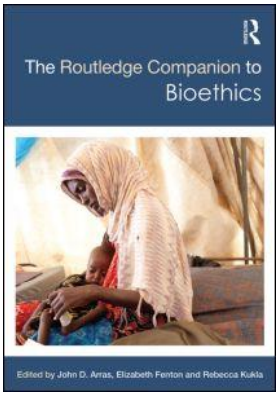

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Research Involving "Vulnerable Populations"

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RESEARCH INVOLVING "VULNERABLE POPULATIONS"

A Critical Analysis

Toby Schonfeld

Much of the contemporary context of research ethics can be understood as a response to the United States Public Health Service Syphilis Study becoming public knowledge. In this study, 400 black men with untreated syphilis from rural Alabama were recruited to participate in a research study that would last 40 years (Jones 1993). The public outcry about this study was substantial, but some of the most scathing criticism centered around the notion that these research participants were particularly vulnerable: They were economically depressed and therefore had strong motivation to participate in order to garner additional income (and later, burial money for their families), they were uneducated and therefore had difficulty understanding the study, and they had little access to healthcare and therefore were likely to agree to participate simply to have access to healthcare professionals (Jones 1993; Reverby 2009).

In addition to arguing for the scientific merit of the study, investigators (from the U.S. government) argued that there were no formal research guidelines to dictate the "proper" conduct of research involving human participants, nor was there any formal designation of populations as "vulnerable" (Reverby 2009). In fact, it was not until much later that considerations about research ethics were codified into U.S. law (Porter and Koski 2008), which can now be found in part 46 of title 45 of the Code of Federal Regulations (CFR). In addition to detailing for investigators and reviewers what constitutes ethical study design and participant recruitment, Subpart A (known as the "Common Rule") also includes guidance for conducting research with groups identified as requiring "additional protections." These groups are referred to as "vulnerable populations": "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects" (45 CFR 46.111b). However, the regulations only include special sections for three specific populations: Pregnant Women, Human Fetuses, and Neonates involved in Research (Subpart B), Prisoners (Subpart C), and Children (Subpart D).

There are at least three problems with these regulations as they stand. (1) It is unclear what defining characteristics make an individual or a subpopulation "vulnerable" and therefore deserving of additional protections. (2) It is unclear whether or not the additional safeguards written into the regulations do in fact protect these subpopulations from their vulnerability. (3) There are other groups of individuals that scholars have argued deserve special protections, including the terminally ill, the politically exiled, and the elderly, among others. It is not clear why federal regulations only apply to the three subpopulations listed above and not others that may in fact be more at risk depending upon the context of the research, regardless of historic instances of abuse. For example, it is difficult to see how a prisoner is at relatively increased risk from participating in a brief anonymous survey (DuBois et al. 2012: 2222), whereas a series of interviews with members of a politically oppressed group are likely to pose substantial risk to participants from the oppressive regime.

In this chapter, I will explore the concept of vulnerability in research, using the situation of pregnant women as our paradigm case. The regulations regarding research conducted with pregnant participants are both problematic and misleading, and therefore focusing on this particular excluded group will demonstrate how the critical analysis of regulations can provide insight into the ethical issues associated with conducting research involving historically excluded participants.

Concepts of Vulnerability in Research

Given that our concern is how regulations influence the notion of vulnerability, it makes sense to begin an analysis of the concept by investigating what a variety of regulatory documents seem to mean by the term "vulnerability." In the United States, that means we begin with the CFR, in which vulnerability is not defined except by pointing to examples of populations that need additional protections (Coleman 2009). For example, the CFR requires institutional review boards (IRBs) to have individuals "knowledgeable about and experienced working with" members of vulnerable groups (45 CFR 46.107a), and to be "particularly cognizant of the special problems of research involving vulnerable populations" (45 CFR 46.111a3). The closest the CFR comes to outlining essential characteristics of these groups is in the section detailing criteria for IRB approval of research. In this section, the regulations include language that says "when some or all of the subjects are *likely to be vulnerable to coercion or undue influence* . . . additional safeguards have been included in the study to protect the rights and welfare of these subjects" (45 CFR 46.111b, emphasis added).

Other international guidelines fail to be more specific or helpful when it comes to definitions. The newly revised Declaration of Helsinki (World Medical Association 2013) includes a section on "Vulnerable Groups and Individuals," but it simply states that "[s]ome groups and individuals are particularly vulnerable and may have an increased likelihood of being wronged or incurring additional harm," and as a result deserve "specifically considered protection." One safeguard included in the Declaration is that the investigators must assure the regulatory body that the proposed research could not be conducted adequately with a non-vulnerable population.

