OBSTETRICS

Review of multicenter studies by multiple institutional review boards: characteristics and outcomes for perinatal studies implemented by a multicenter network

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OBJECTIVE: The objective of the study was to describe characteristics and outcomes of a review of multisite perinatal studies by individual institutional review boards (IRBs) and identify barriers and opportunities for streamlined IRB review.

STUDY DESIGN: We compared the review of 5 collaborative protocols by individual IRBs at National Perinatal Research Consortium centers from 2007 through 2012. Three randomized trials, 1 observational study, and 1 follow-up study of a trial were selected. IRB logs and communications were reviewed and abstracted by trained team members.

RESULTS: Seven or 8 IRBs reviewed each protocol. Monthly IRB meeting frequency varied from 1 to 6. Full board review was required by all IRBs for the primary trials but not by all for the observational protocols. The overall duration from submission to approval ($P = .024$) and number of stipulations ($P = .007$) differed across protocols but not across IRBs. However, times from submission-to-IRB review ($P = .011$) and IRB review-to-initial letter ($P < .007$) differed across sites. Both overall submission-to-approval and initial review-to-approval times increased with the increasing number of IRB review stipulations (both values $P < .001$). Significant delays (>60 days) were few and not consistent across IRBs or protocols. Most stipulations were stylistic or editorial modifications rather than regulatory requests. All protocols were approved without changes, and no more than 1 IRB meeting was needed at each site.

CONCLUSION: Findings confirm unnecessary duplication and variability and some similarities in IRB review processes and outcomes for multisite perinatal studies. This may help guide initiatives to streamline IRB review and reduce research delays and burdens.

Key words: institutional review boards, multicenter studies, perinatal studies

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Whereas an increasingly large proportion of clinical research is conducted at multiple sites, the regulatory review of these multisite studies predominantly continues to follow the model for single-center studies.[1-4] This model typically involves full evaluation of the study protocol by each individual institutional review board (IRB).[1-5] This completely decentralized process is thought by some to be inefficient, to lead to unnecessary delays, and to increase the costs of conducting clinical research.

It has also been proposed that multiple individual IRB reviews may also yield contradictory IRB decisions across multicenter trial sites and carry a paradoxical potential for harm if no IRB takes sufficient responsibility to make needed protocol changes.[1,3,6-9] As a result, there are increasing calls for a more unified IRB review of multisite research. However, other than speculative editorials or commentaries, real objective data describing and comparing multisite and centralized IRB submissions to guide such initiatives are limited.

Specifically, the contributions of local regulations and stylistic editorial changes to potential discrepancies, delays, and costs associated with multisite IRB reviews are not well understood. As a result, there are few ongoing initiatives to accomplish the goal of centralized IRB reviews despite multiple calls.[5,10-12]

The National Perinatal Research Collaborative (NRPC) is currently made

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up of 5 US academic perinatal centers (and their subsites) actively engaged in collaborative multisite perinatal clinical research. A major aim of the NPRC is to facilitate these multisite research endeavors by collaborating on study design and protocol implementation, including the development of a streamlined common IRB review model for its sites. As an initial step toward these goals, the current study reviewed IRB processes and outcomes for recent or ongoing multicenter studies conducted at all NPRC sites. Specifically, we aimed to describe the similarities and differences in IRB processes and outcomes across NPRC sites for different studies and thus identify specific barriers and opportunities for streamlined IRB review.

Materials and Methods

We reviewed the characteristics and outcomes of the review of 5 common protocols submitted to individual IRBs at NPRC centers over a 5 year period from 2007 to 2012. The 5 NPRC centers included Columbia University, University of Alabama at Birmingham, University of North Carolina at Chapel Hill (UNC), University of Texas Medical Branch, Galveston, and University of Utah/Intermountain Healthcare (Utah).

The 5 studies reviewed were projects to be implemented as part of a larger National Institutes of Health–funded perinatal multicenter network in which all NPRC centers (and affiliated sites) participate. Each study protocol was developed by a subcommittee comprised of clinician investigators, research coordinators, and biostatisticians. The study protocol, including a sample consent form, was approved by a steering committee prior to submission to the IRBs at each center.

This review was exempt from IRB review at all participating centers. For each selected study, complete IRB logs and communications at each site (including those for the separate IRBs at subsites) were reviewed. Data abstraction was performed by trained research team members at each of the sites using a pretested data collection form. The data form covered 13 numbered items with several items having multiple subitems. The items covered study design, IRB submission format and review type, submission to final decision time and its subcomponent (submission-to-review, review-to-initial IRB letter and IRB letter-to-final approval) times, and IRB review results including stipulations, risk classification, and age requirements to give consent.

Descriptive measures including proportions and medians (range) were used to summarize the data. The Kruskal Wallis test was used to compare numerical data across site IRBs and across protocols. We used generalized linear regression to explore the relationship between IRB processing times and variables including the number of stipulations and number of IRB meetings per month. SAS software (SAS Institute, Cary, NC) was used to compute descriptive statistics and both SAS and STATA (StataCorp, College Station, TX) were used for linear regression.

Results

The 5 study protocols we examined (designated A-E) and selected characteristics of each study including the goal, study design, and sample size are summarized in Table 1. There was 1 observational study (A) that involved a request for a waiver of consent from the IRB to conduct chart abstraction after delivery (without any patient interaction). Three studies (B-D) were primary randomized clinical trials (RCTs) (the cytomegalovirus trial, D, involved a preliminary screening phase to identify eligible women with primary maternal cytomegalovirus), and 1 study (E) involved secondary follow-up of women and their offspring (5-10 years old) who had previously participated in a mild gestational diabetes mellitus (GDM) treatment trial.

TABLE 1
Characteristics of research studies reviewed

Study	Goal	Year	Design	Planned sample size
A	Determination of quality measures for obstetric care	2007	Observational (IRB waiver for chart abstraction	120,000 women delivering at ≥23 wks
B	Antenatal corticosteroids in late preterm period to reduce respiratory and other morbidity	2010	Placebo-controlled RCT	2800 pregnant women
C	Fetal EKG as an adjunct for intrapartum monitoring to prevent fetal acidemia	2010	RCT (open and masked groups)	11,000 laboring women
D	CMV hyperimmune globulin therapy to prevent congenital CMV	2011	Screening and placebo-controlled RCT	800 pregnant women with primary CMV (to be identified after screening about 120,000)
E	Long-term outcomes of mild GDM and its therapy	2012	Follow-up of women enrolled in a prior mild GDM treatment RCT	About 1500 women-child dyads at 5-10 y after enrollment in the GDM trial

CMV, cytomegalovirus; *EKG*, electrocardiogram; *GDM*, gestational diabetes mellitus; *IRB*, institutional review board; *RCT*, randomized controlled trial.

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