Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Jessica Blackburn Date

Variation in interpretation of Subpart B conditions by stakeholders in the IRB review process of abortion research, United States, 2019

By

Jessica Blackburn

Master of Public Health

Hubert Department of Global Health

_____

Roger Rochat, MD

Committee Chair

_____

Lisa Haddad, MD, MS, MPH

Committee Member

_____

Sarah Cordes, MPH

Committee Member

Variation in interpretation of Subpart B conditions by stakeholders in the IRB review process of abortion research, United States, 2019

By

Jessica Blackburn

Bachelor of Science

University of Georgia

2012

Thesis Committee Chair: Roger Rochat, MD

An abstract of a thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Hubert Department of Global Health

2019

Abstract

Variation in interpretation of Subpart B conditions by stakeholders in the IRB review process of abortion research, United States, 2019

By Jessica Blackburn

Background: Federal regulations for the protection of human research participants in the United States include specific protections for pregnant women, known as Subpart B. These protections are meant to prevent pregnant women from being coerced into abortion but may restrict investigators' involvement in investigational abortion procedures. No published report has evaluated how IRB stakeholders interpret the conditions of Subpart B when applied to abortion research.

Methods: 117 IRB personnel from U.S.-based institutions considered to be stakeholders in the ethical review process for abortion research participated in an online survey. The survey measured participant confidence in applying the conditions of Subpart B to prospectively enrolling research on abortion and specific interpretations of the Subpart B conditions to this type of study. The survey also collected information on participants' personal experience with IRB review of abortion research. Descriptive statistics were run using SAS 9.4.

Results: Confidence in reviewing abortion research under Subpart B is high, with 83.8% of respondents reporting confidence in applying the special protections for pregnant women to this type of study. Despite high confidence in applying the conditions, interpretation of the Subpart B conditions varies, even among participants with high confidence. Overall, 73.9% interpreted that Subpart B prevents investigators from randomizing subjects to different methods of abortion, 68.2% of respondents believe Subpart B prohibits researchers from serving as a study's abortion practitioner, and. 46.6% of participants believe Subpart B prohibits research compensation.

Conclusions: Confidence in applying Subpart B does not correspond to manner of interpreting the conditions of Subpart B. In this study, we were unable to determine a way to predict which IRB personnel will interpret the conditions more literally than others will. Standardization of interpretation of Subpart B may prevent IRB review from serving as a barrier to conducting abortion research.

Variation in interpretation of subpart B conditions by stakeholders in the IRB review process of abortion research, United States, 2019

By

Jessica Blackburn

Bachelor of Science

University of Georgia

2012

Thesis Committee Chair: Roger Rochat, MD

A thesis submitted to the Faculty of the Rollins School of Public Health of Emory University in partial fulfillment of the requirements for the degree of Master of Public Health in Hubert Department of Global Health

2019

Contents

I. Introduction

In the United States, most human subjects research is required to undergo review by an institutional review board (IRB) that is tasked with determining the research meets approval criteria codified in federal regulations or that the research is exempt from those requirements [1]. The Common Rule serves as the baseline level of human subjects protections, but each IRB may follow additional policies and procedures that may further restrict the types of research activities at the institution.

The Common Rule also provides additional protections for three specific vulnerable populations defined as children; pregnant women, fetuses, neonates; and prisoners [1]. The protections for pregnant women include requirements at 46.204 that "(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy; and (i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy" [1]. These conditions appear to limit the influence of the research investigators on women seeking abortion and therefore limit clinical research on the topic of pregnancy termination.

Historical events previously excluded women from participating in clinical research, but those restrictions have gradually relaxed over time "with a shift in advocacy from protecting subjects from risks of research to ensuring the inclusion of subjects in research"[2]. Further complicating matters is the changing political and legal landscape surrounding abortion in the United States. A 2017 study on the federal regulations' impact on abortion research found that IRBs interpret Subpart B in many different ways and these varied interpretations limit investigators' abilities to conduct abortion research [3]. The complementary perspective of IRB

professionals is needed to assess the confidence of IRB professionals in applying Subpart B to prospectively enrolling research on abortion and to discover whether IRB professionals are interpreting specific research regulations in restrictive ways.

Problem statement

IRB review is serving as a barrier to conducting abortion research in the United States.

Purpose statement

To determine if differing interpretations of research regulations impact IRB ethical review and approval of prospectively enrolling human subjects research on abortion.

Research question

In institutions likely to have reviewed research on abortion, how are human research protection program professionals applying the Common Rule's Subpart B to prospectively enrolling research on abortion?

Sub questions:

Which personal and institutional attributes of respondents are correlated with experience of IRB review of abortion research and overall confidence in applying Subpart B to abortion research?

In which Common Rule Subpart B conditions are IRB professionals most and least confident in their interpretation?

What is the geographic distribution of respondents that have reviewed research on abortion and how does this compare to the distribution of abortion services provided in the U.S.?

Which aspects of IRB review are more concerning for IRB professionals reviewing research on abortion than for research on other health topics?

Significance statement

IRB ethical review of human subjects research can influence availability of treatments to people who need them. If IRB review serves as a barrier to research on abortion, this may impact the methods and providers of abortion that are available to women seeking to terminate their pregnancies and may reduce access to safe abortion.

Definition of terms

- Abortion: Induced termination of pregnancy. This definition excludes miscarriage.
- Human Subjects Research: Investigations designed to develop generalizable knowledge that involve living individuals or their private information or biospecimens [1].
- Human Research Protection Program: The institutional body that serves to protect human research participants from harm or risk. This includes the IRB as one component and may encompass other groups at a given institution that are affiliated with compliance, risk management, or clinical research offices.
- Pregnancy: The period of time after fertilization from implantation until delivery. “A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery” [1].
- Prospectively-enrolling: Research involving the enrollment of eligible research subjects through an informed consent process or waiver thereof. This definition excludes research designs such as retrospective medical record review or secondary data analysis.

II. Literature Review

In the United States, federally supported human subjects research is required to undergo ethical review by an institutional review board (IRB) that is tasked with determining the research meets approval criteria codified in federal regulations or that the research is exempt from those requirements [1]. Overall, the Common Rule, so-called because of the now twenty federal agencies that have agreed to follow the rule [4], is meant to standardize ethical review of research conducted or supported by these federal agencies. Despite this standardization, individual differences exist between the way IRBs interpret and apply the federal regulations for research under their review.

Each IRB is comprised of diverse and experienced members who are sensitive to community attitudes while protecting the rights and welfare of human research subjects [1]. Because IRBs are convened at the institutional level, an IRB is expected to represent the community's perspective in reviewing both new studies and ongoing research. Therefore, an IRB at one institution may approve a research proposal that would not be considered approvable-as-written by an IRB at a different institution. The Common Rule sets national standards so that two IRBs in different places across the country apply similar standards to human subjects research, even if the end result of the ethical review process is not completely identical.

Further influencing local review of research, each IRB must establish and follow its own written procedures for initial study review, continuing review of ongoing research, proposed modifications to ongoing research, and prompt reporting to various stakeholders of any problems or errors that arise during the conduct of a research study [1]. These written policies serve to standardize local within-IRB review of research, so that similar studies receive similar treatment by the same IRB over time.

IRB ethical review applies to both biomedical research and social-behavioral research and a myriad of research activities. Research procedures reviewed by IRBs range from participant observation, secondary data or specimen analysis, interviews and focus groups, to clinical trials. IRBs conduct initial review of new studies, continuing review of many studies on at least an annual basis, proposed modifications to approved research, and problems with research [1].

The Common Rule regulations, at 45 C.F.R. Part 46, cover the applicability of the rule, including whether research is exempt from the rule, and provide requirements for IRB Membership, IRB functions and operations, and IRB review of research [1]. At a minimum, for any federally supported research study, the IRB must find and document the Common Rule approval criteria: that risks to subjects are minimized and there is a good risk benefit ratio, that the selection of subjects is equitable, that informed consent will be sought and appropriately documented (or waived if appropriate), and that the study will appropriately monitor data and protect subjects' privacy [1]. The approval criteria leave room for subjective interpretation in how to apply the requirements to each study under review.

The Common Rule also distinguishes additional special protections for populations of research subjects who are vulnerable to coercion or undue influence, specifically defined in the regulations as pregnant women, human fetuses, and neonates; prisoners; and children [1]. These special protections include additional criteria that IRBs must document as met when reviewing and approving any new study targeting, or in some cases, incidentally enrolling these populations [1]. Despite the existence of other vulnerable groups and even other types of vulnerability experienced by the protected populations, the research regulations only require additional protections against coercion or undue influence for these three vulnerable groups.

The Common Rule's regulations, including the protections for vulnerable populations, apply strictly to federally supported human subjects research. There is a long-standing history of restricting federal funding for abortion services that would reduce the likelihood that abortion research be awarded federal funding. This is due to the Hyde Amendment, which has been supported by legislators who oppose abortion and object to the use of federal taxpayer funds for abortion services since 1976 [5]. Due to its wide reach, the Hyde Amendment is now considered a "government-wide imperative" [6] at restricting federal funding, including federal research dollars, from supporting abortion services [7].

