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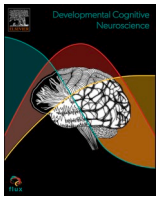

Navigating ethical and legal challenges in the HEALthy Brain and Child Development Study: Lessons learned from the ethics, law, policy working group

Jenny Kingsley [a,b,*], Barbara Andraka-Christou [c], Seema K. Shah [d,e], Paul Spicer [f], Sharlene Newman [g], Pilar N. Ossorio [h], The HBCD ELP WG

[a] Center for Bioethics, Children's Hospital Los Angeles, Los Angeles, CA, United States
[b] Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA, United States
[c] School of Global Health Management & Informatics, University of Central Florida, Orlando, FL, United States
[d] Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, United States
[e] Smith Child Health Outcomes, Research, and Evaluation Center, Stanley Manne Children's Research Institute, Lurie Children's Hospital, Chicago, IL, United States
[f] Department of Anthropology, University of Oklahoma, Norman, OK, United States
[g] Alabama Life Research Institute, University of Alabama, Tuscaloosa, AL, United States
[h] University of Wisconsin Law School, Madison, WI, United States

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ABSTRACT

The HEALthy Brain and Child Development (HBCD) Study, a multi-site prospective longitudinal cohort study, will examine human brain, cognitive, behavioral, social, and emotional development beginning prenatally and planned through early childhood. The HBCD study has faced several ethical and legal challenges due to its goal of enrolling pregnant people (including those with substance use disorder) and their newborns. Challenges not fully anticipated at the outset emerged from the rapidly changing legal landscape around reproductive rights in the United States. By embedding scholars in bioethics and law within research teams and engaging them in conversation with each other and other study personnel, we were able to address many challenges proactively and respond promptly to unanticipated challenges. In this paper, we highlight several important ethical and legal challenges that arose from the first phase of funding through the beginning of participant enrollment. We explain the methods used to address these challenges, the ethical and legal tradeoffs that arose, and the resolution of challenges through the design of the study. Based on this experience, we provide recommendations for research teams, sponsors, and reviewers to address legal risks and promote the ethical conduct of studies with pregnant people and caregivers. We highlight the importance of collaboration with bioethics and legal scholars in studies involving complex and evolving legal risks, as well as the necessity of designing robust approaches to informed consent and maintaining participant trust while navigating ethical challenges in research.

1. Introduction

While the use of prescription and illicit substances in pregnancy has grown in the United States (US) over the previous decades, researchers' understanding of how substance use combines with other environmental, genetic, and biological factors to impact child development remains limited (Rodriguez and Vincent, 2019). The HEALthy Brain and Child Development (HBCD) study aims to address this critical knowledge gap. This multisite, longitudinal, observational study is recruiting 7500 pregnant persons and their newborns to study brain, behavioral, and emotional development in children over time. At least 1875 participants will be recruited from adults using licit or illicit substances during pregnancy. The study will collect data on environmental exposures and personal experiences that could affect child development and uses an observational study design wherein researchers note the resulting effects of exposures without purposefully exposing pregnant people and their children to potential harm.

Though observational in nature, the HBCD study is not without risks for participants, particularly in states where data collection and data sharing about substance use could lead to participants' involvement in

* Correspondence to: Center for Bioethics, Children's Hospital Los Angeles, 4650 Sunset Blvd, MS 12, Los Angeles, CA 90027, United States.
E-mail address: jkingsley@chla.usc.edu (J. Kingsley).

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the child welfare or criminal justice systems. For example, in some states, use of substances during pregnancy is considered child abuse, even without proof of resulting harm to the child (McCourt et al., 2022). Recognizing that these risks warranted serious consideration in the design and implementation of the HBCD Study, the National Institutes of Health (NIH) and study teams worked to embed bioethics and legal scholars both locally within site specific study teams and at a study-wide level within the Ethics, Law, and Policy Working Group (hereinafter "the ELP WG" or "the WG") and the study's Administrative Core.

