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Adolescent Sexual Behavior Research: Perspectives of Investigators, IRB Members, and IRB Staff about Risk Categorization and IRB Approval

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The ethical review of research on adolescent sexual behavior is challenging. Investigators and institutional review boards (IRBs) alike struggle with pediatric risk categorizations for research on sexual health and other sensitive topics, resulting in variable categorization of the same protocols among IRBs, and delays in approvals.[1] In pediatric research, IRB decisions can vary greatly, not only from institution to institution, but also between different review boards within the same institution.[2] These variations suggest that the regulations and laws governing adolescent participation in research are neither uniformly understood nor applied.[3] This is not surprising, given the complex interplay of regulations and laws related to research consent for children and adolescents who are not legal adults. “Children” are defined in U.S. research regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.”[4] Moreover, the regulations reference clinical standards of care in the definition of minimal risk: “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than

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Figure
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those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."[5] The definition of "children" requires investigators and IRBs to be knowledgeable not only about federal regulations but also about complex state health care consent laws[6] regarding adolescent sexual health and reporting requirements. An example of the variability in state law is that while all states allow minor consent for services for sexually transmitted infections (STIs), only a subset cover minor consent for pregnancy services.[7]

Because of the enormous developmental changes in cognitive capacity, family and personal relationships, and health risk behaviors across adolescence, procedures that are best practices for older adolescents (such as 16- and 17-year-olds) may not be best practices for very young adolescents (11- and 12-year-olds), and investigators and IRBs must be aware of developmental differences across adolescence as laid out by professional guidelines.[8] As the leading causes of adverse health outcomes among adolescents reflect certain risk behaviors, much adolescent research covers sensitive and stigmatizing topics, such as sexual behavior and substance use, increasing the difficulty of accurately assessing risks. Studies show that IRBs frequently overestimate risk on sensitive topics and behavioral research[9] and may be less likely to consider a waiver of parental consent for these types of research, even if the study objectively falls within the requirements for this exception.[10] While data exist on variability in the outcome of IRB evaluation of adolescent sexual behavior research, little is known about the process of that evaluation. Thus, the main objective of this study was to examine factors that influence how pediatric investigators, IRB members, and IRB staff members categorize risk in adolescent sexual behavior research and assess whether the IRB should approve such research.

Study Context and Methods

Our study site was a university in Indiana where protocols to conduct research with adolescents are evaluated by one of seven university-wide IRBs. Five of those IRBs (four biomedical and one behavioral) are located at the urban medical campus, one is located at the main university campus, and one is for expedited research. IRB members, IRB staff members, and any investigators who submitted protocols involving minor adolescents (ages 11 to 17 years) were invited via email to participate in an online survey about their knowledge, attitudes, and approach to research with vulnerable populations, including adolescents. Individuals received three email reminders and one telephone call. The response rate was 52%, consistent with similar online surveys.[11]

Participants read a brief hypothetical research scenario of a single, anonymous survey of 11- to 14-year-olds about their sexual behaviors, including oral, vaginal, and anal sex. This scenario was chosen as a representation of a common adolescent research protocol, similar to questions in the Centers for Disease Control and Prevention's Youth Risk Behavior Surveillance System. The investigator in the scenario was planning to obtain parental permission and adolescent assent. Participants were asked to rate the risk categorization (using pediatric risk categories I to IV) of the scenario and to state whether they felt that the study was "IRB approvable," in other words, that it met the regulatory requirements for research with children. We created an outcome variable consisting of a composite score

based on the correct risk classification and assessment of approvability. Correct risk categorization (risk category I, minimal risk) and approvability resulted in higher scores.

> Forty-one percent of the respondents correctly identified the scenario as a risk category I, and 53% reported the study as described as approvable. The low proportion of participants who would approve the protocol suggests that participants may approach protection of adolescents from research harm by limiting access to research.

Predictor variables covered seven topics. Participants' knowledge about minor health care consent laws and reporting requirements was measured using four items related to minor consent (concerning contraception, drug treatment, STI services, and emergency services) and three items related to reporting requirements on statutory rape, drug use, and child abuse (including sex between minors). Questions were based upon Indiana minor consent laws, child abuse laws, and Society for Adolescent Health and Medicine best practices for research with adolescents.[12] Knowledge of federal pediatric research regulations was measured by three items (with Cronbach's alpha = 0.76) covering the participants' knowledge of Subpart D of the federal regulations, which covers research with children, and the report *Research Involving Children* from the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.[13] The most comprehensive and well-known guidelines for research with adolescents are those published by the Society for Adolescent Health and Medicine, and participants were asked about their knowledge of these.[14] We also measured attitudinal factors that might affect review, including beliefs about adolescence (eight items, Cronbach's alpha = 0.65; a sample item being "most adolescents are caring and altruistic) and religiosity and religious participation as measured by the Duke University Religion Index[15] (5 items, Cronbach's alpha = 0.89). Self-efficacy in reviewing adolescent sexual behavior protocols was measured with one item: "I find it challenging to assess risks and benefits of behavioral research with adolescents."

Structural equation modeling (AMOS 21.0; all $p < .05$) was used to evaluate relationships between the outcome variable and predictors, including knowledge about laws, federal research guidelines, and opinions on the submission and approval process. The overall fit of the model was evaluated using the comparative fit index and root mean square error of approximation followed by a close examination of the significance values of each observed variable in the model. Only significant relationships were included in the final model.