Although most abortion research is not federally funded, some institutions may still apply The Common Rule to non-federally funded abortion research for at least two reasons. The first reason is that the Office of Human Research Protection's (OHRP's) federal-wide assurance (FWA) process. This process is a precursor for every institution applying for federal funding for human subjects research, and it used to include an option for institutions to voluntarily pledge to conduct all human subjects research, regardless of funding source, in compliance with the Common Rule [8]. An educational webinar conducted by OHRP in 2013 reported that two-thirds of U.S. institutions voluntarily made this pledge, or pledged to apply all subpart protections to all research, regardless of funding support [8]. The option of documenting the application of the Common Rule to all human subjects research by checking the box on the FWA no longer exists, as this option was removed with revisions to the Common Rule [9]. Despite this change, it is possible that many IRBs have not changed the practice of applying the Common Rule to all research at their institution, if they had done this previously.

A second driver of the broad application of the Common Rule to research that is not federally funded is the human research protection program accreditation process. The

Association for the Accreditation of Human Research Protection Programs, or AAHRPP, promotes quality research ethics review both in the United States and abroad by accrediting human research protection programs, which include IRBs as one component [10]. AAHRPP is an independent, non-profit accrediting body that imparts its own set of standards on accredited groups to promote quality IRB review and improved human subject protection [10, 11]. While the federal regulations influence AAHRPP, the organization sets its own standards above what the Common Rule requires. As a result, institutions with AAHRPP accreditation may impart stricter approval criteria than the Common Rule requires, since AAHRPP recommends that accredited organizations provide equivalent protections to non-federally funded research, and to surpass federal requirements while promoting scientific advancement [12]. AAHRPP accreditation may drive accredited IRBs to apply the Common Rule to research that is not federally funded, including abortion research.

If IRBs apply the Common Rule to non-federally funded research then they should be applying Subpart B, or the specific protections for pregnant women to that research. The Subpart B protections were born from historical events that impacted women and their children in clinical research. One such watershed event was the use of the drug thalidomide. The drug, never approved for use by pregnant women in the U.S. due to a vigilance by FDA, was found to cause birth defects in pregnant women who used the drug in Europe in the 1960s. [2, 13]. This public health victory caused FDA to publish guidance in 1978 that recommended restricting all women of childbearing potential, not just pregnant women, from participating in clinical evaluations of drugs [14]. In the guidance, it was recommended that it consistently be assumed that any investigational drug could cause harm to a fetus and could be passed to infants in breast milk [14]. All women were excluded from clinical drug research on the basis that risks to fetuses or to

breastfeeding infants were too great to rationalize study participation. This policy was not overturned by FDA until 1993 [2] and the National Institutes of Health (NIH) made inclusion of women and minorities in clinical research a requirement within a year of FDA's change [2, 15].

Despite an official reversal of the policy to exclude women from clinical drug research, the practice of limiting pregnant women's participation in research continued due to the Subpart B protections for pregnant women. The special protections were written to protect pregnant women from adverse effects of clinical research on their pregnancies and to prevent pregnant women from being coerced into abortion so that researchers could obtain fetal tissue for research [16, 17]. The Subpart B protections contain ten additional conditions that a study must meet in order to be approved to include pregnant women as a population. The protections include requirements at 46.204 that "(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy; …(i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy"[1]. In addition to the primary intent to safeguard women, the regulatory conditions appear to reduce a research study's influence on abortion procedures, potentially limiting clinical research on abortion that could improve outcomes and access for future women seeking abortion services.

A task force was created by the 21st Century Cures Act at NIH specifically to address the problem of limiting pregnant women's participation in research, called the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC) [18]. PRGLAC has made recommendations to remove the regulatory barriers to the participation of pregnant women in research by modifying Subpart B to remove pregnant women as a vulnerable population [19]. This recommendation was well-received, and the most-recent changes to the Common Rule attempted to address this change to Subpart B [20].

The Common Rule changes were meant to both improve research subject protections and to clarify ambiguity for investigators [20]. Stakeholders from across the United States were invited to offer comments on many proposed changes in the advanced notice of proposed rulemaking (ANPRM), including whether pregnant women should continue to be categorized as a vulnerable population. [20]. “In particular, public comment is sought about whether pregnant women…should be characterized as vulnerable to coercion or undue influence. Whether or not these subpopulations are considered vulnerable to coercion or undue influence would not affect the applicability of Subpart B” [20]. With over two thousand comments published in response to the ANPRM (Federal Policy for the Protection of Human Subjects), the final rule was published and went into effect on January 21, 2019. While the final rule, now known as the Revised Common Rule or the 2018 Common Rule when emphasizing the revisions, did indeed remove pregnant women from the preamble of the regulations, the text at 45 C.F.R. 46 Subpart B still includes pregnant women in its scope as a vulnerable population [9]. As promised, the federal regulations still apply to research including pregnant women despite the Common Rule revisions.

In addition to the conditions of Subpart B, conservative and risk-averse oversight by IRBs reduces participation of pregnant women in research, according to PRGLAC [21]. With IRBs hesitant to accept risk, the environment for research on pregnant women is especially fraught when the research focuses on abortion due to a changing political and legal environment. In 2019, the Guttmacher Institute described a wave of state abortion bans as unprecedented, reporting that there were twenty-seven abortion bans enacted across twelve states [22]. Further, the Trump Administration has repeatedly pushed against access to abortion [5], with Alex Azar, Secretary of Health and Human Services, the parent agency of OHRP, recommending that

United Nations Member States reduce access to abortion since pregnancy termination is not a human right [23]. With government authorities attacking abortion access, IRBs may be hesitant to oppose government political agendas, especially since government regulators oversee IRBs. The political environment may influence IRBs in their ethical review of abortion research.

Abortion research can make abortion procedures even safer and can expand access to abortion by collecting and providing evidence to support new methods or providers of abortion services. Abortion methods need to be rigorously tested before being implemented or serious consequences can result. Investigators from the Centers for Disease Control and Prevention conducting abortion surveillance activities have determined that "new abortion methods should be tested according to a detailed research protocol, under careful scientific and medical supervision…" [24] in order to avoid severe complications or maternal mortality from abortion. Successful IRB review and approval of research proposals aimed at investigating abortion must be achieved before well-designed research studies on the topic can go forward.

Differing practices in applying research regulations, historical factors, and changing legal and political environments challenge IRBs across the United States in conducting ethical review and approving proposed abortion studies. A 2016 survey of IRB chairs and directors by Borgatta and colleagues found that 29% of those who responded expected outright refusal of review of abortion research [25]. A 2017 study by Verma and colleagues interviewed directors of family planning fellowships and found that IRBs interpret Subpart B in many different ways [3]. These varied interpretations limit investigators' abilities to conduct abortion research by limiting investigators' experimental manipulation of abortion procedures [3]. The complementary perspective of IRB professionals likely to have been exposed to abortion research is needed to determine whether Subpart B protections are limiting abortion research.

III. Methods

Introduction

This study involved developing and validating a survey to assess IRB staff, members, and broader human research protection program (HRPP) members' experience and confidence in applying the federal regulations to prospectively enrolling research on abortion. We began developing the survey by first developing a draft version and conducting key informant interviews to improve survey questions, prioritize them, and ensure all relevant demographic information was included in the survey questions. We revised the survey draft after all key informant interviews were completed based on the feedback provided. We then pilot tested the revised survey and further refined it based on feedback before disseminating the survey to the sample. The SurveyMonkey survey was available for about one month, from July 29, 2019 to August 26, 2019, before it was closed to new responses.

Student Contribution

The student was responsible for research activities at all stages of the research project, from study conception and design through analysis and composition of this manuscript. The student designed the initial survey instrument, conducted key informant interviews, pilot tested the survey, and oversaw data collection. After data collection was completed, the student analyzed data and reported the findings. Co-authors included Dr. Roger Rochat, Dr. Lisa Haddad, and Ms. Cordes. All co-authors provided guidance during the data collection and analysis phases of the study and provided feedback on the survey instrument and the manuscript.

Population and sample

The population under study was human research protection program professionals (HRPP) considered to be stakeholders in the IRB review process or compliance oversight for prospectively enrolling research on abortion. The study sample consisted of HRPP staff who were associated with institutions with Family Planning Fellowships, or whose IRB was associated with prospectively enrolling research on abortion published within the last four years or ongoing clinical research. In order to build the sample pool, we first determined the institutions that should be included in the sample. IRBs associated with Family Planning Fellowships are likely to review prospectively enrolling research on abortion since the Family Planning Fellowship vision is "to ensure that quality abortion and contraception are valued as core essential components of women's health," and the fellowship focuses on subspecialist training in research [26]. We conducted a literary search on PubMed using the term "abortion." We reviewed the results for prospective enrollment by excluding case series or retrospective chart reviews, and excluded studies published before 2015. We also collected institutional participation in the targeted research by reviewing ClinicalTrials.gov to determine whether there were ongoing studies whose institutions should be included. Once the institutions were identified, we navigated to their publicly available IRB websites and reviewed the information on the contacts page. We included all email addresses in the sample pool that were included on the first page of contacts. Some institutions included just HRPP staff and some included IRB members or institutional officials in addition to the staff listing. All email addresses included on each institution's main contact page were used in the sample. In total, thirty-two institutions were included, and six hundred and one contact emails were included in the sample.