The most helpful regulatory framework comes in the form of the International Ethical Guidelines for Biomedical Research Involving Human Subjects from the Council for International Organizations of Medical Sciences (CIOMS). Here, there is some attempt

at definition. Guide 13 states the following: "Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength, or other needed attributes to protect their own interests" (Council for International Organizations of Medical Sciences 2002). Subsequent information links the inability to protect their own interests to the process of informed consent, and identifies particular groups as vulnerable to different parts of the consent process. (For example, students may be vulnerable in the context where an instructor with control over their future asks them to agree to participate in a study, whereas these same students would not be vulnerable in a different context.)

The conclusion one can draw, then, is that there is no clear definition of vulnerability to which everyone refers. Scholars' attempts to define vulnerability or vulnerable populations in research include: Susceptibility to exploitation (Macklin 2003), those at an increased likelihood to incur "additional or greater wrong" (Hurst 2008), and those facing "a significant probability of incurring an identifiable harm while substantially lacking ability and/or means to protect oneself" (Schroeder and Gefenas 2009). Others link vulnerability to the precise notions of that to which human subjects are especially vulnerable: Issues with informed consent, the risk/benefit ratio in research, and the distribution of benefits and burdens are commonly cited (Coleman 2009).

Linking the concept of vulnerability to specific protections is another strategy. The Consortium to Examine Clinical Research Ethics suggests that the concept of vulnerability be replaced with the notion of "special scrutiny," and identifies three criteria that should trigger careful attention to a protocol and certain relevant features (Levine et al. 2004). Florencia Luna and Sheryl Vanderpoel (2013) are also concerned with identifying the appropriate safeguard and worry that the traditional ascription of vulnerability to groups of people (the "categorical model") overlooks the notion that an individual can be vulnerable in a number of different respects—and therefore protections must address these multiple "layers" of vulnerability. Additionally, it is clear that individuals who do not fall into traditionally vulnerable subgroups may also need additional safeguards in some circumstances (Luna and Vanderpoel consider the case of middle-class pregnant women who are considering umbilical cord bank storage), and the categorical model offers no way to provide such protections. Instead, they advocate a "layered account" of vulnerability, where researchers and policy-makers are encouraged to attend to the multiple ways in which individuals or groups can be vulnerable, and to develop policies and processes that facilitate the creation of appropriate safeguard for these complex situations.

Lange et al. (2013) take the approach one step further and create a "typology of sources of vulnerability and attendant duties." In their view, vulnerabilities can be inherent (those that are unavoidable features of the human condition), situational (those that pertain to the particular context of the participant), or pathogenic (related to dysfunctional social or personal relationships). Each of these vulnerabilities can be experienced either acutely (what they term "occurrent") or chronically ("dispositional—latent or background"). It is important, they claim, to identify the type of vulnerability in order to properly identify our responsibilities related to the vulnerability-making feature, and in this way it is similar to Luna's layering theory of vulnerabilities. Without the proper identification of the vulnerability, we are likely to make sweeping regulations that are over-inclusive, under-inclusive, or both. In any case, the regulations will miss their mark.

Many scholars who have deep interest in the concept of vulnerability have turned to Ken Kipnis' analysis (Kipnis 2001, 2003). Kipnis expressly challenges what he terms the "subpopulation view" of the concept of vulnerability in research and instead replaces it with analytical categories. Combining two different works, Kipnis identifies seven exhaustive categories that are meant to identify the morally relevant features of vulnerability: Cognitive, juridic, deferential, medical, allocational, structural, and social. He argues that this analysis serves three purposes: (1) To provide a "checklist of circumstances that, along with other conditions, can invalidate the permissibility of research"; (2) to identify the necessary features of vulnerability and determine the "supplementary measures" required to address these vulnerabilities; and (3) to serve as grounds for adjudicating an investigator's culpability in taking unfair advantage of a particular population (Kipnis 2001: G-6). A group is considered "vulnerable" if there is a positive response to any of the questions pertaining to a particular analytic category. Kipnis' analysis will be useful for our considerations here.

