HHS Public Access

Author manuscript

Am J Bioeth. Author manuscript; available in PMC 2023 December 28.

Published in final edited form as:

Am J Bioeth. 2023 June ; 23(6): 113–116. doi:10.1080/15265161.2023.2201201.

Wither Vulnerability? The Over/Under Protection Dilemma and Research Equity

Amelia K. Barwise[a], **Megan A. Allyse**[b], **Jessica R. Hirsch**[a], **Michelle L. McGowan**[a], **Karen M. Meaghar**[a], **Kirsten A. Riggan**[a]

[a]Mayo Clinic Rochester

[b]Mayo Clinic Jacksonville

We are grateful to Friesen and colleagues for drawing attention to the tension between the protection of populations that may experience vulnerability with their inclusion in research (Friesen et al. 2023). Our own research involves groups that have been traditionally categorized as “vulnerable”—including pregnant women, children, and people with limited English proficiency—as well as areas of research not historically held to equal standards —such as public health surveillance and quality improvement. We argue that participant selection is a blunt instrument for advancing health equity. Designating broadly defined groups as “vulnerable” fails to account for temporal or protocol-specific dimensions of vulnerability. The distinction between research that has the potential to interfere in an ongoing state of vulnerability (e.g., imprisonment) versus that in which vulnerabilities may vary or be incidental to the contents of the research (e.g., students) is rarely drawn or navigated. Furthermore, while institutional review boards (IRBs) continue to enforce antiquated protections for outdated categories of vulnerability (e.g., pregnancy), they struggle to account for new vulnerabilities that populations may experience, such as through vast increases in “big data” collection by entities that currently fall outside research regulatory purview. Here, we focus on four examples in which implementation of research regulations has resulted in either systemic exclusion or insufficient scrutiny of vulnerabilities.

PREGNANCY

The federal regulations governing human subjects research were updated to remove the absolute categorization of pregnant people as a vulnerable population in 2019. The designation of pregnant individuals as vulnerable stemmed not from an interest in protecting the pregnant individual per se but out of concern for the fetus. This protectionism is rooted in the tragic impact of drugs such as thalidomide but is also inevitably tied up in the endemic debate over the morality of abortion. The US government’s stance on research that may impact fetal development is summed up in CFR 46.204 part B. The regulation allows for the inclusion of pregnant individuals in research *from which they themselves may benefit*, but

CONTACT Amelia K. Barwise, barwise.amelia@mayo.edu, Biomedical Ethics Research Program, Mayo Clinic, Rochester, MN 55902, USA.

historically IRBs have overwhelmingly focused on potential risk to a fetus to the exclusion of benefit. A key example of this ongoing protectionist stance is the exclusion of pregnant individuals from initial clinical trials pertaining to the safety and efficacy of COVID-19 vaccines. The result was a lack of data on whether the mRNA-based vaccines would impact the pregnancy or confer vertical immunity to fetuses and newborns. Public health officials, clinicians, and pregnant individuals understandably interpreted this lack of data as a sign that the vaccines had not demonstrated safety for pregnancies, leading to delayed uptake and likely increased morbidity and mortality of pregnant people during the pandemic. As qualitative findings demonstrate, many pregnant patients refused vaccination out of such concerns. Some individuals even perceived that obstetrician-gynecologists were actively discouraging vaccination when COVID-19 vaccination first became available (Huang et al. 2022). Professional groups, including the American College of Obstetrics and Gynecology and the Society for Maternal and Fetal Medicine, did not recommend pregnant people receive the COVID-19 vaccine until July 30, 2021, almost eight months after the emergency use authorization was first issued (ACOG 2021). As a result, the CDC finds that the pregnant population has considerably trailed in its uptake of COVID-19 vaccines from other groups, despite being at higher risk for complications from COVID-19 and confirmation of vaccine safety and efficacy in pregnancy.