Research design

A quantitative online survey disseminated by email through SurveyMonkey assessing HRPP professionals' experience and confidence in applying research regulations to research on abortion.

Drafting the survey

We first developed the survey by considering the characteristics that would be most important to collect about the respondents and how their responses could be stratified and displayed with regard to confidence in applying the research regulations to the studied research type. We drafted a table to display descriptive data about the respondents in order to consider the most important information to include in the survey. We drafted the first survey after taking all this information into account. The first draft of the survey included some demographic questions as well as some scenario-based questions that were designed to elicit responses regarding IRB professional methods of applying research regulations to different types of studies.

Key Informant Interviews

We completed four key informant interviews to further inform the draft survey. We drafted an interview guide to cover some of the lingering questions we had about the survey and conducted semi-structured interviews to allow for time to cover new topics we had not yet considered studying. We purposively sampled interview subjects to include the various respondent roles being studied as well as to cover the perspective of abortion researchers. In total, we interviewed two IRB members, one IRB staff-person, and one abortion researcher to inform survey development. Each interview took about twenty minutes to conduct and all were conducted in-person in a private place of the subject's choosing or, in the case of the abortion researcher, by phone. The IRB members provided valuable feedback on how to assess survey

respondents by measuring confidence rather than knowledge and methods of applying regulations. Additionally, one IRB member advised us to ask about institutional policy regarding research on abortion rather than religious affiliation, since institutional policy is the true root cause of systematic treatment of abortion research by HRPPs. Further, one IRB member encouraged us to ask about respondents' personal viewpoints on abortion at the end of the survey as a factor to use to stratify the respondent pool without overly biasing the results. An IRB member also recommended that we ask about respondent recusal from IRB review or pre-review activities based on personal beliefs. We were also advised by an IRB Staff person to ask about how dual roles of abortion researchers (serving as faculty and serving as a medical director for a local clinic, for instance) might be complicating research on this topic. An IRB staff member recommended that we ask about respondent perspective on the value of abortion research compared to research on other health topics to see if personal viewpoints on abortion carry over into differing professional values. The abortion researcher recommended asking whether IRB membership includes women's health practitioners since the perspective of the research community is that the IRB review process is more straightforward when IRB membership reflects the researcher proposing a new study.

Some respondents recommended that we incorporate a way to measure differing state laws' impact on respondents, but there did not appear to be a simple and succinct way to include all of the current and potential future legal nuances in the survey. One respondent also recommended covering the topic of fetal tissue research, but we wanted to keep the survey response rate up by narrowing the focus as much as possible and decided to reserve the topic of IRB management of fetal tissue research for future research projects.

Revising the Survey

We revised the survey based on the feedback we received during the interviews. Also, all collaborators critiqued the survey question wording and made their own suggestions for additional information to collect. We made some changes based on formatting and lay-friendliness. We then entered the survey into SurveyMonkey to prepare for pilot testing.

Pilot testing

Next, we held one pilot testing focus group with four IRB staff from the Emory IRB. Staff were purposively sampled based on role at the IRB and experience level. We wanted to ensure that less-experienced respondents were able to understand the survey questions and provide responses with the same ease as those who have more experience. We selected two participants with just over a year of IRB experience and two participants with over five years of IRB experience. All pilot testers were gathered in a conference room on the Emory University campus where refreshments were provided. After conducting an informed consent discussion and answering questions, the focus group participants were given time to complete the survey and then provide their feedback in a group-based setting. None of the pilot tester survey responses were saved for analysis, in order to encourage greater engagement with the survey and the focus group discussion. The testers used different devices to ensure the survey displayed correctly on tablets, mobile phones, and laptop computers. The pilot testers encouraged us to provide more introduction to the matrix-based questions on each page in which they were presented, so that respondents would know there was continuation from the previous question. The pilot testers confirmed the survey displayed correctly on all devices and made other recommendations for simplification of question wording. We concluded the pilot testing focus group and revised the survey based on focus group participant feedback. The survey was then purposively pilot tested on one additional IRB staff member with experience at multiple institutions in order to promote

clarity in asking about cumulative experience versus institution-specific experience. We also wanted to take the opportunity to ensure the terminology for IRB review processes was not specific to one institution and would be recognized by the sample population regardless of institutional affiliation. The same pilot tester reviewed the survey introduction email and advised us to rename the survey to "IRB Management of Family Planning Research Study" rather than "IRB Management of Abortion Research Study" so as not to discourage responses from those who feel the word abortion is charged. The email text made it clear that abortion research was the focus. The final survey was 36 questions long and incorporated skip logic to advance respondents through questions about previous experience reviewing abortion research if they reported not having such experience.

Survey dissemination

The survey was sent to all 601 email addresses in the sample on July 29, 2019. Recipients received a brief introductory email and a link to the survey through SurveyMonkey. Six emails bounced and were undeliverable to the recipients, while a total of 33 prospective respondents opted out of the survey using the automated unsubscribe function and five requested to be removed from the survey by responding to the invitation email with a request to be removed. Recipients received reminder emails approximately once a week to remind them of the survey while it was available. The survey was closed to responses on August 26, 2019.

Analysis

The confidence matrix responses were each transformed into numerical values 1-5 by coding, with responses of “very unconfident” given a score of 1, “unconfident” given a score of 2, and so on until “very confident” was given a score of 5. Each respondent was given an overall confidence score that was calculated by finding the median of the transformed confidence responses they answered. All calculated confidence scores were rounded up to the nearest whole number, since there is no way to interpret any non-integer value in confidence. The confidence scores were then transformed back into the corresponding text confidence value.

We reviewed all data for trends in confidence applying research regulations, personal experience with IRB review of abortion research, and interpretations of Subpart B conditions. Then, we reviewed the data to see if respondent groups answered uniformly or if there were differences between respondent groups for various questions. We used chi-square tests to compare groups and used an alpha level of .05 for all statistical tests. We also rank-ordered the proportion of “confident” or “very confident” responses for each condition of Subpart B in order to determine which conditions were the most difficult for respondents to apply to prospectively enrolling.

We summarized the descriptive statistics of our population compared to the experience of abortion research as reported by our respondents. We also summarized the reported experience of abortion research by geographic region and compared that data to abortion incidence and rate data reported by the Guttmacher Institute from 2017 [27] to identify whether abortion research appears to be following the trends of abortion services provided in the U.S.

We categorized the free-text responses into different categories and summarized the responses. Data cleaning and creation of the confidence score variable were completed in

Microsoft Excel (2016), which was also used to create a graph comparing abortion rate from 2016-2017 to abortion research experience by geographic region. Survey response analysis was performed in SAS 9.4 (SAS Institute, Cary NC).

Instruments

The key informant interview guide, focus group discussion guide, and survey instrument can be found in Appendix I, II, and III respectively.

Ethical Considerations

This study was determined exempt by the Emory Institutional Review Board under study number IRB00112484. Prospective respondents were provided with an information sheet outlining the elements of informed consent and were required to click "yes" in order to agree to participate in the survey. The information sheet included contact information for the study team and for the Emory IRB. We were professionally recused from all IRB review activities associated with this study.

Limitations/Delimitations

The study sample does not include all HRPP staff who may be involved in the review of prospectively enrolling abortion studies. The sample includes those whose institutions may have approved these types of studies based on published literature or the existence of ongoing clinical research, but not necessarily all those who have received these types of submissions for review. More institutions may be receiving research proposals for abortion studies and determining that the studies are not approvable. Further, the study was designed by interviewing and pilot testing with staff from a single institution through a convenience sample, though some of these subjects have experience in human research protection from different institutions. With this convenience

sample used during survey development, there is a risk that the survey instrument is not validated to be used with staff from different institutions.

There is a risk of selection bias through self-selection to respond to the survey. It is possible that those with more polarized opinions of abortion research chose to respond to the survey and those with more middle-ground views chose not to participate. No compensation was offered to participate in the survey, which may have reduced response. Further, the survey assumed some familiarity with technical vocabulary and research regulatory text that is common in the research administration industry. This language may have been less familiar to individuals with less experience.

We undertook the study to explore whether other HRPP staff feel confident in their review of abortion research, how they are interpreting regulations related to abortion research, and to gauge the frequency that HRPP staff are faced with reviewing these types of submissions. We chose not to sample those unlikely to receive these types of studies as they may not be as familiar with the application of research regulations to abortion research. We excluded Emory University IRB personnel from the sample since many were involved in the survey development and pilot testing stages. While fetal tissue research is another controversial research ethics and research administration topic tangentially related to research on abortion, we excluded it from the survey in order to keep the survey to a manageable size and encourage survey completion.

We discussed attempting follow-up phone call interviews to respondents to try to understand both motivations for participation and hesitancy to participate that may have contributed to the lower response rate. After discussion, we decided that those who were hesitant to respond to the survey might also be hesitant to take part in a follow-up interview, especially

with the same study staff. Therefore, we do not know why some eligible participants chose not to participate.

