protocols or after individual studies are complete. In chapters 4, 7 and 8 I focus specifically on how it encourages the view that the primary moral concerns in the field arise within one-time or single-shot interactions between private parties and that the primary, if not the exclusive, focus of research ethics is on the terms that IRBs use to regulate these interactions. This focus is inadequate, in part, because there are a range of ethical issues that fall squarely within the nexus of concerns that are recognized in orthodox research ethics that simply cannot be addressed through the evaluation of individual protocols (§4.9). More fundamentally, as I show in chapters 2, 4, 7, and 8, this frame obscures the extent to which research is a cooperative social endeavor, extended over time, involving numerous parties, and that the regulation of this activity is an exercise in what economics calls mechanism design—the design of institutions and rules that regulate the conduct of multiple stakeholders and that fundamentally shape the strategic environment in which they interact. This strategic environment includes the goals they are likely to pursue, the constraints on their pursuit, and the incentives that are used to shape stakeholder conduct.

1.2.4 Research as Functional Role

Fourth, the parochialism of orthodox research ethics has been nourished by a tendency to conceptualize research in functional terms. In other words, research ethics tends not to treat research as a social activity involving the distribution of labor across multiple stakeholders over long periods of time. Instead, it treats research as a function—a set of goals and purposes—that an individual adopts or pursues, often in contrast to the goals and purposes that are treated as definitive of clinical medicine.

This functional understanding of research helped to facilitate research oversight by demarcating when a particular individual is acting as a caregiver versus when they are acting as a researcher. In chapter 2 I show how early scandals that shaped the development of the field involved researchers using prerogatives that they enjoyed by virtue of their role as caregiver to advance the ends of research. So, it was useful to demarcate the role of caregiver as making decisions around the goal of advancing the medical best interests of the individual patient while demarcating the role of researcher as making decisions around the goal of generating generalizable scientific knowledge. Conceptualizing research in these terms also allows it to be represented as an activity that fits neatly within the bounds of the IRB triangle. Although this has a certain practical utility, it reinforces a view of the field in which larger social connections, including issues of justice, are difficult to make salient.

In chapter 5 I show how this way of framing matters reinforces the perception that there is an ineluctable dilemma at the heart of research. When research and medical care are understood functionally, they are treated as two sets of goals, purposes, and constraints that are adopted by a single decision maker. Because these goals and constraints are conceptually or logically distinct, they appear to make incompatible demands on the individual professional. If the same decision maker cannot simultaneously maximize what are represented as competing and incompatible demands, then there appears to be a deep dilemma at the heart of research ethics. This idea has played a significant role in structuring discussions of risk in research including the formation of the concept of equipoise and discussions of its strengths and weaknesses.

1.2.5 Two Dogmas of Research Ethics

This functional treatment of research and medicine is closely connected to a fifth feature of the conceptual ecosystem of orthodox research ethics, namely, the widespread acceptance of what I refer to in chapter 5 as two unquestioned dogmas of research ethics. The first is that the fundamental norms in this domain are grounded in, and derive from, the role-related obligations of medical professionals. In particular, to be a clinician is to occupy a social role that is defined by a singular commitment to advancing the medical best interests of the individual patient. The second is that research is an inherently utilitarian activity. To be a researcher is thus to occupy a social role defined by a singular commitment to advancing the ends of science.

Conceptualizing research this way allows it to fit neatly into the confines of the IRB triangle without having to appeal to larger social relationships or obligations, facilitating the practical goals of research oversight. But understanding research and medical practices as goals and ends that are adopted by individuals, abstracted away from any larger division of social labor, makes it appear almost true by definition that research generates a thorny social dilemma by requiring compromises to individual welfare that are inconsistent with the individual clinician's fiduciary duty of care.