Application of Vulnerability

Before proceeding, it is useful to describe a few representative studies that may be helpful to keep in the back of one's mind when assessing the forthcoming analysis. Essentially, why does it matter if vulnerable populations are included as research participants? Consider an experimental dermatological ointment that is not thought to be systemically absorbed. Even if a pregnant woman suffers from an uncomfortable or embarrassing skin condition, some IRBs may interpret the regulations in such a way as to prevent pregnant women from participating in this research, despite the low probability of harm from this topical medication (for either the woman or the fetus) and potential for benefit. Or consider a case from the world of pediatrics: Suppose researchers are proposing a trial of medical countermeasures (or vaccines, etc.) to combat (or as prophylaxis against) a biological attack. Surely, in the event of such an event we want to have effective methods of treating children who might have been exposed to the agent. Yet to have compelling evidence about therapeutic options, we will have to expose children to the risks of the treatment (and perhaps even the agent, should intentional exposure studies be warranted) without the possibility of direct benefit to the child (Presidential Commission for the Study of Bioethical Issues 2013).

In either case, there may be good reasons for proceeding with the research—carefully, respectfully, and with sufficient safeguards to minimize risks. Yet the regulations often serve as an impediment to research by limiting meaningful conversations about research with pregnant women. In this way, the regulations can in fact create harms—or vulnerabilities—rather than mitigate them. In what follows, I will briefly describe how Kipnis' analysis of vulnerability (originally applied to pediatric research) supports the argument that regulations can create or exacerbate vulnerabilities by demonstrating the harms obtaining to vulnerable populations (predominantly pregnant women and fetuses here) from the so-called "additional protections" of the federal requirements. (For a full treatment of this topic, see Schonfeld 2013.)

First, consider cognitive vulnerability, which Kipnis claims is obtained when potential participants have some intellectual barrier to participating fully in an informed consent process. Certainly this does not apply to pregnant women (or if it does apply to a particular pregnant woman, it is not by virtue of the pregnancy that it does so). And while it may be true that the fetus is cognitively vulnerable in that it cannot make

decisions for itself, there is no reason to think that having a woman make a decision for the fetus is any more inappropriate than it is once the child is born and the parent is required to make decisions for him/her. That is, it is not clear that the regulations offer any additional protections greater than those that would normally be the case of the appropriate proxy decision-maker.

Cognitive vulnerability is also interesting in the context of prisoners. While some prisoners may be cognitively vulnerable, this vulnerability is not due to the incarceration itself. In fact, it is a common stereotype that prisoners have some cognitive vulnerability (because surely someone whose rationality was intact would not commit a crime!). So in one sense, ascribing vulnerability of this kind to prisoners may in fact *increase* their vulnerability as it makes them more susceptible to the biases and prejudices of others.

Medical vulnerability is commonly cited as a reason to offer additional safeguards to research participants; the idea is that because of their medical situation, research participants with medical vulnerabilities may be more likely to consent to participate in a study regardless of the attendant risks. Consider here the pregnant woman who is willing to do *anything* to preserve the health of her fetus, or the parent who is willing to do *anything* to improve the health of his/her (acutely or chronically) ill child.

While it is true that pregnant women may be selected for inclusion in research specifically because of their condition, it is not clear that such selection makes them medically vulnerable to the extent that they would be willing to take risks they would otherwise deem unreasonable (Kipnis 2003: 115). There may be occasions, however, when the fact of pregnancy *coupled* with another medical problem confers medical vulnerability on the pregnant woman. The classic example would be a pregnant woman with a newly diagnosed cancer, where treatment for the cancer may require a woman to consider therapies that put her fetus at heightened risk. If there is an experimental therapy that purports to shrink her tumors without exposing the fetus to radiation, for example, she might be inclined to choose that option over a regimen that has a higher probability of success at curing her cancer but also a higher probability of fetal harm. In this way, she is in a situation of medical vulnerability, when she chooses a research option that she might otherwise not consider. Yet one could plausibly argue that the cancer is responsible for the medical vulnerability here, not the pregnancy, even though treatment decisions about one will invariably affect decisions about the other. Such a situation might require a particularly nuanced consent process in order to separate these issues, but it is not clear whether additional regulatory protections are required for this above and beyond the standard guidance for adequate informed consent.