IV. Results

Response

120 respondents clicked the SurveyMonkey survey link in their emailed invitation. and six email invitations were undeliverable to their recipients. The response rate was 20.2%. Three respondents were presented with the informed consent information sheet and declined to participate.

A total of 117 respondents continued to the survey. There were 87 complete responses and 30 partial responses. One participant did not provide any answers to demographic questions but responded to the remainder of the survey questions beginning with questions about confidence in applying Subpart B conditions to prospectively enrolling research on abortion. 18 (15.4%) respondents withdrew from the survey before completing any confidence in applying Subpart B matrix-based questions and an additional eight (6.8%) participants withdrew between webpages of the confidence applying Subpart B questions. There did not appear to be any trends in respondent confidence among those that partially completed confidence questions. Three participants completed all questions except questions about specific interpretations of subpart B conditions.

Study Population

The demographic and descriptive characteristics of our study population are presented in Tables 1 and 2. The majority of our participants identified as female (76.9%) and reported personally being pro-choice with regard to their beliefs about abortion (59.0%). Most of our respondents (60.7%) had over five years of experience working with a human research protection program, with over 40% of the study population reporting that they had ten or more years of overall experience in the field. Most of our respondents (79.4%) worked in a role directly related

to the IRB as an analyst or coordinator, IRB staff leader, IRB member, or IRB chair. The remainder characterized their roles as “other” or administrative in nature. Some (46.2%) reported that they held the Certified IRB Professional (CIP) certification. Most participants had experience with both biomedical and social-behavioral research (53.9%) or biomedical research only (38.5%).

Table 1. *Reported personal experience of abortion research by respondent personal characteristics*

Characteristic	Experience (n, %)	Experience-naïve (n, %)	Experience missing (n, %)
Experience in years			
0-1	0 (0)	8 (13.3)	0 (0)
2-5	12 (22.6)	23 (38.3)	2 (6.3)
6-9	14 (26.4)	9 (15.0)	0 (0)
10+	27 (50.9)	20 (33.3)	1 (2.0)
Gender			
Female	42 (79.3)	46 (76.7)	2 (2.2)
Male	10 (18.9)	14 (23.3)	1 (4.0)
CIP-Certified			
Yes	31 (58.5)	22 (36.7)	1 (2.0)
No	22 (41.5)	38 (63.3)	2 (3.2)
Role			
Administrative	6 (11.3)	9 (15.0)	0 (0)
IRB Analyst/Coordinator	17 (32.1)	39 (65)	1 (1.8)
IRB Staff Leader	15 (28.3)	10 (16.7)	1 (3.9)
IRB Member	2 (3.8)	0 (0)	0 (0)
IRB Chair	7 (13.2)	1 (1.7)	0 (0)
Other	6 (11.3)	1 (1.7)	1 (12.5)
Personal Belief			
Pro-choice	20 (71.4)	47 (82.5)	2 (2.9)
Pro-life	3 (10.7)	3 (5.3)	0 (0)
Neutral	2 (7.1)	5 (8.8)	1 (12.5)
Undecided	1 (3.6)	0 (0)	0 (0)
Other	2 (7.1)	2 (3.5)	0 (0)

Our respondents represented most regions of the United States except for the West South Central portion including Texas, Oklahoma, Arkansas, and Louisiana. The region most heavily represented was the Pacific (29.9%), including respondents from Washington, Oregon, California, Alaska, or Hawaii. More than three quarters of our respondents reported working for

an institution that was AAHRPP-accredited (78.6%). About half of the respondents (51.3%) reported that abortion procedures are performed by individuals at their institutions. Some respondents (45.3%) reported that they had personally experienced IRB review or pre-review activities for prospectively enrolling research on abortion.

Table 2. *Reported personal experience of abortion research by institutional characteristics*

Institutional Characteristic	**Experience n (%)**	**Experience-naïve n (%)**	**Experience Missing n (%)**
Region			
New England (ME, NH, VT, MA, RI, CT)	5 (9.43)	5 (8.3)	1 (33.3)
Middle Atlantic (NY, NJ, PA)	6 (11.3)	11 (18.3)	0 (0)
East North Central (OH, IN, IL, MI, WI)	3 (5.7)	9 (15.0)	0 (0)
West North Central (MN, IA, MO, ND, SD, NE, KS)	5 (9.4)	2 (3.3)	0 (0)
South Atlantic (DE, MD, D.C., VA, WV, NC, SC, GA, FL)	4 (7.6)	7 (11.7)	0 (0)
East South Central (KY TN, AL, MS)	2 (3.8)	4 (6.7)	0 (0)
Mountain (MT, IO, WY, CO, NM, AZ, UT, NV)	6 (11.3)	10 (16.7)	1 (33.3)
Pacific (WA, OR, CA, AK, HI)	22 (41.5)	12 (20.0)	1 (33.3)
AAHRPP-Accredited			
Yes	38 (71.7)	52 (86.7)	2 (100)
No	15 (28.3)	8 (13.3)	0 (0)
Majority of Active Studies			
Social-behavioral only	0 (0)	2 (3.3)	0 (0)
Biomedical only	17 (32.1)	20 (33.3)	1 (33.3)
Both Social-behavioral and Biomedical	36 (67.9)	37 (61.6)	1 (33.3)
Other	0 (0)	1 (1.7)	1 (33.3)

Abortion Research IRB Submissions

Of those that reported experiencing IRB review of abortion research (n=53), most (55.8%) reported that they are personally involved with one to four research protocols a year, though 25% of those with abortion research experience reported personal involvement with more

studies on an annual basis. The type of research reported for abortion research studies reviewed by respondents followed the pattern of overall research experience, with 40.4% reporting experience with both biomedical and social-behavioral abortion research and 42.3% reporting biomedical abortion research experience only. A minority of those who have experienced IRB review of abortion research (36.5%) reported they felt abortion research has changed over time. Two respondents reported that they had experienced IRB review for a study not considered approvable under the Common Rule that was reviewed by the Secretary of the Department of Health and Human Services (HHS). Despite this response, personal communication received from Misti Ault Anderson, Senior Advisor for Public Health Education at the Office for Human Research Protections under HHS [28], confirmed that no research proposal has been submitted for consideration under this part of the regulations since it went into effect on December 13, 2001.

Comparison of Abortion Research Reported to Abortion Services Provided

Table 3 summarizes the number of reported abortions in 2017 (the most recent data available, published by the Guttmacher Institute [27]) and the number of women of childbearing potential in 2016 (the most recent complete state-level data available, published by the March of Dimes [29]) for each geographic region compared to survey response and abortion research experience of respondents. The Pacific had a high proportion of respondents who have experience reviewing abortion research (62.9%) and is also the only geographic region from which participants reported ten or more protocols involving abortion personally reviewed on an annual basis. Despite having the second-highest proportion of respondents with abortion research experience, the Pacific appears to be the region with the most abortion research density, since more respondents with abortion research experience reported a larger quantity of abortion

research protocols reviewed annually. The Pacific performs 19% of abortions in the United States. The West North Central region had the greatest disparity between abortion research experience and abortion rate, with 71.4% of respondents reporting abortion research experience but only performing 3.5% of the abortions in the United States in 2017. This region had an abortion rate of only 7.5 abortions performed per thousand women aged 15-44 in 20 while the rate for the entire United States was 13.5. Figure 1 presents this information graphically.

Table 3. *Geographic region by annual number of protocols involving survey respondents with abortion research experience compared to abortion services provided in 2017*[abc]