1.2.6 Paternalistic Foundations

The sixth feature of research ethics I want to call into question is the widespread perception that its central purpose and normative justification are fundamentally paternalistic. Against the background assumption of an inherent conflict between the interests of study participants and the goals of science, research ethics is naturally portrayed as having one moral purpose—to protect potential and actual study participants from harm or abuse at the hands of researchers. Outside oversight is required because research activities are seen as inherently in conflict with the best interests of study participants and because the complexities of research make it difficult, if not impossible, for study participants to effectively safeguard their own interests.

In chapter 7 I show how understanding the purpose and justification for research ethics in fundamentally paternalistic terms plays a critical role in shaping which issues fall within the scope and purview of research ethics. If the reason for the existence of this field is to protect the rights and interests of study participants, then issues that cannot be cast in terms of safeguarding the interests of study participants are invisible, or must be shoehorned into such terms in order to be seen as relevant. Once again, which questions research addresses, which methods are used to answer those questions, where research takes place, and how the information generated from this process is later used must either be cast as issues related to study participant welfare or be treated as falling outside of the purview of the field.

1.2.7 Justice without Social Institutions

The seventh feature of orthodox research ethics, illustrated in chapter 2, is a conceptual ecosystem in which considerations of justice have almost no substantive role to play. This is ironic in two ways. First, influential documents in research ethics, such as the *Belmont Report* (discussed in detail in chapter 2), list justice as one of the core values or principles of research ethics, alongside respect for persons and beneficence. There it is also recognized that injustice can arise from the way research is embedded in larger social systems. For example, the *Belmont Report* states that "whenever research supported by public funds leads to the development of therapeutic devices and procedures, justice demands both that these not provide advantages only to those who can afford them and that such research should not unduly involve persons from groups unlikely to be among the beneficiaries of subsequent applications of the research." Second, as the philosopher John Rawls (1971, 3) famously said, justice is the "first virtue of social institutions" and research is a social activity that involves a complex division of social labor, carried out over time, often with the participation of important social institutions, and often with the goal of improving the capabilities of actors or agents within those social institutions.

But when research is understood in purely functional terms, and the moral epicenter of the field is located in discrete interactions between researchers and participants, considerations regarding the terms on which important social institutions operate fall entirely outside the purview of the discipline. For example, there is no discussion in the *Belmont Report* about how the use of public funds should shape the priorities for, or nature of, the research that is carried out with those funds. There is a tacit assumption either that research always produces socially valuable knowledge, or that forces external to research ethics—such as the profit motive of firms, the desire for credit on the part of researchers, or some larger humanitarian impulse on the part of each of these parties—are sufficient to ensure that public funds are directed to socially valuable purposes. Notice, however, that if those funds are instead used to support research that is lucrative for firms but lacks social value then the requirement quoted previously from the *Belmont Report* would entail, perversely, that the use of public funds requires that this low-value intervention ought to be made available to those who are unable to pay for it, presumably through some form of social subsidy. This is perverse to the extent that it would require scarce resources to be directed at the purchase and delivery of an intervention that generates revenue for a private actor without producing sufficient social value to warrant its provision.

Although tensions of this sort are often not salient in the context of domestic research, they emerge with powerful force when we turn to research that is sponsored and conducted by entities from high-income countries (HICs) but carried out in communities from low- or middle-income countries (LMICs). As we see in chapters 3 and 8, guidelines governing international research stipulate a range of requirements that implicate the activities of a broad set of stakeholders and that are grounded in the value of justice. One of these requirements holds that research that is carried out in LMICs must be responsive to the health needs and priorities of host communities. Another holds that prior to the initiation of such research, a wide range of stakeholders must agree to the terms on which the fruits of successful research will be made reasonably available to members of the host community. Without a conception of justice as a value that governs the operation of social institutions and their effects on the rights, liberties, and interests of community members, research ethics has struggled to provide consistent justifications for and interpretations of these requirements.

