Institutional Review Board Approval of Practice-based Research Network Patient Safety Studies

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Abstract

Background: Institutional review board (IRB) approval of research that involves the collection of medical error reports is a major challenge. The process includes issues of confidentiality, privacy, discoverability, informed consent, and Web site security. The challenges are more complex for multisite research. This paper describes the approaches taken by the American Academy of Family Physicians (AAFP) and the University of Colorado (CU) to address the challenges and barriers created by the IRB approval process for multisite patient safety research studies. **Methods:** Between 2001 and 2004, the AAFP and CU conducted several patient safety studies involving primary care practices in three practice-based research networks (PBRNs). The AAFP conducted two pilot studies in 18 primary care clinics in which error reports were submitted by physicians, staff, and patients. The AAFP sought approval from 15 different IRBs for these studies. CU conducted a 3-year project that collected medical errors from 38 primary care practices affiliated with seven separate IRBs. **Results:** AAFP successfully obtained approval from all 15 IRBs. Several sites required approval from risk management and legal departments. CU obtained approval for the primary study from seven IRBs and two hospital research committees. Secondary studies required additional approvals. Overall, the two projects had a high level of success in obtaining IRB approval. There was great variation in submission requirements, level of review, length of time to obtain approval, and required revisions. **Conclusion:** PBRN research often includes atypical, multisite research activity, with practices simultaneously serving as research subjects and investigators. The high-risk nature of patient safety work further complicates this situation. Investigative work with the Office for Human Research Protections and the Agency for Healthcare Research and Quality to create a central IRB process could greatly facilitate work of this nature.

Introduction and background

Primary care practice-based research networks (PBRNs) are composed of physicians, other clinicians, and practices committed to the investigation, analysis, description, and understanding of the phenomena of primary care—its content, structure, processes, and outcomes. The number of PBRNs has increased dramatically in family medicine, internal medicine, pediatrics, and nursing over the past few years, although their origins can be traced to the 1970s in the United

States and earlier in other countries.[1] The ultimate goal of network investigations is to improve health care delivery to patients and communities and to enhance the health status of all patients. Although ambitious, the goal appears feasible since most patients usually receive most of their health care in primary care settings.[2, 3] As Lindbloom, Ewigman, and Hickner assert, "PBRNs will continue to evolve as the laboratories necessary to generate research from primary care practice, translate research into practice, and accelerate the flow between scientific discovery and practical clinical care."[4]

Institutional review boards (IRBs) were developed in the 1970s to ensure protection against reported horrific abuses experienced by human subjects in federally funded research. IRBs were established to review research protocols that involve human subjects, approve consent forms (where applicable), monitor ongoing studies, and investigate reports of alleged adverse events in approved studies. Most studies conducted to date in PBRNs have been observational, making use of data collection at the point of care, including patient records/chart reviews, interviews, and surveys. These studies rarely involve invasive procedures with patients; consequently, they are typically designated by IRBs as presenting low to minimal risk for the subjects participating in them.

Despite the relatively low risk associated with most PBRN studies, challenges remain for investigators seeking IRB approval for these investigations.[5] Arguably the most daunting challenge is the situation where a given research protocol is to be executed across multiple practice sites and where the practices are affiliated with different IRBs. This situation is in stark contrast to a research study conducted across multiple sites where the practices are affiliated with only one or a very few IRBs, or a research study conducted across multiple sites where none (or only few) of the practices reports directly to an IRB (in which case the site clinicians are designated as "unaffiliated investigators"). Regardless of the IRB status of the PBRN's participating practices, however, the sponsoring organization must receive approval of the research protocol from its own IRB of record, mandated by its Federalwide Assurance (FWA) issued by the Department of Health and Human Services Office for Human Research Protections (OHRP).[6]

While multisite studies requiring several to many local IRB reviews are common among the growing number of State, regional, and national primary care PBRNs, little has been written about experiences encountered in these situations. Our impression—based on numerous conversations over time with PBRN leaders and researchers—suggests that the observed variation in local IRB requirements and reviews amounts to more than "local contextual effects." Reports documenting problems encountered in multisite clinical trails and genetic epidemiological studies in the United States and England have been published.[7–15] Reported problems include time for approval, delays in subject recruitment, application requirements, consent forms, level of review, revision of protocols, documentation required, and IRB knowledge and compliance with Federal regulations. Based on such problems, Burman et al. observed, "There is increasing controversy about the appropriate role of the local institutional review board in the review of multicenter clinical studies."[7]