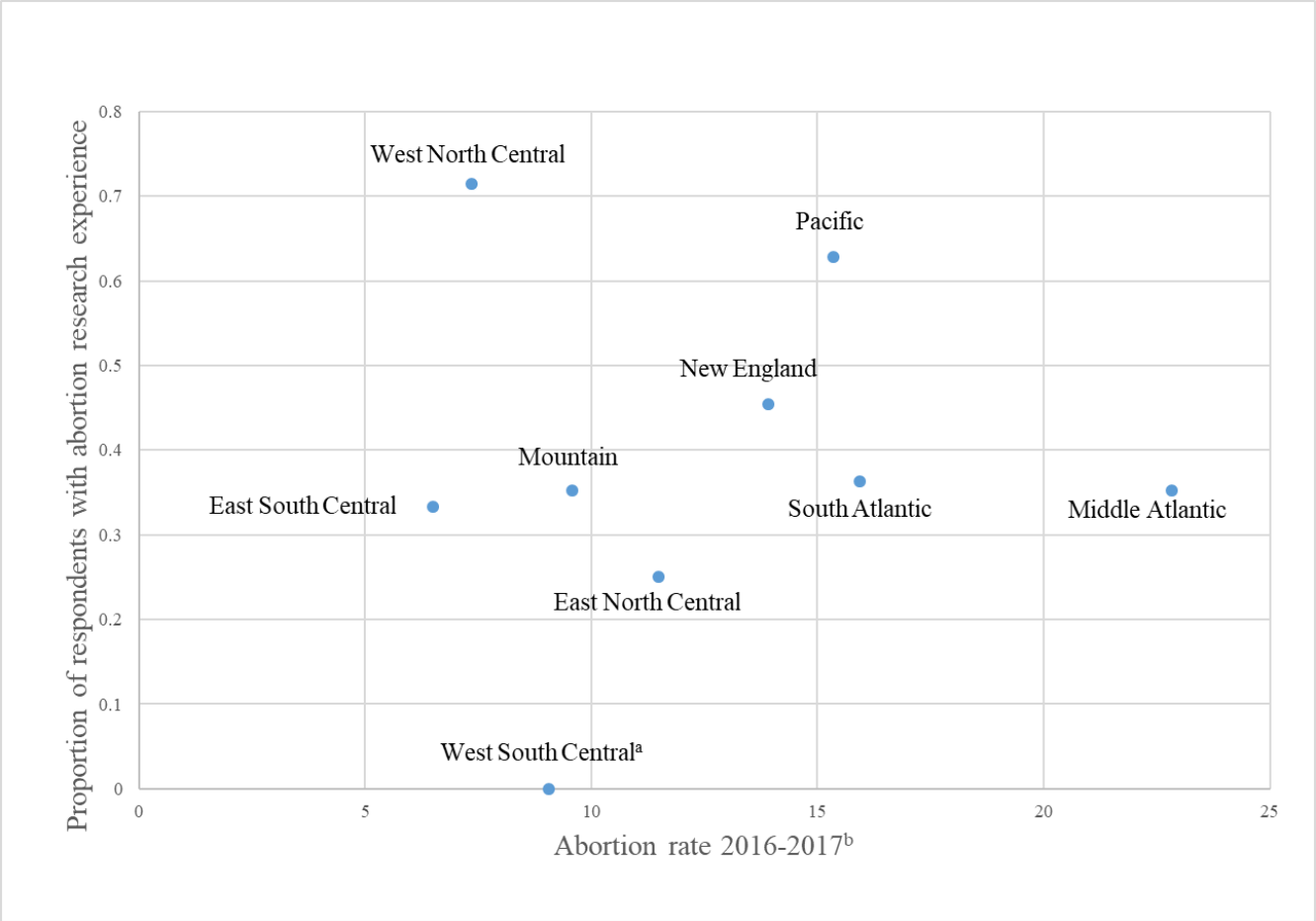
Region	Respondents	Respondents with Abortion Research Experience n (row %)	Annual Number of Abortion Research Protocols Involving Respondents				Abortion Incidence n (%)	Number of women aged 15-44 n (%)	Abortion rate per 1000 women aged 15-44
			1-4	5-9	10+	Not Sure			
New England (ME, NH, VT, MA, RI, CT)	11	5 (45.5)	4	1	0	0	39,550 (4.6)	2,842,414 (4.5)	13.9
Middle Atlantic (NY, NJ, PA)	17	6 (35.3)	5	0	0	0	184,750 (21.4)	8,091,819 (12.7)	22.8
East North Central (OH, IN, IL, MI, WI)	12	3 (25.0)	1	0	0	2	103,410 (12.0)	8,995,713 (14.1)	11.5
West North Central (MN, IA, MO, ND, SD, NE, KS)	7	5 (71.4)	3	0	0	2	29,720 (3.5)	4,047,563 (6.4)	7.3
South Atlantic (DE, MD, D.C., VA, WV, NC, SC, GA, FL)	11	4 (36.4)	3	0	0	1	197,970 (23.0)	12,420,896 (19.5)	15.9
East South Central (KY TN, AL, MS)	6	2 (33.3)	1	0	0	1	24,000 (2.8)	3,699,797 (5.8)	6.5
Mountain (MT, ID, WY, CO, NM, AZ, UT, NV)	17	6 (35.3)	3	2	0	1	45,100 (5.3)	4,709,878 (7.4)	9.6
Pacific (WA, OR, CA, AK, HI)	35	22 (62.9)	9	5	5	3	164,520 (19.0)	10,712,819 (16.8)	15.4
West South Central[b] (TX, OK, AR, LA)	-	-	-	-	-	-	73,340 (8.5)	8,092,115 (12.7)	9.1
Total	116	53	29	8	5	10	862,320	63,613,014	13.5

[a]Abortion services data reported by Guttmacher Institute, 2017 [27] and population of women aged 15-44 data reported by March of Dimes, 2016 [29]

[b] No survey response was received from the West South Central United States. Abortion data included in the table for reference.

[c]One respondent with abortion research experience did not disclose the number of protocols they experience annually

Figure 1. *Proportion of respondents with abortion research experience compared to abortion rate, 2016-2017 by geographic region*



[a]No survey response was received from the West South Central United States. Abortion rate data included in the table for reference.
[b]Abortion services data reported by Guttmacher Institute, 2017 [27] and population of women aged 15-44 data reported by March of Dimes, 2016 [29]

Confidence applying Subpart B

Overall, confidence scores in applying Subpart B to prospectively enrolling research on abortion were high. 83.8% of respondents who answered at least one question about confidence in applying the regulations to this type of study (n=94) had an overall confidence score of "confident" or "very confident". Table 4 summarizes the distribution of confidence responses to each condition of Subpart B. When the proportion of responses of "very confident" and

"confident" were compared between all ten conditions of Subpart B, Condition H received the highest proportion of confident responses (89.0%). In descending confidence, the remainder of the conditions were Condition J (86.8%), Condition F (86.2%), Condition I (85.7%), Condition G (79.1%)), Condition B (73.7%), Condition D (73.4%), Condition E (73.4%), Condition A (72.7%), and Condition C, which received the lowest confidence response (69.7%).

Table 4. *Distribution of respondent confidence in applying the Subpart B conditions to prospectively enrolling research on abortion.*

Subpart B Condition	Very Unconfident n (row %)	Unconfident n (row %)	Neutral n (row %)	Confident n (row %)	Very Confident n (row %)	Response total
A. "Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;" [a]	1 (1.0)	4 (4.0)	22 (22.2)	47 (47.5)	25 (25.3)	99
B. "The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;" [a]	1 (1.0)	6 (6.1)	19 (19.2)	47 (47.5)	26 (26.3)	99
C. "Any risk is the least possible for achieving the objectives of the research" [a]	0 (0)	4 (4.0)	26 (26.3)	46 (46.5)	23 (23.2)	99
D. "If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part" [a]	1 (1.0)	5 (5.3)	19 (20.2)	41 (43.6)	28 (29.8)	94
E. "If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability,	1 (1.0)	4 (4.0)	20 (21.3)	43 (45.7)	26 (27.7)	94

incompetence, or temporary incapacity or the pregnancy resulted from rape or incest." [a]						
F. "Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;" [a]	1 (1.0)	2 (2.1)	10 (10.6)	51 (54.3)	30 (31.9)	94
G. "For children as defined in § 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;" [a]	2 (2.2)	7 (7.7)	10 (11.0)	40 (44.0)	32 (35.2)	91
H. "No inducements, monetary or otherwise, will be offered to terminate a pregnancy;" [a]	0 (0)	3 (3.3)	7 (7.7)	29 (31.9)	52 (57.1)	91
I. "Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and" [a]	1 (1.1)	3 (3.3)	9 (9.9)	33 (36.3)	45 (49.5)	91
J. "Individuals engaged in the research will have no part in determining the viability of a neonate." [a]	0 (0)	1 (1.1)	11 (12.1)	37 (40.7)	42 (46.2)	91

a[1]

We observed some trends in confidence score based on participant characteristics, and some associations reached statistical significance by chi-square test (Table 5). Characteristics found to be statistically significantly associated with confidence score included geographic region of residence ($p<.0001$), years of experience ($p=.0048$), AAHRPP accreditation ($p=.0351$), IRB membership including women's health providers ($p=.0030$), type of research experience (biomedical or social-behavioral) ($p<.0001$), and whether abortions were performed at the respondent's institution ($p<.0001$). We found that gender, CIP certification, personal experience with abortion research, personal beliefs about abortion, position within the HRPP, and the existence of a written institutional policy governing abortion research were not associated with confidence score.

Table 5. *Characteristics associated with confidence score*

Characteristic	χ^2 (df)	p
Geographic region of residence*	114.9 (21)	<.0001
Years of experience*	22.1 (9)	.0048
CIP certification	2.7 (3)	.8598
Gender	3.5 (3)	.6241
Experience with Abortion Research	6.5 (3)	.0889
Abortion Belief	12.6 (12)	.3999
IRB membership including women's health providers*	22.7 (6)	.0030
Position (IRB chair, member, etc.)	22.6 (15)	.2768
AAHRPP accreditation*	1.8 (3)	.0351
Type of research experience*	106.1 (9)	<.0001
Abortions performed at institution*	11.2 (6)	<.0001
Written policy on abortion research	8.5 (6)	.2018

* Groups are significantly different ($p<.05$)

Interpretation of Subpart B Conditions

Of those who responded to specific questions about their interpretation of specific Subpart B Condition I, which reads "Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy" [1] (n=88), 68.2% interpreted that Condition I prohibits researchers from serving as a study's abortion practitioner. 18.4% were not sure, and 21.6% did not interpret the condition that way. 73.9% interpreted that Condition I prohibits researchers from randomizing subjects to different methods of abortion. 6.8% were not sure and 19.3% did not interpret the condition that way. 31.8% interpreted that Condition I prohibits researchers from assigning pain management regimens during an abortion procedure. 15.9% were not sure and 52.3% did not interpret the condition that way.