Ironically, the most plausible account of ways in which pregnant women are medically vulnerable is as a direct result of their *lack* of inclusion in research. We know that women are consistently prescribed medication during pregnancy, and many of those prescriptions involve a drug of either unknown teratogenicity or drugs that had demonstrated teratogenic effects (Daw et al. 2012; Yang et al. 2008; Andrade et al. 2004). Women who have a chronic health problem are four times as likely to be exposed to risk to themselves and their offspring via pharmaceuticals during their pregnancy as are women without chronic illness (Yang et al. 2008: 272). This is a pressing concern, since, as Françoise Baylis notes, "pregnant women get sick and sick women get pregnant" (Baylis 2010). Additionally, since approximately half of all pregnancies in the United States are unplanned (Guttmacher Institute 2012), fetuses are exposed to medications when their mothers unexpectedly become pregnant (Lyerly et al. 2009).

What this means is that any of the medications used to treat women during pregnancy are used "off label," that is, without specific guidance from the U.S. Food and Drug Administration or the manufacturer, or data on their likely outcomes. We know that pregnancy changes the way women's bodies respond to medications, and it is often difficult to predict the specific changes that a woman may experience (Lyerly et al. 2009). Therefore, clinicians cannot rely on standard evidence-based practice in order to prescribe medications for pregnant women, since the data available from clinical trials that included only non-pregnant women may be inaccurate or misleading in this context (Lyerly et al. 2009; Baylis 2010; Lyerly et al. 2008; Chambers et al. 2008).

This does more than create a situation of uncertainty; rather, it is a failure to respect the principle of justice. Pregnant women deserve to have effective treatment during pregnancy, and this goal can only be fostered by responsibly including pregnant women in clinical research (Baylis 2010). As Lyerly et al. argue, " . . . a pregnant woman is not just a woman with a bigger belly . . . if we are to treat pregnant women's illnesses effectively—something crucial to the health of *both* pregnant women and that of the children they may bear—we must study medications in pregnant women" (Lyerly et al. 2009: 4).

Finally, consider the case of juridic vulnerability. Juridic vulnerability is obtained in situations when others have legal authority over the decisional processes of others. This is certainly the standard case in the parent–child relationship until the child reaches the "legal age" of decision-making. The pediatric context is the easiest in which to see the justification for protections related to jurdic vulnerability: Given that cognitive development is such that children are often willing to forego long-term risks in favor of short-term rewards, it is important that others who have developed the skills to evaluate a risk/benefit ratio appropriately do so on behalf of the child. The idea is to ensure that children are safe and healthy in order to enable them to develop the appropriate cognitive skills that will enable them to make well-informed decisions later in life.

It is difficult to see how any of this could apply, however, to pregnant adult women (leaving aside, of course, the situation of pregnant children).[1] Assuming typical cognition, pregnant women are not under the juridic control of others. Some argue, however, that it is the fetus that is juridicially vulnerable, in some ways no different from children: Others have to make decisions on their behalf. The difficulty lies in how the regulations have addressed this vulnerability. The federal regulations confer juridic authority to *both* the biological mother and biological father in certain instances of research: Namely, when the research holds out the prospect of direct benefit solely to the fetus (provided that the father is not unavailable, incompetent, or temporarily incapacitated or that the pregnancy resulted from incest or rape) (45 CFR 46.204e). The parallel to this situation in the regulations is for research involving children that is greater than minimal risk to the child (45 CFR 46.406–407). In those cases, consent from both parents is required (with similar exceptions as those listed above).

The "protections" offered for the juridically vulnerable fetus, then, are the same as for children being considered for research that is greater than minimal risk. The justification for two-parent consent in the latter case is that the increased level of risk requires an increased level of protection; ostensibly, the child's welfare is better safeguarded with both parents providing permission for research participation than simply one parent doing so (recognizing, of course, that there are exceptions to this situation). The implication with fetuses, therefore, is that all research involving the potential for direct benefit to the fetus alone must be considered of a sufficient risk to require what is known as "two parent consent." Yet recall that the fetus exists dependently with the woman; as

a result, many things that confer risk to a fetus also confer risk to a woman. A particularly vivid example of this are the rare instances of fetal surgery that confer significant risk (but the possibility of benefit) on the fetus, but also involve surgical procedures on the woman herself. But there are other examples as well: Interventions to reduce preterm labor, placental insufficiency, or other issues of necessity affect the woman (either because they are ingested by her or bodily affect her in some way, such as cervical cerclage or stitching) despite the potential for fetal benefit. And while there may not be significant risk to the woman with these agents, they are still actions being taken within her body. The implication of conferring juridic authority on the father, then, is that it gives him the power to consent to research that will happen to someone *who does not lack decisional authority*. This is odd, to say the least. The regulations remain silent on what happens if the mother and the father disagree about research participation in these instances, although presumably refusal by one would fail to meet the criterion that consent is obtained by both parties. Regardless, the purported juridic vulnerability of the fetus has the paradoxical effect of *making* the pregnant woman juridically vulnerable, which gives others authority over choices affecting her own body—a situation we would judge unethical in any other population retaining cognitive decisional capacity (Cantor 2012). Therefore, as it stands, the regulations do *not* protect the rights and welfare of pregnant women who are research participants; rather, they serve to *create* additional vulnerability for them.