This paper reports on the experience of two PBRNs in the execution of three separate patient safety studies funded by the Agency for Healthcare Research and Quality (AHRQ)—studies in which practice site clinicians, office staff personnel, and in some cases the practices' patients were asked to report either anonymously or confidentially on perceived medical errors committed in these practices. The aims of this report are to (1) assess the feasibility and challenges of human subjects review required for medical error reporting in primary care settings and explore solutions to the challenges; and (2) provide recommendations for other PBRNs to facilitate IRB reviews, especially recommendations for multisite studies requiring coordination of multiple review processes and procedures.

Methods

To address our specific research aims, the staffs of two organizations involved in patient safety research in PBRNs came together to assess and outline respective IRB activities, challenges, and solutions. All pertinent IRB documentation for the patient safety projects for both organizations were reviewed and summarized. Teleconferencing facilitated the discussion and development of this manuscript.

For background purposes, this section describes the overall design of both the American Academy of Family Physicians (AAFP) and the University of Colorado Department of Family Medicine (CU-DFM) patient safety projects. The settings and participants, systems used for patient safety reporting (PSRS), and the regulatory processes that guided project implementation within the three primary care PBRNs participating in the projects are also described.

Design

The AAFP Developmental Center for Research and Evaluation in Patient Safety–Primary Care (DCERPS) of the AAFP National Research Network carried out two patient safety studies: Physician, Staff, and Patient-reported Errors in Primary Care (General Errors); and Estimating Rates and Describing Causes and Consequences of Testing Process Errors Detected in Family Physician Offices (Testing Process Errors). Both studies were descriptive in nature, using a Web-based and paper PSRS. The General Errors study collected anonymous event reports from clinicians, staff, and patients. The Testing Process Errors study collected anonymous event reports from clinicians and staff and also included focus groups and redesign investigations.

The CU-DFM carried out a primarily descriptive study: Applied Strategies for Improving Patient Safety (ASIPS). This study was designed to collect and analyze medical error reports from clinicians and staff in two PBRNs, and to perform secondary analysis of malpractice claims and Medicaid claims data guided by the these reports. The ASIPS PSRS accepted clinician and staff reports of errors anonymously or confidentially. Clinicians and staff who signed informed consent forms also participated in a confidential, linked system-satisfaction survey. Secondary data analysis is being performed through data use agreements with two

malpractice carriers in the State of Colorado and the State Department of Health and Human Services.

Setting and participants

The AAFP studies took place in 18 family medicine practices recruited from the AAFP National Research Network (National Network). The General Errors study involved five family physician offices and five family medicine residency clinics. These 10 practices included 401 clinicians and staff who signed consent forms to participate in the study and/or participated in onsite training sessions (for the practices that did not require consent forms). This study also elicited reports from patients of these 10 practices. The Testing Process Errors study involved eight family practice offices. These 8 practices included 160 participating clinicians and staff.

The 18 practices in the two AAFP studies were distributed throughout the United States (five in the Northeast, four in the Midwest, seven in the South, and two in the West). Six practices identified themselves as urban, six as suburban, and six as rural. Seven practices were residency programs and 11 were nonresidency clinics. Six participants were academic practices.

ASIPS involved 35 practices recruited from the Colorado Research Network (CaReNet) and the High Plains Research Network (HPRN). These 35 practices included more than 500 clinicians and staff. Fourteen practices were rural and 21 were urban/suburban. Nine were residency sites, 8 were community health centers, and 18 were urban/suburban nonresidency offices.

Instruments

The AAFP PSRS accepted anonymous reports from clinicians, staff, and patients concerning events that happened in the practice "that should not have happened and that you don't want to happen again." For the General Errors study, these could be any type of events, including office process or knowledge and skill errors, errors of commission or omission. For the Testing Process Errors study, reported events were related only to laboratory tests, diagnostic imaging tests, or other tests. Clinicians and staff were given the choice of two methods of reporting: via a secure Web site or via written reports. Patients could report via a secure Web site, written reports, or an automated telephone system. The ASIPS PSRS accepted anonymous and confidential paper, Web-based, and telephone reports on all types of errors. All studies convened focus groups involving clinicians and staff. Both groups conducted onsite analyses of process pathways in selected practices.