Of those who responded to questions about interpreting Subpart B Condition H which reads "No inducements, monetary or otherwise, will offered to terminate a pregnancy"[1]

(n=88), 46.6% interpreted that Condition H prohibits compensation for research participation. 12.5% were not sure and 40.9% did not interpret the condition that way. Of those who responded to a follow up question about the same condition prohibiting reimbursement for time and travel for research participation (n=87), 25.3% interpreted Condition H to prohibit reimbursement, 18.4% were not sure, and 55.7% did not interpret the condition that way.

We did not observe any trends in the interpretation of either Condition H or Condition I based on personal beliefs about abortion. Respondents who considered themselves pro-choice or pro-life both interpreted the conditions about the same way, with a variety of responses across the interpretation spectrum for each question. The same can be said for interpretation of either Condition H or Condition I by confidence in applying the relevant condition to abortion research: there is no pattern in interpretation among those with a high confidence in application of the condition.

For example, among those who described themselves as very confident or confident in applying Condition H that also answered the corresponding interpretation question (n=79), 44.3% interpreted that the condition prohibits compensation for research and 43.0% did not. Among those who described themselves as very confident or confident in applying Condition H that also answered the relevant interpretation question (n=78), 24.4% interpreted that the condition prohibits reimbursement for time and travel for research participation and 56.4% did not. As previously noted, Condition H was the Subpart B condition that respondents felt most confident in interpreting and applying to abortion research. Confidence in applying Subpart B conditions to abortion research appears to be independent from manner of interpreting the conditions.

IRB Focus for Abortion Research

None of the participants reported that they had ever recused themselves from the IRB review process for personal beliefs, but some reported they had witnessed others recuse themselves for this reason (16.2%). 90.6% of respondents reported that their IRB's membership included representatives from obstetrics and gynecology or other women's health providers. Nearly one-fifth (19.6%) reported that their institution has a written policy about studies involving abortion.

Participants were asked about which aspects of IRB review they are more concerned with for an abortion research study compared to other studies in a "select all" type of response question. Participants could select as many of the options we provided as they wanted. Of the 249 total selections made by the 90 participants who responded to this question, participants were most concerned with local context (i.e. institutional policies and state law) (18.5%). In a rank ordering of responses, participants were then concerned with cultural context (16.5%), privacy and confidentiality (16.1%), informed consent (14.9%), and research procedures (10.0%). 7.6% of the respondents were no more concerned with any aspects of IRB review for an abortion research study than for any other type of study. The three least concerning aspects of IRB review for an abortion research study were scientific review (6.0%), principal investigator qualifications (5.2%), and funding source (5.2%). The respondents were slightly more comfortable with their IRB serving as the IRB of record (40% answered "comfortable" or "very comfortable") than ceding review to an external IRB (37.8% answered "comfortable" or "very comfortable") for multisite collaborative research on abortion.

Respondent Comments

Sixteen respondents entered text into the free text response for survey comments. The field did not require text entry in order to complete the survey, but three respondents entered information such as “N/A” or “no.” Three respondents offered clarification of some survey forced answer choices such as, “Some of your forced choice answers preclude the nuanced ethical discussions that should be had around this sort of topic..,” “Many of the qx [questions] about interpreting regulations would be best answered by ‘it depends’,” and “In response to question 34– [regarding value of abortion research compared to other health research] I think it is more difficult to approve studies that involve abortion, but the information obtained is important.” One respondent offered criticism of political changes that have affected research, “The current administration has pulled federal funding for such research studies... effectively preventing important research from being done to pander to a voting base.”

Two respondents called for further study of IRB management of fetal tissue research, with one respondent providing the comment, “A discussion on use of fetal tissue resulting from abortions would be good too. This is a difficult area with many ambiguous laws on the books.” Three participants provided further information about their handling of research proposals involving abortion with comments including “Equivalent protections have been used with non-federally funded studies that would not have been approvable under the Common Rule,” “The requirement to register with CT.gov [clinicaltrials.gov] for applicable clinical trials is also problematic as there is little interest on the part of the researchers or the institution to advertise this type of research,” and “We would have to be sure a woman has already decided to have an abortion with a clinician who is not involved in the research. The clinician performing the abortion should not be a research subject either...at least in the same study.” Four participants

expressed gratitude or wishes for results of the survey to be shared with researchers and regulators including comments “I hope that the results are shared with regulators, and result in clarification in regulatory language via guidance that make more clear how to approve abortion research in compliance with subpart B,” “We need regulations that offer stringent protections but also allow researchers to do research related to all aspects of the abortion process, to make the procedure as safe as possible for women who make the difficult choice to terminate their pregnancy,” and “This area of research needs more discussion and interpretation of the regulations as I can see where there probably are differing opinions among regulators...”

V. Discussion

Our study aimed to determine if differing interpretations of research regulations impact IRB ethical review and approval of prospectively enrolling human subjects research on abortion. Our respondents were mostly female, were well-experienced with HRPPs, hold higher-level positions with IRBs, and mostly considered their personal beliefs to be pro-choice. Many reported personal experiences with the review of abortion research. Our respondents demonstrated that IRBs in the Pacific review more abortion research than any other geographic region by research density yet the Pacific does not conduct the most abortion procedures according to data from 2017 [27]. Overall, abortion research is not commensurate with the number of abortion services provided by region.

Respondents reported they were most concerned with local context, including institutional policies and state law when reviewing abortion research, likely due to the increasingly complex state laws governing abortion procedures. Investigators submitting abortion research for ethical review should be prepared for increased IRB scrutiny of the proposed study's cultural context, plans for privacy and confidentiality, informed consent process, and the research procedures. Our study did not find any association between respondents' personal beliefs and confidence applying subpart B to abortion research or between respondents' personal beliefs and their specific interpretation of the subpart B conditions. Investigators should not expect a difference in IRB review between those who consider themselves pro-choice and those who consider themselves pro-life.

There did not appear to be any hesitancy in executing reliance agreements for single IRB review for multisite collaborative abortion research, but respondents were more comfortable with

their IRB serving as the IRB of record rather than ceding IRB review to another institution. The respondents' increased concern with local context may have influenced some respondents to favor their IRB as the single IRB best able to ensure compliance with local policies and state laws.

Overall, confidence in applying the conditions of Subpart B to prospectively enrolling research on abortion is high. 83.8% of respondents were confident or very confident in applying the conditions of Subpart B to this type of study. The high confidence in applying Subpart B to abortion research reported by participants may be due to the respondents' length of experience and role with IRBs, or even possibly a motivation to approve abortion research to support respondents' pro-choice personal beliefs. Despite a potential inclination to approve abortion research, interpretation of the conditions of Subpart B vary even among participants who consider themselves to be pro-choice.

The majority of respondents believe that Subpart B prohibits research staff from randomizing subjects to different methods of abortion and from serving as a study's abortion practitioner. Overall, most respondents did not believe Subpart B prohibits compensation or reimbursement for research participation. We were not able to determine a pattern in disagreement in interpretation of Subpart B conditions between respondent groups based on confidence in applying Subpart B or personal abortion beliefs. There does not appear to be a way to predict which IRB personnel may interpret the conditions of Subpart B more literally than others.

To our knowledge, the Office for Human Research Protections does not provide guidance detailing specifically how to apply Subpart B to research on abortion. Moreover, human research ethics industry leaders do not provide continuing education resources. These leaders include

PRIM&R [30, 31] and AHHRPP, whose website's search tool [10] returned zero results after a search for the term "abortion". In addition, a search of a discussion board commonly used by HRPP professionals to discuss complex human research ethics issues and to develop consensus about how to apply research regulations, IRB Forum [32], did not reveal any discussion threads about applying the research regulations to research on abortion.

Limitations

This study recruited human research protection program professionals from institutions that are considered stakeholders in the research ethics review process for abortion research. Our sample only included ethics review personnel from the United States that have experience with the U.S. federal regulations. We did not recruit any participants from IRBs unlikely to review abortion research, so the results of this study are only representative of the attitudes of the sampled population. Further, we only disseminated the survey to IRB personnel with publicly available IRB webpages. This excluded IRBs known to review abortion research such as the Guttmacher Institute IRB or commercial IRBs, such as Advarra IRB.

We anticipated a low response rate for this study since IRB personnel might be hesitant to respond to a survey that would collect information on potential non-compliance with human research protection regulations. We tried to mitigate any hesitancy to taking the survey by collecting as few identifiers as possible, yet we only achieved a 20% response rate. We do not know why some eligible participants chose not to participate. As a result of trying to collect as little identifying information as possible, we have only regional location data rather than more precise location information in our survey results. Due to the low response rate and sampling only those with publicly available contact information, we cannot be sure our results are representative of the total population of IRB stakeholders in the abortion research review

process. During analysis we discovered that high confidence in applying the conditions of Subpart B does not correspond to specific interpretations of the Subpart B conditions. Therefore, we did not perform any regression analysis to predict IRB personnel confidence in applying Subpart B, since confidence applying Subpart B appears to have little impact on the end result of applying Subpart B to abortion research.