Consequences of Additional Protections

This creation of vulnerabilities is not restricted to pregnant women. In the creation of their typology of vulnerability, Lange et al. (2013) worry that failing to connect protections precisely to the type of vulnerability a participant is experiencing may result in those extra protections exacerbating or creating vulnerability. In 2011, the National Institute of Mental Health (NIMH) convened an interdisciplinary panel to investigate the concept of vulnerability in research and to suggest approaches to reduce such vulnerabilities or protect the vulnerable in the research context (DuBois et al. 2012). Interestingly, one of the first findings by this panel was that efforts to protect groups from harm may in fact create new harms for that same population—in this case, those with mental illness. Indeed, they identified five problems with the "status quo" approach to research protections for vulnerable populations: (1) Saddling groups with the label of "vulnerable" can reinforce, rather than reduce, stigmas associated with that group; (2) labeling groups as vulnerable may discourage researchers from including particular individuals in research when they in fact retain decisional capacity; (3) current policies regarding vulnerable subjects may create artificial barriers to research, and as a result create harms or injustice to those populations; (4) "vulnerability" becomes an easy scapegoat for reasons to exclude particular populations when system or other problems are the actual causal factors in a potential participant's inability, for example, to understand a proposed study; (5) denying individuals the ability to choose to participate in research when they are capable of making such choices, even if they are members of a traditionally "vulnerable" group, unjustifiably impedes the exercise of their autonomy (DuBois et al. 2012).

It seems, then, that some of our "additional protections" may in fact be backfiring: Rather than safeguarding subpopulations from abuse, these protections are actually creating the vulnerabilities they purport to resolve. Yet this is not the only harm possible from the improper use of additional protections. Many research protocols also offer the

prospect of benefit to the participants; to the extent that particular subpopulations are excluded without justification from participation, they are denied this benefit, which violates the principle of justice (Koffman et al. 2009). But even more than this, if members of certain subpopulations are denied the ability to participate in research, then the results of any studies will not apply to them; and as in the case of medical vulnerabilities, this denies pregnant women the benefits of medical advances relevant to their needs or situation" (Koffman et al. 2009: 440). Similar results have been described regarding patients requiring palliative care (Koffman et al. 2009), older people (deKlerk 2012), indigenous native populations (Clough et al. 2013), and mental health research among internationally displaced people (Siriwardhana et al. 2013), among others.

Possible Remedies for Exclusion

To address the barriers to the protection of vulnerable groups in research, the NIMH panel recommends a series of six guidelines designed for researchers and ethics review boards. The hope is that by attending carefully to these guidelines, those who are truly vulnerable will be identified and additional measures can be established to protect them; and others who have the ability and desire to participate in research will not be unjustly barred from doing so. Interestingly, the authors claim that their guidelines are consistent with current federal regulations, which makes them even more appealing. The overall approach is to design a system of considerations that demonstrates "genuine respect" for research participants while at the same time attending to broader considerations of vulnerabilities. Their recommendations are as follows (DuBois et al. 2012):

1. Risk: Rather than starting with the additional protections, the panel recommends investigators start by evaluating carefully the risk involved in the research. This will ensure that any safeguards deployed are appropriate and proportionate to the risk itself.
2. Protections: The additional measures should be proportionate to the risk, that is, offer the minimum additional safeguards necessary in relation to the actual risk. This recommendation ensures that individuals will not be unjustly prevented from participating in research because of procedures that do not relate to the risks in the study.
3. Consent Assessments: Attending carefully to the actual level of risk of a study, require universal consent assessments. That is, whenever we are significantly concerned about potential participants understanding the risks involved in a study, screen all of the potential participants for capacity rather than just those who might fall into a category of vulnerability. This policy will ensure that all potential participants have a sufficient understanding of the risks of participation, regardless of one's inclusion in a vulnerable group or not. Singling out members of particular populations disregards both individual variation and respect for persons who will be the ones to assume the risk once enrolling on the protocol.
4. Evidence: Just as medicine should be evidence based, so too should the development of additional protections in research be related to evidence about the actual risk in a particular study. Relying on high-quality evidence minimizes the impact of false assumptions based on (sometimes unconscious) bias or stereotypes and ensures that the suggested protections will actually safeguard against the identified risks.
5. Labels: Given that assessments in research are really designed to test the potential participant's understanding of the particulars of the research study in which the person may participate, the panel suggests that attending to the "subjective outcome of the