International research represents a context in which it is clear that powerful parties can influence the conduct of research to advance their own interests to the detriment of other stakeholders, including the communities that host such research and the individuals who participate in it. But when research is understood in functional terms, divorced from a larger division of social labor involving diverse parties with their own often quite powerful parochial interests, the field struggles to articulate the moral purpose of research and, with this, the reasons that it is a moral wrong to co-opt the research enterprise to advance the parochial interests of powerful parties. Without established criteria for connecting the research enterprise to some larger social purpose—to some notion of the common good—it is difficult to hold these diverse parties accountable for advancing, or subverting, such larger social purposes.

1.2.8 Reducing Justice to Mutually Beneficial Agreements

Finally, stripped of a diverse set of actors whose activities are morally beholden to some larger set of social purposes, I show in chapters 2 and 8 how research ethics has operationalized justice in terms that reduce it to the satisfaction of the other values that come to function as the twin pillars of research ethics—respect for persons and beneficence. The pragmatic desire to avoid controversial philosophical questions about the nature of justice encourages the tacit acceptance of what I refer to as the minimalist approach to justice. On this view, justice is a function of beneficence and respect for autonomy in the sense that discrete transactions between researcher and participants are regarded as just if they are mutually beneficial and freely undertaken. Although this allows issues of justice to be formulated in a way that fits neatly within the confines of IRB deliberations, reducing justice to a function of the other pillars of research ethics severs important connections between the research enterprise and the institutions of a decent social order.

The allure of this kind of view has been felt most keenly in the context of international research where an approach to the evaluation of cross-national clinical trials with many of these features has been articulated under the banner of the “fair benefits” approach (Participants 2002, 2004). The way that this view follows naturally from core commitments of orthodox research ethics is discussed in chapter 8. Proponents have advocated for this approach on the basis of its ability to satisfy a set of intuitive requirements such as ensuring that benefits to participants and host communities increase as the burdens of research increase, that benefits to sponsors should increase as the benefits to others increase, and that the benefits various parties receive should track their relative contributions to research. Even if these are regarded as ethically appropriate constraints on international research, I argue that there are no grounds to think that the fair benefits approach will jointly satisfy these requirements and that there are compelling reasons to believe that the fair benefits approach will operate in practice in ways that flout each of these requirements.

International research has been at the epicenter of protracted and sometimes divisive debates in research ethics for more than three decades. One reason for this is that the parochialism of orthodox research ethics relied heavily on tacit assumptions about the way that domestic research would connect to a set of domestic institutions and practices whose governance and regulation are treated as falling outside of the scope of the field. When biomedical research began moving in volume from HICs of the Global North to LMICs of the Global South, many of these tacit assumptions could no longer be maintained. As a result, research ethics struggled to find ways to align its overriding focus on ethical issues that arise within the IRB triangle with highly salient concerns about the way that research in settings of deprivation and injustice can be morally problematic. These struggles are discussed in chapters 2 and 8.

The allure of the fair benefits approach, as well as the problems that it faces, stem from tensions latent in the problematic commitments of orthodox research ethics that I have summarized here. The depth of these tensions is illustrated dramatically in chapter 3 in provocative work by Alan Wertheimer. In particular, Wertheimer has argued that even if certain transactions in research are unfair, unjust, or exploitative they should not be prohibited. Instead, “there should be a very strong presumption in favor of principles that would allow people to improve their situations if they give appropriately robust consent, if doing so has no negative effects on others, and this even if the transaction is unfair, unjust, or exploitative” (Wertheimer 2008, 84).

Although the position that Wertheimer articulates is unlikely to garner significant support in the mainstream research ethics community, its philosophical relevance should not be underestimated. Wertheimer's view draws on core assumptions of orthodox research ethics, but from these assumptions it derives conclusions that undermine the field's paternalism and a range of requirements that are typically seen as grounded in this normative foundation. In particular, Wertheimer's view adopts the near exclusive focus on the relationship between researchers and participants that typifies orthodox research ethics. It treats the relationship between these parties as largely private, unmoored from larger social purposes and the imperatives they might ground. Instead, it emphasizes the fundamental importance of the twin pillars of research ethics—namely, the voluntary and informed consent of participants and beneficent concern for welfare understood as requiring a mutually beneficial distribution of a potentially wide range of benefits and burdens.