CHILDREN

Another instance in which we have experienced institutional protectionism in relation to populations that may experience heightened vulnerabilities is in federally funded research involving children. Federal regulations continue to treat children as universally vulnerable even though a multitude of pediatric clinical and research ethics guidelines recommend increasingly engaging young people in clinical and research decision making as they mature. Even in pediatric genomic research that has been informed by adolescent engagement (Blumling et al. 2021), IRBs and associated entities have taken overly protectionist stances, treating all children as equally vulnerable to the potential harms of participation when the study is only enrolling healthy adolescent research volunteers and is explicitly studying a model of shared decision-making proposed by adolescents for learning personal genomic information with their parent or legal guardian (McGowan et al. 2018). Despite meeting with the IRB and institutional social media gatekeepers, concerns about children's vulnerability prevented the implementation of adolescent-facing recruitment strategies that were recommended in community engagement efforts. Relying on protectionist parent-driven enrollment into pediatric research may inadvertently subject older minors to more pressure to participate in research and undermine adolescents' emerging autonomy to learn personal genomic information than if they were recruited directly by the research team.

LIMITED ENGLISH PROFICIENCY

Although not explicitly listed in federal regulations as a vulnerable population, participants with language barriers or limited English proficiency can encounter unique hindrances to their inclusion in research and are provided extra protection during the informed consent process. While federal regulations strongly encourage investigators to consent participants via the written consent process in the participants' preferred language, federal regulation

allows for the use of a short form consent when supplemented with an oral presentation of the long consent form in prospective participants' preferred language. Both these approaches require attestation from a witness who speaks both English and the prospective participant's language, usually an interpreter, to confirm the participant has provided informed consent. In our institution it transpired that during clinical trial recruitment and consent, interpreters were not comfortable with the process, procedures, and documentation for seeking informed consent and their responsibility to confirm participant understanding of the risks and benefits of the research. Following the challenges created by these conditions with recruiting populations with language barriers to clinical trials at our institution, we collaborated with language services, study coordinators, and our IRB to modify the informed consent process by re-centering the documentation on study coordinators rather than interpreters (Barwise, Sharp, and Hirsch 2019). This structural change supported improved clinical trial research opportunities among those with language barriers and is a key example of a collaborative approach between IRBs and researchers to expand opportunities for research participation of this population rather than succumbing to logistical barriers that would result in their exclusion.

PUBLIC HEALTH

Public health has also faced difficulties with a protectionist paradigm, despite an explicit carve out for surveillance activities. The contrast we wish to draw here with a protectionist stance is how advancement of health equity goals sometimes requires institutional structures to make research *possible*. One good way to avoid politically inconvenient data from emerging is to create obstacles (including bureaucratic ones). Population health data are also political data: they can demonstrate government failure of constituencies. Moreover, by elucidating shared aspects of health that might be previously unrecognized, such research (and public health practice) can disrupt the status quo by generating new constituencies. The United Kingdom's 1980 Black Report documenting perpetuation of health inequities based on socioeconomic status was so politically charged, the conservative government only printed a small number of copies (Gray 1982). In the United States, chronic underfunding of. U.S. gun violence research leaves us with an incomplete understanding of the unjust toll of violence in our communities (Rajan et al. 2018). Reforming our research oversight approaches to increase IRB familiarity with epidemiological study design is an initial step. The lines between public health, quality improvement, and research activities are not always simple and pose challenges to IRBs and researchers alike (Carter et al. 2017). These distinctions are also concerning to affected community members in the era of "big data," where health information is increasingly flowing between population and individual care contexts (Molldrem, Smith, and McClelland 2022). Solutions may also highlight the importance of partnerships between Offices of Research Compliance and academic leaders, such as Deans of Research. Candidate policies include reinvigorating academic freedom and supporting faculty critical review of agency funding priorities to identify and institutionally redress underfunded health equity research domains.

RECOMMENDATIONS

While respecting the important role of IRBs within the scientific enterprise, the tendency toward an overly protectionist stance may impede scientific advancement, and more importantly, contribute to research inequities and exclusion of already marginalized groups and socially important lines of research. Such protectionism may also violate, rather than uphold, participant autonomy to engage in research based on their own assessment of personal risk and individual and community values. To balance participant autonomy with respect for the need for structural review and protections, we offer several pragmatic suggestions for IRBs to improve their oversight of research on populations with perceived vulnerability (Box 1). Crucially, all these constructive suggestions are consistent with regulatory compliance:

CONCLUSION

Considerable work remains to unpack how perceptions of vulnerability impact how populations are included and excluded from research. We share Friesen and colleagues' concern and argue that a protectionist stance is a structural driver of broad evidence gaps for the very groups it was designed to protect and simultaneously undervalues research protections that may be warranted for other populations to promote equitable population health. Expanding IRB and research university's toolbox to incorporate approaches beyond inclusion criteria would advance more inclusive and diverse research agendas and promote health equity.