The ELP WG meets regularly to discuss current and potential ethical and legal concerns related to the HBCD study. When appropriate, the WG provides advice to local study sites, other WGs, and the study leadership. To inform its discussions and decisions about legal and ethical concerns, the WG draws on existing theoretical frameworks. In particular, the WG has drawn on the framework described by Emanuel et al. (2000, 2004) for implementing ethical clinical research. This framework, which has been widely used to guide numerous clinical studies in the US and abroad, has eight considerations: collaborative partnership, social or scientific value, scientific validity, independent review, fair subject selection, favorable risk-benefit ratio, informed consent, and continuing respect for potential and enrolled subjects. Though each of these considerations is generally relevant to the HBCD study, some are more germane than others. Additionally, applying the framework requires navigating trade-offs among these considerations. As described by the Ethics Group from the Adolescent Brain and Cognitive Development study (another recent longitudinal cohort study involving minors), investigators, administrators, funding agencies, parents, and children may have competing interests (Clark et al., 2018). Moreover, variations in the interpretations of these ethical considerations and changes in the legal landscape at each site raise the level of complexity involved in planning and executing ethical research. And in some cases, legal obligations conflict with ethical ones, raising questions about whether to make changes in study design that necessitate ethical trade-offs.

The goal of this paper is to describe emerging legal and ethical challenges faced by researchers in the HBCD study. Below we summarize ethical and legal concerns discussed by the WG, including planned or potential responses to these concerns.

1.1. Background regarding the HBCD study and the Ethics, Law, and Policy WG

The HBCD study is funded by the NIH's Helping to End Addiction Long-term (HEAL) initiative, the National Institute on Drug Abuse (NIDA), and ten other NIH Institutes and Centers. It establishes a nationwide, multi-site, multi-modal, longitudinal cohort study that prospectively examines the brain and behavioral development from birth through childhood and will provide multifaceted and detailed information on neurodevelopmental trajectories and the long-term impact of high-risk environments, including the impact of substance exposures during pregnancy on childhood development (HEAL NIH,). The study will utilize data from magnetic resonance imaging, electroencephalograms, biospecimens (saliva, urine, blood, and nail samples), an array of survey measures regarding parental health, substance use, culture and environment, nutrition, and behavioral assessments over the study period. The study is comprised of 27 sites, 17 working groups, and 3 different committees. More information about the organizational structure of the study may be found on the study website.(HBCD, 2024)

Given potential legal and ethical concerns related to the vulnerable populations who serve as participants, including children, pregnant people, and people with substance use disorder (SUD), study leaders created several working groups, including the ELP WG (Jordan et al., 2020; Shah et al., 2022). The ELP WG provides a forum for bioethics scholars, legal scholars, and other study personnel to discuss legal and ethical concerns. The WG works in parallel with a Bioethics and Medical Oversight Group (the BMO) and the external Observational Study Monitoring Board (OSMB) - both of whom safeguard the interests of study participants through assessment and review of study procedures and guidelines. The study has 27 research sites in twenty states around the country. Concerns may be brought to the WG by individual WG members, study leadership, the NIH, or from other working groups. The WG meets at least monthly for one hour via Zoom and functions primarily as a consultative group that provides advice to the study's leadership teams and local sites. As of early 2024, the WG has had 23 meetings about the HCBD study. The members of the WG and their roles and affiliations with academic institutions are listed in Supplement A for reference.

2. Legal & ethical challenges

Legal and ethical challenges brought to the WG since the beginning of the HBCD study have included the following: (a) community engagement with parties who may present risks to participants; (b) withdrawal of participants who do not complete study measures; (c) participant compensation; (d) optimizing use of study navigators without influencing study outcomes; (e) inclusion of incarcerated people; (f) navigating legal reporting obligations; (g) sharing incidental findings with participants; and (h) navigating legal risk and ethical obligations in the setting of possible unknown fentanyl exposure.

Table 1
Challenges addressed by the ethics and law working group with relevant ethical or legal considerations in tension.