In effect, Wertheimer uses the core commitments of orthodox research ethics to undermine the deontological bulwarks that are a hallmark of the field. Without a social imperative to conduct research, researchers have broad discretion about whether and with whom to partner in conducting clinical trials. In such a context, strong norms against exploitation, or other forms of unfair, unjust, or disrespectful treatment effectively erect a barrier to conducting studies among desperately needy people by raising the "cost" of conducting such studies. If researchers decide to take their studies elsewhere (depriving potential participants of the associated benefits), this safeguards a vulnerable population from exploitation and unfairness but leaves them prey to the ravages of lethal neglect. But if desperate individuals prefer, and so would choose, exploitative or unfair but beneficial interactions to potentially lethal neglect, then Wertheimer's position—that we ought not to prohibit exploitation even if it is morally wrong—follows from the two values that remain as the pillars of traditional research ethics, namely, beneficence and respect for autonomy. If there is something morally suspect with this conclusion then it reflects a deeper problem with the way the core commitments of orthodox research ethics have evolved in the conceptual ecosystem I describe here.

Wertheimer's revisionist arguments highlight a deep tension in research ethics between the way it balances three moral pitfalls. The first pitfall involves sanctioning neglect. For Wertheimer, erecting deontological barriers around the interests of people who are in desperate situations may protect them from wrongdoing, but it leaves them vulnerable to poverty and disease. The second pitfall involves sanctioning wrongdoing. Orthodox research ethics errs on the side of neglect because of the worry that connecting research to larger social purposes will involve sanctioning wrongdoing in the name of social progress. In contrast, Wertheimer defends permitting some wrongdoing in order to allow desperate people to advance their interests in the face of potentially lethal neglect. The third pitfall is that it is unfair to saddle a narrow range of stakeholders with overly demanding moral requirements. This concern is evoked with special intensity by the prospect that if research ethics requires researchers and sponsors to rectify larger injustices in the world, then it will simply lead them to avoid research in LMICs, consigning more people there to the ravages of neglect.

The eight views just discussed represent sometimes explicit but often tacit presuppositions of orthodox research ethics. They provide the intellectual background that sets the terms in which problems are articulated, the parameters on what an acceptable resolution will look like, and the nature of the considerations that are germane to analysis and reasoning. It is my contention that each of these positions is problematic and the positive program I outline in this book rejects them all.

1.3 The Common Good and a Just Social Order

1.3.1 The Basic Interest Conception of the Common Good

The positive program that I defend here understands research as a scheme of social cooperation that is one small element within a much larger division of labor. In chapter 4 I argue that the role of this larger division of social labor in a just social order is to advance the common good, understood not as the preservation or perfection of the community as an aggregate entity, but as a set of interests that are shared by all persons. In particular, although individuals in a diverse society are likely to embrace different and potentially conflicting conceptions of the good and to find fulfillment in the pursuit of widely different activities, every person can recognize themselves as sharing a more basic or generic interest in being able to form, pursue, and revise a life plan of their own.

To say that a just social order advances the common good, on this conception, is to say that its basic institutions—its social, political, legal, economic, and health-related institutions—are organized on terms that secure and advance the basic interests of that community's members. This conception of the common good thus dovetails with a conception of justice as primarily concerned with the regulation of social institutions, and in chapter 4 I show that this conception of the common good can be formulated within a range of social and political theories that begin from different starting points and cash out its implications within different intellectual and political traditions.

1.3.2 Free and Equal Persons

The basic interests of persons play a dual role in shaping the terms on which the basic structures of a decent social order can operate. In particular, they help to define the social goal that these institutions are required to advance and the constraints under which they are required to advance those goals. This is because they define the respect in which individuals in a diverse society have a claim on one another to be treated as morally free and equal.