FUNDING

Michelle L. McGowan's work is supported by National Human Genomic Research Institute HG010166.

REFGERENCES

ACOG (American College of Obstetricians and Gynecologists). 2021. ACOG and SMFM recommend COVID-19 vaccination for pregnant individuals. Accessed March 9, 2023. https://www.acog.org/news/news-releases/2021/07/acog-smfm-recommend-covid-19-vaccination-for-pregnant-individuals.

Barwise A, Sharp R, and Hirsch J. 2019. Ethical tensions resulting from interpreter involvement in the consent process. Ethics & Human Research 41 (4):31–5. doi:10.1002/eahr.500025. [PubMed: 31336041]

Blumling AA, Childers-Buschle KE, Lynch JA, Myers MF, and McGowan ML. 2021. The underdeveloped "gift": Ethics in implementing precision medicine research. The American Journal of Bioethics 21 (4):67–9. doi:10.1080/15265161.2021.1891352.

Carter EJ, Mastro K, Vose C, Rivera R, and Larson EL. 2017. Clarifying the conundrum: Evidence-based practice, quality improvement, or research? The Journal of Nursing Administration 47 (5):266–70. doi:10.1097/NNA.0000000000000477. [PubMed: 28422932]

Friesen P, Gelinas L, Kirby A, Strauss DH, and Bierer BE. 2023. IRBs and the protection-inclusion dilemma: Finding a balance. The American Journal of Bioethics 23 (6):75–88. doi:10.1080/15265161.2022.2063434.

Gray AM 1982. Inequalities in health. The black report: A summary and comment. International Journal of Health Services: Planning, Administration, Evaluation 12 (3):349–80. doi:10.2190/XXMM-JMQU-2A7Y-HX1E. [PubMed: 7118327]

Huang L, Riggan KA, Ashby GB, Rivera-Chiauzzi EY, and Allyse MA. 2022. Pregnant and postpartum patients' views of COVID-19 Vaccination. Journal of Community Health 47 (5):871–8. doi:10.1007/s10900-022-01118-z. [PubMed: 35841461]

McGowan ML, Prows CA, DeJonckheere M, Brinkman WB, Vaughn L, and Myers MF. 2018. Adolescent and parental attitudes about return of genomic research results: Focus group findings regarding decisional preferences. Journal of Empirical Research on Human Research Ethics: JERHRE 13 (4):371–82. doi:10.1177/1556264618776613. [PubMed: 29806518]

Molldrem S, Smith AK, and McClelland A. 2022. Predictive analytics in HIV surveillance require new approaches to data ethics, rights, and regulation in public health. Critical Public Health :1–7. doi:10.1080/09581596.2022.2113035.

Rajan S, Branas CC, Hargarten S, and Allegrante JP. 2018. Funding for gun violence research is key to the health and safety of the nation. American Journal of Public Health 108 (2):194–5. [PubMed: 29320291]

Box 1.

- Generate normative and regulatory pathways to approve research engaging understudied populations
- Train IRB members on population health, action research, and community-engaged research methods
- Engage subject matter experts to determine study risk to populations with perceived “vulnerability”
- Evaluate research design for capacity to inform population health interventions
- Reassess procedural mechanisms that automatically designate populations as vulnerable without scientific scrutiny of study purpose, design, and methods
- Consider implementation of ancillary committee reviews that work in concert with IRB (e.g., Pediatric Advisory Board, Education Research Committee, Community Advisory Groups)
- Address financial and structural limitations that have historically impeded participants from joining research studies, e.g., reevaluating participant remuneration and social media recruitment policies
- Assess adequacy and appropriateness of policy mechanisms outside research protection, including university academic freedom, gaps in funding priorities that advance health equity.