Challenges	Relevant Ethical or Legal Considerations in Tension	Recommendations
Community engagement	**Collaborative partnership** with relevant stakeholders may compromise maintaining a **favorable risk/benefit ratio.**	1. Careful study design to minimize legal risk.
Administrative withdrawal	Preserving **scientific validity** of study data may conflict with maintaining a **favorable risk/benefit ratio** and **respect for recruited participants.**	1. Explicit and transparent criteria for withdrawal that appeal to ethical principles and are detailed in the informed consent process.
Participant compensation	Ensuring **respect for recruited participants** must be balanced by maintaining a **favorable risk/benefit ratio**.	1. Allowing for flexibility in timing of visits to minimize financial risk. 2. Providing up-front payment to minimize financial burden on participants.
Study Navigators	Preserving **scientific validity** of the study data may conflict with maintaining **respect for recruited participants.**	1. Creation of a working group specifically aimed at addressing these concerns.
Incarcerated people	**Legal constraints** on participants may compromise **fair subject selection**.	1. Case by case review by central IRB.
State reporting requirements	**Legal reporting requirements** may compromise maintaining a **favorable risk/benefit ratio.**	1. Careful study design to minimize legal risk. 2. Utilize robust informed consent process.
Incidental findings	Ensuring **respect for recruited participants** must be balanced by maintaining a **favorable risk/benefit ratio**.	1. Return only clinically actionable findings. 2. Utilize robust informed consent process.
Managing risks	Balancing different risks (of compromising confidentiality with risk of drug exposure) to maintain a **favorable risk/benefit ratio.**	1. Adhere to promised confidentiality to minimize legal risk. 2. Implement harm reduction measures. 3. Utilize robust informed consent process.

Table 1 provides a summary of these challenges, including the specific ethical or legal consideration(s) in tension. We will discuss each of these challenges and our recommendations for addressing them below.

2.1. Community engagement with parties who may present legal risk to participants

Collaborative partnership requires consideration of how to engage communities, participants, and other interested parties. The HBCD study strives to develop authentic community engagement to inform study design, recruitment, enrollment, and retention. Many of the approaches to community engagement were addressed at the site level, with sites setting up community advisory boards to provide input into the study. Additionally, during the pilot phase of the study, researchers planned to minimize legal risks to participants by engaging prosecutors' offices to obtain Memoranda of Understanding (MOUs) under which prosecutors would agree not to seek data from the study to prosecute pregnant participants who used substances. This strategy had been used in some previous studies (Shah et al., 2023a). However, after HBCD began, it became clear that the prosecutors most willing to enter into MOUs were located in places where laws were least punitive and where treatment was most accessible. In contrast, concerns were raised that prosecutors in states with more punitive laws would be less likely to enter into MOUs, rendering these efforts futile. The WG felt it unwise to share information with prosecutors that could increase, rather than decrease, the legal risk to which participants were exposed. The WG instead recommended careful study design to minimize legal risk. Therefore, although the study initially planned broad consultation with different interested parties, investigators instead created protocols to minimize legal risk as further described in section F of this article.

2.2. Withdrawal of participants who do not complete study measures

It is unethical to expose participants to risks or inconvenience with no purpose; a study that collects or analyzes data without rigor produces meaningless results and is, therefore, unethical. To produce valid data, HBCD's methods have been rigorously assessed, chosen, and then developed into protocols by working groups with subject matter expertise. Numerous quality control checks of the data are conducted. In addition, the study design working group includes deep expertise in statistics and has modelled study design choices, data missingness, and other variables to help ensure that the study will produce valid data.