Roughly speaking, to say that persons are morally equal is to say that they each have a deep and abiding interest in being able to formulate, pursue, and revise a life plan of their own and that, relative to this interest, there are no grounds for promoting the interests of one person over another. Similarly, the claim to be treated as morally free is understood as a social claim to the physical, social, environmental and other conditions that are necessary to have the real ability to exercise these interests in practice without the arbitrary or unwarranted interference from others.

As a result, justice and fairness require that the basic norms and institutions in a community strive to advance the basic interests of every community member with equal efficacy and efficiency. They also require that efforts to advance these ends must be consistent with respect for the freedom and equality of the community members who take on the responsibility of advancing these goals or whose interests are implicated in their efforts.

1.3.3 Reconnecting to Social Institutions

A wide range of social institutions affect the ability of individuals to function as free and equal persons. In part, this is because the capacity of individuals to formulate, pursue, and revise an individual life plan can be thwarted by a range of threats. These threats include poverty and various forms of indifference or antipathy as well as sickness, injury, and disease. But the ability of social institutions to fill this role depends on the quality of the information that they possess about the sources and nature of such threats and the likely effects of alternative strategies, policies, or interventions for addressing them.

On the view I defend here, the research enterprise is also understood on fundamentally social terms. It is a division of social labor between a diverse range of stakeholders that requires the exercise of social authority and the utilization of social resources in order to fulfill a distinctively social purpose. I argue that the moral purpose of this social enterprise is to generate the knowledge and the means necessary to enable the basic social institutions of a community to effectively, efficiently, and equitably secure and advance the basic interests of their respective members. In the context of health, this means that the social function of the research enterprise is to generate the knowledge and the means necessary to enable the institutions of public health and clinical medicine to secure and advance the basic interests of community members from health-related threats.

1.3.4 Producing a Unique Public Good

Although research may be a conduit for a wide range of benefits, and different actors may be drawn to some of these benefits more than others, the pursuit of these various benefits must not compromise the ability of this scheme of social cooperation to produce a unique social and public good. This good is the knowledge that is required to bridge shortfalls or gaps in the ability of the basic social institutions of a community to safeguard and advance the basic interests of its members.

This knowledge is a *unique* good in the sense that it often cannot be generated by other means. It is a *public* good in the sense that it is nonrival and non-excludable. It is nonrival in that its use by one party does not hamper the ability of others to use it. It is non-excludable in that it is difficult to prevent others from using this information once it has been discovered and disseminated.

It is also a *social* good in the sense that a wide range of stakeholders rely on it to discharge important social responsibilities. Policy makers in government, health systems, and the public or private mechanisms that communities use to pool risk and share resources (such as insurance agencies) rely on this information to make decisions that implicate how scarce resources are allocated. These decisions impact the effectiveness, the efficiency, and the equity with which basic social systems address the needs of the stakeholders who rely on them.

Additionally, health systems, public health experts, clinicians, and other providers rely on this information to understand health needs, to determine the relative merits of alternative strategies for addressing these needs, and to make decisions that impact the ability of individuals to exercise the capacities they need to form, pursue, and revise a life plan in practice. Patients and community members rely on this information to understand their health status, to understand the nature of various threats to that status, and to make momentous decisions that impact their ability to exercise their basic interest. The character and quality of this information is also a critical input into future research. It constitutes the knowledge base used to formulate hypotheses about the pathophysiology of disease and to identify targets and strategies for diagnoses or intervention.

1.4 The Egalitarian Research Imperative

In chapter 4 I argue that the relationship between the information that research produces and the ability of basic social institutions to safeguard and advance the basic interests of community members grounds what I call the *egalitarian research imperative*:

The Egalitarian Research Imperative: There is a strong social imperative to enable communities to create, sustain, and engage in research understood as a scheme of social cooperation that respects the status of stakeholders as free and equal and that functions to generate information and interventions needed to enable their basic social systems to equitably, effectively, and efficiently safeguard and advance the basic interests of their constituent members.