Implications and Future Studies

Future studies should include qualitative research to understand the perspectives of IRB stakeholders on abortion research, and they should also aim to understand motivations and hesitations for participating in a study like this one. Addressing participant concerns over research participation may help to raise future response rates from IRB personnel and develop more generalizable conclusions. Future quantitative research should collect more specific geographic information and explore whether state laws or local policies have an impact on interpretation of Subpart B.

A few of our study's participants shared a desire for a similar study on fetal tissue research, which also came up as a potential research topic during key informant interviews. A survey study on this topic appears to be welcomed by IRB stakeholders in the abortion research review process.

Conclusions

IRB review of abortion research should be standardized as much as possible, since differing interpretations of regulations by IRB personnel can cause IRB review to serve as a barrier to abortion research being conducted in the United States and may exacerbate the regional differences between abortion research conducted and abortion services provided. The comment by one survey respondent that "equivalent protections have been used with non-federally funded

studies that would not have been approvable under the Common Rule" shows that some IRBs have already developed their own standards for abortion research outside of the federal regulations. IRBs should share best practices for this type of study and work with ethicists and other stakeholders to develop a consensus on this topic.

References

1. *OHRP Common Rule*, in *45*. 2018, Government Publishing Office: Electronic Code of Federal Regulations.
2. Davis, A.L., *The Study Population: Women, Minorities, and Children*, in *Institutional Review Board Management and Function*. 2006, Jones and Bartlett Publishers: Sudbury, Massachussetts. p. 129-133.
3. Verma, N., et al., *Exploring the impact of federal regulations on abortion research.* Contraception, 2017. **96**(4): p. 276.
4. *Federal Policy for the Protection of Human Subjects ('Common Rule')*. [cited September 21, 2019]; Available from: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html.
5. Alina Salganicoff, L.S., Amrutha Ramaswamy. *The Hyde Amendment and Coverage for Abortion Services*. Women's Health Policy 2019. [cited September 22, 2019]; Available from: https://www.kff.org/womens-health-policy/issue-brief/the-hyde-amendment-and-coverage-for-abortion-services/.
6. Adashi, E.Y. and R.H. Occhiogrosso, *The Hyde Amendment at 40 Years and Reproductive Rights in the United States.* JAMA, 2017. **317**(15): p. 1523.
7. Estelle H. Rogers, S.C. *Acess Denied: Origins fo the Hyde Amendment and Other Restriction on Public Funding for Abortion*. 2019. [cited September 22, 2019]; Available from: https://www.aclu.org/other/access-denied-origins-hyde-amendment-and-other-restrictions-public-funding-abortion.
8. *When the Assurance Comes a 'Knocking': Everything You Need to Know About OHRP's FWA*. 2013, Office for Human Research Protections (OHRP).
9. *Redline of Unofficial Final Revised Common Rule (January 18, 2017) Against Health and Human Services ("HHS") Common Rule At 45 C.F.R. Part 46, Subpart A (2005),* January 19, 2017. [cited December 4, 2019]; Available from: http://www.verrilldana.com/files/uploads/Images/Redline-of-Final-Revised-Common-Rule-FINAL-DRAFT_1-19-2017.pdf.
10. *Our Mission, Vision, and Values*. About AAHRPP [cited September 22, 2019]; Available from: http://www.aahrpp.org/learn/about-aahrpp/our-mission.
11. *Founding Members*. About AAHRPP [cited September 22, 2019]; Available from: http://www.aahrpp.org/learn/about-aahrpp/founding-members.
12. *Accreditation Principles* [cited September 21, 2019]; Available from: http://www.aahrpp.org/apply/web-document-library/accrediation-principles.
13. *Frances Oldham Kelsey: Medical reviewer famous for averting a public health tragedy*. February 1, 2018 [cited September 26, 2019]; Available from: https://www.fda.gov/about-fda/virtual-exhibits-fda-history/frances-oldham-kelsey-medical-reviewer-famous-averting-public-health-tragedy.
14. J.Richard Crout, M.J.F., *General Considerations for the Clinical Evaluation of Drugs*, E. U.S Department of Health, and Welfare, Editor. 1978: Rockville, MD. p. 1-11.
15. *NIH Guidelines on the Inclusion of Women and Minorities as Subjects in Clinical Research*, National Institutes of Health, Editor. 1994.
16. *Ethical and Policy Issues in Research Involving Human Participants*, National Bioethics Advisory Commission, Editor. 2001: Bethesda, Maryland.

17. Green, R.M., *Research Involving Fetuses and In Vitro Fertilization*, in *Institutional Review Board Management and Function*. 2006, Jones and Bartlett Publishers: Sudbury, Massachussetts. p. 356-362.
18. *Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)*. Advisory Groups, August 13, 2019 [cited September 29, 2019]; Available from: https://www.nichd.nih.gov/about/advisory/PRGLAC.
19. *List of Recommendations from the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC)*. 2018 [cited December 4, 2019]; Available from: https://www.nichd.nih.gov/about/advisory/PRGLAC/recommendations.
20. *Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators*, HHS, Editor. 2011, National Archives: Federal Register.
21. Calis, K.A., *IRB Interpretation of 45 CFR 46 Subpart B*, in *Scientific Meetings and Events*. 2017, NIH.
22. Nash, E. *Unprecedented Wave of Abortion Bans is an Urgent Call to Action*. May 31, 2019 [cited September 29, 2019]; Available from: https://www.guttmacher.org/article/2019/05/unprecedented-wave-abortion-bans-urgent-call-action.
23. Azar, A., *Remarks on Universal Health Coverage*. 2019, U.N. General Assembly Press: New York, New York.
24. Rochat, R.W., et al., *Maternal and Child Health Epidemic-Assistance Investigations, 1946–2005.* American Journal of Epidemiology, 2011. **174**(suppl_11): p. S80-S88.
25. Borgatta, L., et al., *Research concerning miscarriage and abortion and IRB (institutional review board) barriers.* Contraception, 2016. **94**(4): p. 392-393.
26. *What is the Fellowship in Family Planning?* [cited October 6, 2019]; Available from: https://www.familyplanningfellowship.org/what-fellowship-family-planning.
27. Jones, R.K., Witwer, Elizabeth, and Jerman, Jenna. *Abortion Incidence and Service Availability in the United States, 2017*. 2019 [cited November 18, 2019]; Available from: https://www.guttmacher.org/report/abortion-incidence-service-availability-us-2017#fn1a.
28. Anderson, M.A., *Recommendations to learn more about "research not approvable..."*, J. Blackburn, Editor. 2019.
29. *Population of women 15-44 years: United States, 2016*. [cited December 2, 2019]; Available from: https://www.marchofdimes.org/peristats/ViewSubtopic.aspx?reg=99&top=14&stop=128&lev=1&slev=1&obj=18.
30. *PRIM&R Program Archives*. [cited November 18, 2019]; Available from: https://www.primr.org/ProgramArchives.aspx?tag=Human.
31. *Research Ethics Publications*. [cited 2019 November 18, 2019]; Available from: https://www.primr.org/Publications.aspx?tag=Human.
32. IRB Forum; Available from: https://www.irbforum.org/.

Appendix 1: Key Informant Interview Guide

1. Tell me about your experience with IRB review of abortion research.
2. Pre-review
    a. If IRB personnel: Did you find that many revisions were required to the IRB submission before the study (ies) were approvable? If yes, what kind?
    b. If abortion researcher: Do you remember the IRB pre-review process? Can you tell me more about it?
3. How long have you been working in your field?
    a. Probe: (If longer than 7 years), Have you noticed any difference in IRB review of abortion research over time?
        i. If yes- probe for what those differences are and how they could be studied in a survey
4. Specific Regulations—Provide participant with a copy of Subpart B regulatory text. Prompt: Take a moment to review the text of these regulations. What stands out to you when you consider your experience with abortion research?
5. What questions do you have for other IRB personnel about the review of abortion research?
6. Provide table one draft: What characteristics of respondents do you think would be the most productive to track?
7. I plan asking survey respondents to see how they choose to apply Subpart B regulations. Do you have any suggestions for the best way to collect this type of information?

Appendix 2: Survey Instrument

IRB Management of Family Planning Research Survey

Thank you for your interest in our IRB Management of Family Planning Research study. We would like to tell you everything you need to think about before you decide whether or not to join the study. It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.

1) The purpose of this study is to understand the knowledge and confidence of research ethics professionals in applying research regulations to research on abortion.

2) This study will take about 10 minutes to complete.

3) If you join, you will be asked to take a brief survey about your confidence in applying research regulations to research on abortion. The survey will ask questions about your personal experience. This survey is not a test with right or wrong answers.