Recognizing that participation in the study is time-intensive and potentially invasive (e.g., biospecimens, like blood and fingernail samples, are collected), study leadership anticipated some participants may not complete all study measures. To protect the data integrity, the design working group questioned what threshold should be used to administratively withdraw a participant. Administrative withdrawal is supported when necessary to protect a participant from excessive risk or to maintain the integrity of the study's data. However, administrative withdrawal also infringes on a participant's autonomy and may introduce bias and inequity. Therefore, preserving the scientific validity of the data may conflict with the considerations of respect for recruited participants. The WG was required to consider potential circumstances where administrative withdrawal would be appropriate, including the threshold when data integrity is jeopardized, how to notify participants about withdrawal, and when to stop providing incentive payments to participants who have been withdrawn. The ELP WG advised that criteria for withdrawal should be explicit, transparent, and widely advertised. Ultimately, study leadership, with input from the Design and ELP-WGs, decided that administrative withdrawal would be appropriate if participants failed to attempt to provide any biospecimens, failed to complete certain demographic data prior to the child's birth, or failed to complete more than half of the questions on 80 % of the remaining questionnaires at visit 1. Given that the study aims to include a portion of participants with substance use disorder, care was taken to allow for an attempt to provide biospecimens (rather than completion of biospecimen collection) because of potential difficulties that may arise from vestiges of previous substance use (e.g., such as scarring that may make venipuncture difficult or past trauma that may make participants less open to multiple blood draw attempts). Finally, the informed consent document was revised to ensure that participants were made aware of the conditions for administrative withdrawal.

2.3. Participant compensation

To respect the time and resources required of participants during such a long and intensive study, HBCD planned to compensate participants and cover transportation costs. Challenges surrounding the appropriate timing of payment for transportation costs came to the attention of the WG, including whether to reimburse participants for costs or to pay for costs upfront. While not considered a direct benefit of participating in the study, financial compensation/reimbursement may be necessary to prevent harm to participants and to prevent undersampling of people from lower socioeconomic backgrounds, including many people with substance use disorder. Therefore, the WG recommended that, as much as reasonably possible, sites should provide funds upfront for participants costs (e.g., provide funds to participants to cover transportation costs; hotel costs) or sites should pay providers of services (e.g., taxis, hotels) directly. The latter approach could help prevent the need for participants to report such payments as income to the Internal Revenue Service, which could engender legal or financial risk. Alternatively, sites could distribute funding for costs to participants over time, to prevent participants from receiving funds crossing the threshold necessitating IRS reporting in any given year.

2.4. Optimizing involvement of study navigators without influencing study outcomes

Ethical considerations for research require ongoing respect for potential and enrolled participants and fair selection. Given the multiple and overlapping vulnerabilities expected among study participants, including pregnancy, substance use, ethnic and racial minorities, and low socioeconomic status, the study leadership believed study navigators with lived pregnancy and/or substance use experience should be hired as study staff to assist study participants in navigating the research process. Additionally, such study navigators could provide emotional support and connect participants to community resources, like housing or SUD treatment, if desired by participants.

The ELP WG discussed how best to optimize use of study navigators to provide support for participants and connection to community resources without unduly influencing study outcomes or compromising scientific validity. While researchers hoped study navigators could positively impact study recruitment and retention by helping address barriers to study involvement, concerns were raised that access to study navigators might inadvertently serve as a study intervention and introduce bias into study results and compromise their scientific validity. For example, concerns were raised that activities or support from a study navigator could lead to participants engaging in activities they would not do otherwise (e.g., obtaining SUD treatment). Concerns were also raised about the emotional distress navigators might experience while seeking to assist vulnerable populations, as well as the need to help navigators recognize professional boundaries (e.g., not using personal funds to pay for transportation or food for participants.) A Study Navigator WG was formed with the intention of staying in regular contact with the ELP WG. Given that study navigators are among the study staff most likely to regularly engage with participants, study navigators could bring WG attention to some of the ethical or legal concerns related to the study that are affecting study participants. Additionally, several training courses were planned for study navigators to address such issues. The ELP WG also encouraged sites to hire navigators who would be interested in participating for the duration of the 10-year study, as data

suggest that the positive relationships formed between study participants and study navigators could help facilitate retention (Shah et al., 2023b).