This imperative is egalitarian in two respects. First, it is grounded in the goal of ensuring that the basic social structures of a community have the knowledge and the means necessary to secure and advance the basic interests of community members. These interests define the respect in which community members have a claim to equal moral regard. Second, the division of labor through which these goals are advanced must themselves respect the status of individuals as free and equal.

To secure the cooperation of such diverse stakeholders over time, this enterprise must be justifiable to its various stakeholders as an avenue through which they can advance the common good without being subject to forms of treatment that deny or compromise their status as free and equal. Understanding research as a voluntary scheme of social cooperation among free and equal persons entails that strong norms of respect are not external constraints on this activity. They are integral, enabling components. Together, the arguments in chapter 4 show that a moral imperative to carry out important research with humans can be grounded in a conception of the common good that does not license the abrogation or the denigration of the status of study participants or other stakeholders in this enterprise.

1.5 The Integrative Approach to Risk Assessment

1.5.1 Dissolving the Dilemma

The argument in chapter 4 undermines the claim that embracing an imperative to conduct socially valuable research necessarily requires compromising the rights and welfare of individual participants. Nevertheless, such an abstract, philosophical claim may appear untenable in practice since research participation is widely viewed as antithetical to the interests of individual participants. In fact, the idea that research is an inherently utilitarian undertaking, requiring that the welfare of study participants be weighed against and traded off for benefits to future patients, is so intuitive that it constitutes an unquestioned dogma of research ethics.

Chapter 5 illustrates how some of the common commitments of orthodox research ethics outlined in §1.2 structure the perception that study participation poses a moral dilemma for study participants and for clinicians. This chapter introduces the concept of equipoise and shows why the most common and intuitive way of formulating this concept is also doomed to failure. In particular, its earliest proponents regarded it as a way to use the norms and duties that are treated as definitive of the doctor-patient relationship to constrain the inherent utilitarianism of the research enterprise. But within the conceptual ecosystem of orthodox research ethics, this position is unworkable.

Chapter 5 carefully examines a progression of arguments that purport to show that research with humans requires a compromise or sacrifice of participant welfare. This includes the claim that research participation has the form of a coordination problem known as the prisoner's dilemma. In each case I argue that these arguments rest on questionable presumptions and often reflect an overly paternalistic conception of the norms of clinical medicine and an overly narrow conception of individual welfare. Ultimately, I argue that these arguments fail. At the social level, this means that research can be organized in a way that does not give rise to a prisoner's dilemma.

Instead, I argue that if organized on the terms I defend here, research participation has the structure of a strategic interaction known as a stag hunt—a coordination problem in which it is rational for individuals to participate as long as they are convinced that doing so will produce information that is sufficiently valuable and that enough others will be willing to participate that studies will function as planned. One of the overarching themes of the rest of the book is that we should reject the idea that research ethics and oversight is a fundamentally paternalistic undertaking and instead see their purpose as creating an institutional and social order in which participants are justified in seeing research as an avenue through which they can help to produce an important public good.

1.5.2 The Principle of Equal Concern

In chapter 6, I defend what I call the *integrative approach* to risk management. This approach is integrative in the sense that it seeks to reconcile respect for the basic interests of study participants with the social goals of producing scientifically sound and socially valuable evidence. The integrative approach is grounded in the following principle of equal moral concern:

Principle of Equal Concern: As a necessary condition for ethical permissibility, research with humans must be designed and carried out so as not to undermine the standing of any research participant as the moral and political equal of their compatriots, by either knowingly compromising participant basic interests or by showing less care and concern for their basic interests than the interests of those the research is intended to serve.

When this condition is satisfied, free and equal persons have credible social assurance that research participation offers an avenue for contributing to the common good without making participants subject to neglect, abuse, or domination at the hands of the other stakeholders on whom the research activity depends.