Study Results

Respondents (n = 159) included 117 investigators, 68 IRB members, and 9 IRB staff members (with the possibility that participants held more than one of these roles). Over half (58%) were female, most were white (85.7%), and the average age was 46.7 (SD = 10.7). Of the IRB-member participants, 64% had served for five years or less, and 58% of IRB staff members had worked in the IRB office for under two years. Investigators included those who conducted research with adolescents as well as subspecialists such as pediatric oncologists and gastroenterologists whose research participants include adolescents. Forty-one percent of the respondents correctly identified the scenario as a risk category I, and 53% reported the study as described as approvable. ANOVA results indicate no differences in risk

categorization or approvability between IRB staff members, IRB members, and investigators (F[2,156] = .402, p = NS; F[2,156] = .285, p = NS). Respondents who answered correctly about Indiana health care consent law for sexually transmitted disease diagnosis and treatment scored better on their overall assessment of the scenario's risk category and approvability (β = .22). Respondents who knew that health care providers in their state do not need to report consensual sex between two 14-year-olds similarly scored better on their overall assessment of the scenario's risk category and approvability (β =.12). However, beliefs that an adolescent in their state may consent for contraception services predicted lower scores (β = −.17). We note that Indiana does not have a minor consent law related to contraceptive use or family planning, and this ambiguity in the law may have meant that knowledgeable investigators were less likely to identify the scenario's risk category correctly. We found no relationship between outcomes, risk categorization, and approvability with knowledge and beliefs about the following: health care consent laws for emergency services and drug treatment, reporting requirements on statutory rape and drug use, federal research regulations, Society for Adolescent Health and Medicine guidelines, and self-efficacy in reviewing protocols. We additionally found no relationship between conservative beliefs about adolescents or the Duke Religion Index. The model showed good fit with a comparative fit index of .98 and a root mean square error of approximation of .067 (Figure 1, available via the *IRB: Ethics & Human Research* web page).

Discussion

Less than 50% of study participants categorized the sample protocol as category 1, and just over 50% identified this lower risk protocol as IRB approvable. These findings are consistent with related research describing large variability in how IRB chairs would classify pediatric risk for a study of adolescent sexual behaviors.[16] The low proportion of participants in our study who would approve the protocol suggests that participants may approach protection of adolescents from research harm by limiting access to research, a well-described tension in pediatrics.[17] These findings highlight the need for IRBs to include members who are adolescent research specialists and for IRB members and staff members to obtain specialized training about ethical considerations related to adolescent sexual behavior research.

Greater understanding of the state minor consent laws and state mandatory reporting laws were the best predictors of appropriate risk categorization of a minimal risk protocol. This suggests that having legal and regulatory expertise specific to adolescent health may help facilitate the timely and appropriate review of protocols for research involving adolescents and sensitive topics. Given the apparent value of specific expertise and the lack of association between appropriate risk categorization and participants' attitudes toward adolescence and religiosity, the findings also suggest that additional education of pediatric investigators and IRB members and staff members should concentrate on improving knowledge and appropriate application of relevant legal and clinical care guidelines, rather than on shifting intrinsic beliefs about adolescents and sensitive topics.

The study was limited to a single large institution in a Midwestern state that did not have a single pediatric IRB but, instead, reviewed pediatric protocols in IRBs with content-specific expertise (for example, oncology and behavioral health). Results thus may not be applicable

to institutions that have different IRB structures or that are in a different region. Further investigation into IRB decision-making would benefit greatly from qualitative data regarding how individual IRB members understand risk-benefit calculations as well as legal and clinical guidelines. Future research may seek to elucidate factors influencing IRB decisions about guardian waiver for adolescent sexual health research and about how IRB appraisals of risk and approvability may differ with studies with more complex methodologies as well as increases in real or perceived risk to adolescent subjects. Even with these limitations, this study adds to our understanding of how investigators and IRB members may make decisions about pediatric risk categorization and indicates how educational interventions may be improved.

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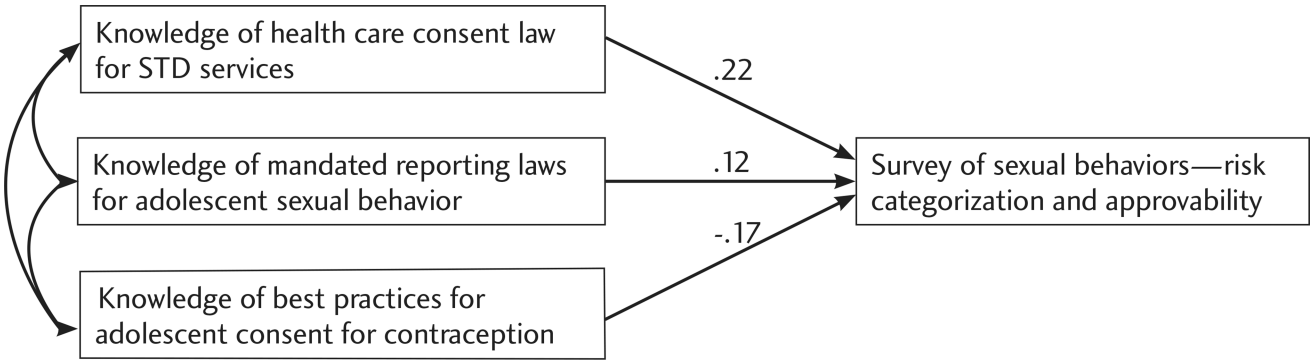

Figure 1.
Path Analysis of Relationships between Knowledge and Risk Categorization and Approvability