2.5. Inclusion of incarcerated people

To promote justice, fair subject selection requires that the benefits and burdens of research are distributed fairly among groups and participants. While research among populations traditionally labeled as vulnerable – such as pregnant people and their children – was long avoided to protect participants *from* research, recent ethical guidance has shifted to recognize the importance of protecting groups *through* research that addresses their unmet needs (Lyerly et al., 2021). Because the study aims to specifically examine substance use in pregnancy, and because many pregnant people who use substances are involved with the carceral system in some manner, investigators anticipated that some eligible participants might meet the regulatory definition of a prisoner, either at the time of recruitment or after entering the study (Steely Smith et al., 2023). People who are prisoners are vulnerable because their liberty and autonomy is severely limited and, thus, they may lack opportunities to make voluntary, uncoerced decisions about whether to participate in research.

HBCD researchers had numerous questions regarding the point at which a person is considered "detained" in a treatment facility. For example, it was unclear whether a person receiving treatment in an unlocked residential treatment facility by court order was considered detained. It was also unclear whether a person is considered detained if they participate in a locked residential treatment facility, because they perceive such treatment would lower the risk of child removal by the welfare system. In such a case, the extent of coercion or duress leading to residential treatment may be difficult for researchers to ascertain. Entry into the justice system is often complex, and both researchers and participants may lack the full information necessary to determine whether someone has been "detained" for purposes of federal regulations.

Given the IRB requirements for enrolling prisoners, the WG asked these questions of the central IRB and ultimately deferred to their determination to examine recruitment from residential facilities on a case-by-case basis. Maintaining the option to enroll from residential facilities was important to sites who wanted to ensure that the population enrolled in HBCD was not merely "convenient" but truly reflected the population from which investigators wished to learn, particularly people with SUD, in keeping with the principle of fair subject selection.

2.6. Navigating reporting requirements

Participants cannot expect to derive direct benefits from participating in observational research; therefore, researchers must minimize risks to participants to maintain a favorable risk-benefit ratio. Ensuring confidentiality and carefully designing the informed consent process are critical for ensuring an appropriate risk-benefit ratio. In the HBCD Study, participant risk largely stems from researchers' knowledge of sensitive information related to a participants' life (e.g., their substance use) without the researcher having a plan to intervene to prevent harm (e.g., provide SUD treatment). In addition to information about substance use, researchers in the HBCD study might obtain data indicating that a participant child is experiencing developmental delays or behavioral challenges, that a participant is exposed to domestic violence, or that a participant has severe mental health disorder symptoms.

The WG was particularly concerned about substance use information from study participants who live in states where substance use during pregnancy is considered child abuse, even without evidence of harm to the child. HBCD relies on the willingness of participants to provide valid substance use reports; yet, in some states researchers are required to report substance use during pregnancy to child welfare agencies, potentially leading to harm to the participant and their family via arrest, detention, prosecution, custody loss, or stigmatization. Therefore, the ELP WG weighed in on how to balance the need to collect information about substance use, while attending to potential legal risks to participants who disclose their substance use. One solution was to have substance use questionnaire data and toxicology data sent to a central processing site without identifiable data being accessible to the local study site. Study sites would only obtain aggregate deidentified results regarding substance use. This solution attempts to mitigate legal risk to the pregnant person by protecting participants' privacy via blinding researchers and has the added benefit of maintaining scientific data integrity. Though some may criticize the study's efforts to create ethically permissible workflows that circumnavigate state law, the ELP WG sought a solution to prioritize respect for potential and enrolled subjects, minimize risk, and preserve the integrity of the research and relationships with participants. The ELP WG emphasized the importance of alerting participants during the informed consent process of what might fall under the requirements of mandated reporting.

The WG nevertheless recognized that some information may generate ethical obligations to report information and/or intervene. Such information could include self-disclosure or spontaneous sharing of information regarding intimate partner or domestic violence, concerns of child abuse or neglect other than substance use during pregnancy, or suicidal ideation. However, reporting of such information requires setting aside an obligation to protect participant autonomy and confidentiality and may result in a loss of trust between participants and the research team. Moreover, without resources and standard operating procedures (SOPs) in place, reporting may be subject to bias, inequity, and may lead to further harm and jeopardize the study's success (Raz, 2017). The ELP WG recommended that site personnel interpret their role as mandated reporters narrowly, not permissively, and focus on reporting *only* when mandated. Additionally, the WG recommended deferring to local site training and already established institutional SOPs.