The integrative approach articulates three criteria that give the principle of equal concern greater operational clarity and a set of practical tests for determining whether or not these criteria are met in practice. The first operational criterion ensures that risks associated with research participation are not gratuitous or arbitrary. The second ensures that no study participant receives a level of care for their basic interests that is substandard or medically inappropriate. The practical test for this operational criterion is similar to what Benjamin Freedman (1987) called "clinical equipoise" and it requires that study participants can only be allocated to an intervention if at least a reasonable minority of well-informed expert clinicians would recommend that intervention for that patient.

The third operational criterion for ensuring equal concern ensures that risks to the basic interests of participants that are not offset by the prospect of direct benefit to participants themselves are consistent with the level of risk that is regarded as acceptable in other social activities that are oriented toward advancing meritorious social purposes. The incremental increase in risk associated with study participation should be consistent with socially enforced limits on risk that are incurred in other social activities with a similar structure. In this case, similarity of structure is explicated in terms of activities in which individuals are exposed to risks in the performance of tasks or activities that advance a meritorious social goal.

1.5.3 Integrating Equal Concern and Social Value

In the framework I propose, the egalitarian research imperative and the principle of equal concern work hand in hand to ensure the proper functioning of the research enterprise. The egalitarian research imperative seeks to align research activities with the common good, understood as providing the information necessary to bridge gaps between the health needs of community members and the capacity of the institutions in that community to meet those needs. The principle of equal concern ensures that individuals can contribute to advancing the common good with credible, social assurance that their status as free and equal persons will not be denigrated in that process.

In chapter 6, I connect the integrative approach to risk management with the notion of a learning health system (Institute of Medicine 2007). In particular, the ideal of a learning health system reflects two ambitions. The first is making better use of medical information to continuously improve medical practice. The second is altering clinical practice in ways that will better generate medical information that facilitates this learning process. One way to advance these ambitions is to employ adaptive study designs that adjust the treatments that patients receive on the basis of measured outcomes and that provide a platform for delivering care to patients over a longer term.

These adaptive design features are often thought to be particularly difficult to reconcile with the requirements of clinical equipoise. Since the integrative approach incorporates elements of clinical equipoise, it is thus important to demonstrate that these trial design features are not inconsistent with the approach to risk management defended here. I therefore show that when we explicitly recognize that research is a social undertaking and we design studies to model the behavior of fully informed experts in a diverse community, it is possible to reconcile the egalitarian research imperative, the principle of equal concern, and several additional moral requirements.

1.6 Non-Paternalistic Research Ethics

Within the narrow confines of orthodox research ethics, the idea that the field is grounded in, and charged with advancing, fundamentally paternalistic objectives seems almost analytic. The very rubric of "human subjects protections" evinces a paternalistic goal. Although a system of research ethics and oversight can be grounded in such a moral foundation, it need not be.

In chapter 7, I argue that the broader conception of research ethics that I defend here opens up the possibility for reconceiving research ethics on non-paternalistic foundations. In particular, the view that I defend recognizes that research is a fundamentally social undertaking, often requiring the coordination and cooperation of diverse parties over extended periods of time. Each of the parties to this undertaking often has a range of interests that motivate their participation in the research enterprise. These motives can include profit, fame, career advancement, prestige, and access to medical care including access to investigational agents. Because these parties often do not possess the same information, skills, or abilities, and because they are dependent on one another to achieve their shared and their distinctive ends, their interactions are susceptible to cooptation by powerful parties and to coordination problems such as the tragedy of the commons and what is known as the “lemons” problem.

I argue that a better understanding of research ethics is to see its proper social functioning as providing credible public assurance that the division of labor between these parties is organized on terms that satisfy the egalitarian research imperative and the principle of equal concern. In other words, the goal of an effective system of research ethics, policy, and oversight should be to align the parochial interests of these diverse parties with the production of the distinctive social good that provides the normative ground for the social support of the research undertaking and to ensure that this undertaking is carried out in terms that respect the status of study participants, as well as other stakeholders, as free and equal persons.