4) The survey will be sent to over 600 email addresses. The survey will not collect any identifying information, including IP addresses. There will be no way for the research team to link responses with individual participants. You can skip any questions you do not want to answer, and you can stop participation at any time.

5) You may feel uncomfortable answering some survey questions. If this happens you can skip any questions you do not want to answer or stop participation. As with any research study, there is a possible risk of breach of confidentiality.

6) This study is not intended to benefit you directly, but we hope this research will benefit the research ethics community in the future.

7) Your privacy is very important to us. We will keep all research data protected by storing it electronically on password protected devices. No identifiers will be collected during this study, so data will not be stored with identifiers.

Contact Information
If you have questions about this study, your part in it, your rights as a research participant, or if you have questions, concerns or complaints about the research you may contact the following:

Jessica Blackburn, Principal Investigator: 678-468-4920 or jessica.blackburn@emory.edu

Emory Institutional Review Board: 404-712-0720 or toll-free at 877-503-9797 or by email at irb@emory.edu

This study was determined exempt by the Emory IRB: study number IRB00112484.

* 1. Do you agree to participate in the study?

- ◯ Yes
- ◯ No

2. In which region of the United States do you live?

- 1. New England (Maine, New Hampshire, Vermont, Massachusetts, Rhode Island, Connecticut)
- 2. Middle Atlantic (New York, New Jersey, Pennsylvania)
- 3. East North Central (Ohio, Indiana, Illinois, Michigan, Wisconsin)
- 4. West North Central (Minnesota, Iowa, Missouri, North Dakota, South Dakota, Nebraska, Kansas)
- 5. South Atlantic (Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida)
- 6. East South Central (Kentucky, Tennessee, Alabama, Mississippi)
- 7. West South Central (Arkansas, Louisiana, Oklahoma, Texas)
- 8. Mountain (Montana, Idaho, Wyoming, Colorado, New Mexico, Arizona, Utah, Nevada)
- 9. Pacific (Washington, Oregon, California, Alaska, Hawaii)

3. Overall, how many years of experience have you had working as IRB staff, an IRB member, or as a member of the broader human research protection program (HRPP)?

- 0-1
- 2-5
- 6-9
- 10+

4. Do you currently hold the Certified IRB Professional (CIP) certification?

- Yes
- No

5. Do you currently hold any other certification relevant to research ethics or clinical research?

- Yes
- No

6. How would you describe your current primary role with the IRB?

- ◯ Administrative
- ◯ IRB Analyst/Coordinator
- ◯ IRB Staff Leader
- ◯ IRB Member
- ◯ IRB Chair
- ◯ Other

7. What is your gender?

- ◯ Female
- ◯ Male
- ◯ Non-Binary

8. Which type of research has made up the majority of your IRB experience?

- ◯ Biomedical research
- ◯ Social/Behavioral/Educational research
- ◯ Both Biomedical and Social/Behavioral/Educational research
- ◯ Other

9. Has the majority of your IRB experience been at an institution that is accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP)?

- ◯ Yes
- ◯ No
- ◯ Not sure

10. Which type of research makes up the majority of your institution's active studies?

- ◯ Biomedical research
- ◯ Social/Behavioral/Educational research
- ◯ Both Biomedical and Social/Behavioral/Educational research
- ◯ Other

IRB Management of Family Planning Research Survey

11. Does your institution have a written policy regarding the review of studies involving abortion?

- ◯ Yes
- ◯ No
- ◯ Not sure

12. Does your IRB include membership from Obstetrics and Gynecology or other women's health care providers?

- ◯ Yes
- ◯ No
- ◯ Not sure

13. Do individuals at your institution perform abortion procedures?

- ◯ Yes
- ◯ No
- ◯ Not sure

14. Have you ever recused yourself from the review (or pre-review activities) for any study due to conflict with personal beliefs?

- ◯ Yes
- ◯ No
- ◯ Not Applicable- I do not conduct IRB pre-review or reviews

15. Has any IRB member at your institution recused him- or her-self from the review of any study due to conflict with personal beliefs (to your knowledge)?

- ◯ Yes
- ◯ No
- ◯ Not sure

16. Have you personally ever processed, reviewed, or provided guidance during the submission of research related to abortion at your IRB?

- ◯ Yes
- ◯ No

17. About how many research protocols involving the topic of abortion are you involved with annually?

- ◯ 1-4
- ◯ 5-9
- ◯ 10+
- ◯ Not sure

18. Which type(s) of studies have made up the majority of your experience with abortion research?

- ◯ Biomedical research
- ◯ Social/Behavioral/Educational research
- ◯ Both Biomedical and Social/Behavioral/Educational research
- ◯ Other (please specify)

19. Have you noticed any change in abortion research type over time as state laws and political climates have changed?

- ◯ Yes
- ◯ No
- ◯ Not sure

20. Does your experience with research on abortion include research conducted in the following locations?

- ◯ Within my institution only
- ◯ Outside my institution only
- ◯ Both inside and outside my institution
- ◯ Not sure

21. Do you have experience reviewing research on abortion where one or more of the investigators were affiliated with multiple sites?

- ◯ Yes
- ◯ No
- ◯ Not sure

22. Have you ever experienced the review of abortion research not otherwise approvable that presented an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women that was referred to the Secretary of Department of Health and Human Services (HHS)?

- ◯ Yes
- ◯ No
- ◯ Not sure

23. Was the outcome of research that was referred to the Secretary of HHS that the research could go forward?

- ◯ Yes
- ◯ No
- ◯ Not sure

24. The following questions are to determine your confidence in interpreting and applying research regulations. How confident are you in applying the following conditions to prospectively enrolling research on abortion?

	Very Unconfident	Unconfident	Neutral	Confident	Very Confident
Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses	○	○	○	○	○
The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means	○	○	○	○	○
Any risk is the least possible for achieving the objectives of the research	○	○	○	○	○

25. The following questions are to determine your confidence in interpreting and applying research regulations. How confident are you in applying the following conditions to prospectively enrolling research on abortion?

	Very Unconfident	Unconfident	Neutral	Confident	Very Confident
If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions	○	○	○	○	○
If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest	○	○	○	○	○
Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate	○	○	○	○	○

26. The following questions are to determine your confidence in interpreting and applying research regulations. How confident are you in applying the following conditions to prospectively enrolling research on abortion?

	Very Unconfident	Unconfident	Neutral	Confident	Very Confident
For children who are pregnant, assent and permission are obtained in accord with the provisions of subpart D (additional protections for children)	○	○	○	○	○
No inducements, monetary or otherwise, will be offered to terminate a pregnancy	○	○	○	○	○
Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy	○	○	○	○	○
Individuals engaged in the research will have no part in determining the viability of a neonate.	○	○	○	○	○

IRB Management of Family Planning Research Survey

27. Please rate your comfort in the following IRB oversight scenarios for multi-site research, regardless of whether your experience includes IRB Reliance.

	Very Uncomfortable	Uncomfortable	Neutral	Comfortable	Very Comfortable
Ceding IRB review for a multi-site prospectively enrolling research study on abortion	○	○	○	○	○
Serving as the IRB of record for a multi-site prospectively enrolling research study on abortion	○	○	○	○	○

28. Are there any aspects of IRB review that you are more concerned with when reviewing a prospectively enrolling research study on abortion than you are with other types of studies?

- ☐ Funding source
- ☐ PI qualifications
- ☐ Scientific review
- ☐ Research procedures
- ☐ Informed consent process
- ☐ Local context (i.e. institutional policies and state law)
- ☐ Cultural context (political climate)
- ☐ Privacy and confidentiality
- ☐ None- I share the same concerns as I do with any other study

29. Do you interpret the following condition to effectively prohibit researchers from serving as the study's abortion practitioner if a study involves an abortion procedure?

Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy

- ◯ Yes
- ◯ No
- ◯ Not sure

30. Do you interpret the following condition to effectively prohibit researchers from prospectively assigning subjects to different methods for an abortion procedure?

Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy

- ◯ Yes
- ◯ No
- ◯ Not sure

31. Do you interpret the following condition to effectively prohibit researchers from prospectively assigning subjects to different regimens for pain management during an abortion procedure?

Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy

- ◯ Yes
- ◯ No
- ◯ Not sure

32. Do you interpret the following condition to prohibit compensation for research participation if a study involves an abortion procedure?

No inducements, monetary or otherwise, will be offered to terminate a pregnancy

- ◯ Yes
- ◯ No
- ◯ Not sure

33. Do you interpret the following condition to prohibit reimbursement for time and travel for research participation if a study involves an abortion procedure?

No inducements, monetary or otherwise, will be offered to terminate a pregnancy

- ◯ Yes
- ◯ No
- ◯ Not sure

34. How would you describe your personal beliefs about abortion?

- ◯ Pro-choice
- ◯ Pro-life
- ◯ Neutral
- ◯ Undecided
- ◯ Other

35. Do you believe that research on abortion presents the same opportunity to understand, prevent, or alleviate a serious problem affecting health or welfare as research on other healthcare topics?

- ◯ Yes
- ◯ No
- ◯ Not sure

36. Do you have any other comments, questions, or concerns about the topic that were not already addressed?