2.7. Sharing incidental findings

By conducting an observational study, HBCD researchers are positioned to discover findings that have potential to impact health but are beyond the aims of the study, therefore prompting study leadership to question when individualized findings should be disclosed to participants. It was noted that participants may be motivated to participate or be retained in the study due to a perceived benefit of obtaining test scores about themselves and their children. Nevertheless, the purpose of such testing is for research, not clinical care.

Questions arose about how to navigate disclosure of clinically actionable, incidental findings from a child's developmental results or findings from biospecimens that may pose a threat to child or family welfare. For example, it was unclear whether participants should be told that their child scored below average on childhood development assessments performed during the study, even though the assessments were done for research rather than clinic purposes. Additionally, sites expressed concerns about navigating clinical alerts from screens for depression or adverse childhood experiences that do not qualify for mandatory reporting but raised concerns about participant welfare. The WG discussed the threshold that ought to be used to determine when individualized results are returned to participants, how results would be returned, and how to respond to participant concerns about results. Cognizant that not all study staff are clinicians and may not be equipped to interpret results or answer questions about results, the ELP WG recommended returning only *clinically actionable* findings, reviewed by content experts and utilizing well-established local resources for participant support. Again, the WG recommended utilizing the informed consent process to emphasize that, as participants in an observational research study, subjects will not be provided individualized results and referrals to care unless a clinical alert requires it. Providing clarity to participants about the specific types of results parents can expect to be

returned about their child and what kinds of concerns would trigger a clinical alert was also recommended.

2.8. Managing risk related to potential fentanyl exposure

Finally, to illustrate the complexities of managing risk in the HBCD study, we present the particular case of fentanyl positive biospecimen results for a participant who did not report having used that drug. People who use substances may become unknowingly exposed to fentanyl (e.g., due to a contaminated drug supply). Such individuals are at high risk for drug overdose and death. In the beginning phases of HBCD, the study's steering committee and BMO became aware of a discrepancy between a small number of participants' disclosure of fentanyl and biospecimens indicating the presence of fentanyl; such discrepancies could result from incomplete disclosure or intentional withholding of information, or they could indicate lack of awareness of substances being used.

Some members of the leadership team asked whether the site staff ought to consider linking individual biospecimen data back to participants, despite a prior commitment not to do so (see above), and warn these individuals of fentanyl risks. One interpretation of a researcher's obligation to maintain a favorable risk-benefit ratio would be to inform participants of fentanyl exposure, enabling participants to use this information to prevent future exposure and harm, Nevertheless, the ELP WG recommended against this approach for several reasons. First, biospecimen data is batched and tested at discrete intervals that could be temporally separated by months from when the sample was taken and the fentanyl exposure occurred, limiting the utility of that information. Second, returning results to individual sites could introduce legal risk to the participant if that site is in a state that requires reporting substance use during pregnancy to the child welfare system. Third, researchers promised during the informed consent process, not to link biospecimen data to individual participants, so returning individual level results could harm the foundation of trust on which the staff-participant relationship is built. Instead, the ELP WG recommended providing aggregate feedback to participants about this scenario and giving all participants harm reduction resources to mitigate the potential risks of unintentional fentanyl exposure, including education, naloxone (an overdose reversal medication), and fentanyl test strips. The ELP WG worked in conjunction with the BMO, the Steering Committee, and the NIH Bioethics Consult Service to produce a procedure for addressing this concern.

3. Discussion

Several legal and ethical challenges emerged in the initial phase of our work in the ELP WG of the HBCD study. While addressing bioethical and legal challenges, the ELP WG has leaned heavily on the informed consent process to ensure that participants are fully aware of the risks of participating in the study. Informed consent, borne out of a need to respect participants' autonomy and voluntary participation in research, is an ethically imperfect process (Grady, 2015). Informed consent ensures individuals control whether they enroll in clinical research when it is consistent with their values and interests. The HBCD informed consent has undergone a series of iterative and necessary revisions to capture the nuance needed to fully explain such a long and complicated study. Most bioethics scholars agree that informed consent is a representation and beginning of the relationship between participant and researcher (Pietrzykowski and Smilowska, 2021; Mandava et al., 2012, 356–365). In that vein, the ELP WG recommended that researchers revisit the informed consent process throughout the study to ensure that participants' informational needs are being met. Additionally, because the informed consent document contains so much essential information (from attendant legal risks to conditions for administrative withdrawal), it is important that participants have ready access to information in a form that is easy to understand. Creating a 'frequently asked questions' (FAQ) page on a public facing website was recommended to help accomplish that goal.