I argue that even within the paternalism of orthodox research ethics, prospective review before bodies of diverse representation helps to solve the coordination problems to which an unregulated system would be prone. But the mismatch between the paternalistic justification for IRB review and the social benefits that it actually provides creates tensions that threaten to undermine stakeholder trust. Adopting the framework that I propose here would better align the justification for prospective review with the social benefits that it produces. It would also illuminate the need for new institutional structures that incentivize a wider range of stakeholders to advance the twin goals of the egalitarian research imperative.

The argument in chapter 7 constitutes a defense of prospective research review as a mechanism for providing warrant for the social trust on which the research activity crucially depends. However, because the current system of research oversight is so narrowly focused on the IRB triangle, it lacks the ability to hold other stakeholders accountable for the way that they influence the research enterprise. These shortcomings are illustrated in the difficulties research ethics has had in addressing issues of justice and fairness in international research.

1.7 Justice and the Human Development Approach to International Research

The egalitarian research imperative guides and constrains the way labor is divided between the system that produces practical knowledge and the basic social institutions of a community that put that knowledge into practice. It guides the way labor can be divided by requiring that research activities be directed at advancing the common good of community members. This idea is operationalized, in part, as identifying and then attempting to bridge gaps between the health needs of community members and the ability of the health systems in a community to address those needs. The egalitarian research imperative constrains the activities of stakeholders in the research enterprise by prohibiting activities that might undermine or detract from this social mission, including activities that involve abrogating the status of any stakeholder as free and the moral equal of every other. Activities that might undermine the warrant for public trust in the research enterprise are morally problematic and it is, therefore, a legitimate function of oversight structures to discourage or prohibit such activities.

In chapter 9, I argue for what I call the *human development approach to international research*. In this view, the egalitarian research imperative is understood within the context of a larger conception of human development. Every community has an obligation to undertake a larger program of human development, understood as the project of ensuring that the basic social structures of that community are organized and function on terms that secure and advance the basic interests of community members. Research has a unique role to play in this process by generating the knowledge and the means necessary to bridge shortfalls in the ability of those structures to fulfill this mission.

Although every government has a duty to undertake this process domestically, affluent communities have a duty to support and assist this process in less-affluent communities. This duty includes creating incentives and structures aimed at aligning the parochial interests of stakeholders with the goal of promoting research that targets knowledge gaps that represent development priorities for those communities.

The human development approach extends the egalitarian research imperative into the international context and it connects the requirements of responsiveness and reasonable availability with the conditions of a just research enterprise. In this respect, it provides a coherent foundation for norms that are grounded in justice, in a field that largely lacks a conception of justice that has sufficient content to ground and interpret those requirements.

Additionally, the human development approach provides a coherent and consistent account of the standard of care that should govern domestic research in HICs, domestic research in LMICs, and cross-national research.

Borrowing from the integrative approach to risk assessment and management, it holds that study participants should be provided with what is called the *local de jure* standard of care. This states that participants in research are entitled to a level of care for their basic interests that does not fall below what experts judge to be the most effective strategy for preserving or advancing those interests under conditions that are attainable and sustainable in their community.

1.8 Conclusion

Ultimately, the human development approach to international research illustrates how the basic interests conception of the common good, the egalitarian research imperative, and the integrative approach to risk assessment and management provide a coherent and unified framework for evaluating domestic and international research. This framework provides clear guidance for promoting research that generates social value without abrogating the rights and interests of study participants in the process. It situates research within a larger social context and does a better job of identifying the grounds for holding a wider range of actors accountable for decisions that affect the questions that are asked; the methods that are used to address them; the terms on which studies are carried out; and the prospects for incorporating the resulting knowledge, practices, and interventions into the social systems charged with safeguarding and advancing the basic interests of community members.