assessment process" is more appropriate than making global pronouncements about a subject's decisional capacity in general (DuBois et al. 2012: 2223). What is, or should be, relevant for investigators is whether or not the potential participant is able to adequately understand the trial and consider his or her options from among other alternatives. Individuals may be able to demonstrate this capacity without demonstrating capacity for larger issues, and that should be sufficient for the conduct of research. In this way, cognitive or other deficits that impair the broader concept of decisional capacity may not prove to be a barrier for research participation in particular contexts.

6. Additional Safeguards: Policies and procedures regarding additional safeguards should be considered in context: Community attitudes and priorities are relevant to the development and implementation of protection measures. Two examples offered by the panel are how payment for research participation can be viewed as respectful or manipulative in different contexts, or how the inclusion of patient advocates can be seen as either beneficial or as an invasion of privacy. In this way, investigators can ensure that the measures they propose to mitigate risk do not in fact confer additional vulnerabilities on participants because of external factors.

Scholars have also been working on the issue of how to include pregnant women in research responsibly. As a beginning, researchers are encouraged to take advantage of "low hanging fruit"—observational studies that incur no risk of harm to the mother or the fetus. Prospective studies including pregnant women and fetuses will require some sort of regulatory reform—a necessary step in order to make true progress. Already, researchers have initiated preliminary investigations by asking women themselves how they would feel about participating in research relative to reproductive risk (Schonfeld et al. 2009; Lyerly et al. 2012). This information may serve as the basis for regulation revision, as well as give insight into new procedural recommendations regarding informed consent. In addition, careful analyses of the risks appropriate for children to bear in the context of research, as well as the appropriateness of the consent process, may also yield fruitful directions for revised policies (Wendler et al. 2005; Nelson et al. 2013). Efforts are also underway regarding the reconsideration of issues in pediatric research. This includes justifying pediatric research without the possibility of direct benefit (Wendler 2012), reconsidering the concept of "minimal risk" (Glass and Binik 2008; Wendler 2009), and meaningfully involving children in decisions about research participation (Joffe et al. 2006; Wilfond and Diekema 2012).

What is clear from the analysis of vulnerability and its attendant protections is that one size clearly does not fit all. Investigators ought to consider carefully the appropriate population for research apart from any labeling of "vulnerability," rather than rely exclusively on regulatory frameworks to dictate when an individual participant may be "vulnerable," and how that vulnerability should be addressed. Attending carefully to contextual features will enable researchers to create a study design and process of participant recruitment that conform to ethical norms that not only cohere with regulation, but also meaningfully respect the participation of the individuals who make the study possible.

Related Topics

Chapter 14, "Biomedical Research Ethics: Landmark Cases, Scandals, and Conceptual Shifts," Jonathan D. Moreno and Dominic Sisti

Chapter 16, "The Future of Informed Consent to Research: Reconceptualizing the Process," Paul Appelbaum

Note

1 The section on juridic vulnerability comes verbatim from Schonfeld (2013: 194–5).

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Further Reading

For extended reflections on women and vulnerability, see Mackenzie, C., Rogers, W. and Dodds, S. (eds.) (2013) *Vulnerability: New Essays in Ethics and Feminist Philosophy*, New York: Oxford University Press. Three texts deal importantly and differently with the involvement of children in research: Wendler, D. (2010) *The Ethics of Pediatric Research*, New York: Oxford; Ross, L.F. (2006) *Children in Medical Research*, New York: Oxford University Press; Kodish, E. (ed.) (2005) *Ethics and Research with Children*, New York: Oxford University Press; for a regulatory perspective on including prisoners in research, see Institute of Medicine (2007) *Ethical Considerations for Research involving Prisoners*, Washington: National Academies Press; for a case study involving prisoners in research, see Hornbulm, A.M. (1998) *Acres of Skin*, New York: Routledge.