The ethical and legal challenges encountered in this study demonstrate that observational studies, not just interventional studies, must involve careful consideration from bioethical and legal experts. Challenges are heightened when the study involves participants with overlapping vulnerabilities and high-risk behaviors. HBCD researchers will likely be aware of potentially harmful behavior, be privy to clinically actionable results that are outside of the scope of the study or witness the sometimes-harsh realities that coincide with living life in a country without strong social support for pregnant and parenting people. Boots-on-the-ground study personnel will likely experience the moral dilemma of being bystanders to difficult situations and need to navigate a decisional calculus about when to intervene or not. Intervening – either through clinical alerts and referrals, resources, or access to peer navigators – will introduce bias, alter study results, and potentially undermine the scientific integrity of the observational study. Not intervening may result in personnel feeling morally culpable or experiencing moral injury or may erode trust with participants. Because it will not be possible to anticipate the many scenarios that may come up, study personnel will benefit from ongoing support from the BMO, the ELP WG, and locally embedded bioethics scholars to address these scenarios. Raising awareness of these kinds of scenarios and creating a cohesive and standardized plan to address them will be important for maintaining scientific integrity and equity among sites and participants. More broadly, additional research may help delineate researchers' obligations in observational studies where known inequity exists.

While the details and context of any study clearly matter a great deal for the ethical resolution of challenges like those discussed here, we have three high level recommendations based on our experience for studies where participants face evolving legal risks related to information obtained during the research. First, the inclusion of legal and ethics experts within study teams can be helpful in studies where ethical and legal challenges are likely to arise that are difficult to anticipate. While research ethics consultation services can provide some guidance, we have found that intensive engagement and collaboration is often required to navigate complex ethical tradeoffs. Second, while community engagement and coordination with local officials can minimize legal risks for participants and help with a study's success, in contexts where participants face legal risks, this may not be possible. Alternative ways to protect participants include limiting access to information from individual participants at the site level and analyzing data centrally. Finally, restrictive legal regimes can have unintended consequences for research that can undermine the protection of children and families. The more challenging it is to conduct research with pregnant people and children facing adverse experiences during childhood, the more difficult it will be to understand how to intervene and improve outcomes for children and families in the future.

4. Conclusion

While navigating the challenges discussed above, the ELP WG worked to maintain participant trust as an overarching and repeated goal. The ethical and legal trade-offs that are incumbent in the execution of this study require careful consideration to reduce participant harm by avoiding legal risk and protecting participant privacy and to prioritize participant respect. We hope that this discussion contributes to the growing literature on ethical and legal issues in observational studies with pregnant and substance using individuals by clarifying the complex considerations and balancing required in the practical application of an established framework to ensure ethical clinical research.

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Data Statement

Data not available to be shared. The raw/processed data required to reproduce the above findings cannot be shared at this time due to legal/ethical reasons.

CRediT authorship contribution statement

Sharlene Newman: Writing – review & editing, Conceptualization. **Paul Spicer:** Writing – review & editing, Conceptualization. **Seema K Shah:** Writing – review & editing, Writing – original draft, Formal analysis, Conceptualization. **Barbara Andraka-Christou:** Writing – review & editing, Formal analysis, Data curation, Conceptualization. **Jenny Kingsley:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **the HBCD ELP WG:** Conceptualization. **Pilar N. Ossorio:** Writing – review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. Jenny Kingsley reports financial support was provided by National Institutes of Health. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.dcn.2024.101460.

Data availability

Data will be made available on request.

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