Regulatory processes

The AAFP studies were submitted to 15 separate institutional review boards to secure 16 IRB approvals. The primary National Network IRB, the University of Missouri–Kansas City Social Science IRB (SSIRB), approved both AAFP studies.

One of the AAFP sites did not receive local institutional approval and was not able to participate. This site was replaced by a new site.

The ASIPS application was submitted to seven different IRBs and two post-IRB institutional financial reviews. The ASIPS staff helped two participating institutions obtain FWAs that designated the University of Colorado IRB (COMIRB) as the IRB of record.

All data collected in these studies were protected from discoverability by statute. That is, all identifiable research data obtained for AHRQ research projects were protected by the statutory provision of the Public Health Service Act, 42 U.S.C. §299c-3(c), and could not be disclosed without the consent of the supplier of the data.

Outcome measures

We examined the following information from the review process for the three studies: application submission requirements, type of review required by each IRB, consent considerations, other approvals required, ability of practices to fully participate, number of inquiries and modifications requested, estimated network resources required to obtain approval, and length of time to obtain approval. We also described each network's approach to obtaining IRB approvals and the staff effort involved.

Results

Network approach to obtain approvals

Both the AAFP and CU elected to submit IRB applications in a sequential fashion. That is, both waited for approval from their primary IRB before submitting to secondary IRBs. This approach lengthened the time necessary to obtain full approval for all sites, but eased the communication and tracking burden as protocol or consent adjustments were requested. All 3 protocols were granted expedited review by the two primary IRBs and averaged 29.3 days (a range of 20–40 days) for obtaining approval. Approval of the 3 protocols by 19 secondary IRBs averaged 19 days (1–48 days). In total, the 3 protocols were submitted 23 times to 21 IRBs. AAFP submitted both protocols to its primary IRB, and one of the IRBs reviewed both the ASIPS protocol and one of the AAFP protocols.

Both networks utilized approaches to extend primary IRB coverage to sites not affiliated with an IRB at the time these protocols were submitted. The two groups obtained unaffiliated investigator agreements for 19 sites, and ASIPS helped two institutions complete the FWA process to be associated with the primary IRB. Table 1 describes the complexity of the IRB structure for the practices that participated in the three studies.

Table 1. Description of IRB status of the practices participating in patient safety studies, by organization

Organization	No. of primary IRBs	No. of secondary IRBs	No. of practices with FWA associated with primary IRB	No. of practices with unaffiliated investigator	No. of practices with multiple sites (practices/ sites)
AAFP	1	14	0	5	0/0
ASIPS	1	6	5	9	7/25

The 23 protocol reviews required for the 3 studies varied considerably, as described in Table 2. Eight submissions required full board reviews and 15 were granted expedited reviews. Many of the IRBs conducted expedited reviews, as defined in the Code of Federal Regulation Title 45, Part 46, Protection of Human Subjects. The expedited procedure requires review and approval by the chair or other qualified IRB member only. However, some IRBs approved the protocol as expedited only after review with a full board, having no mechanism for chair-only review. Practice co-investigators were required to be present at two of the reviews. Though meeting all local and Federal requirements was very time consuming, most IRBs approved the protocols with minimal revisions required.

Table 2. Number of IRB submissions according to characteristics of IRBs and the type and time of review required for approval

	Total reviews	Full review	Expedited review	Consent required	Days for approval (mean/range)
Type of IRB (N = 23)					
University	10	2	8	9	23.6/(9–40)
Hospital	11	4	7	11	15.5/(1–48)
Private or Federal	2	2	0	0	30.0/(29–31)
Volume handled by IRB (# protocols reviewed/yr) (N = 22)*					
Low (≤200)	12	5	7	11	14.1/(1–38)
High (>200)	10	3	7	8	24.6/(4–40)
Study (N = 23)					
AAFP General Errors	9	4	5	6	23.4/(4–40)
AAFP Testing Process Errors	7	2	5	7	24.9/(9–48)
ASIPS	7	2	5	7	11.6/(1–20)
Days for approval (mean/range)		24.4/ (5–48)	18.1/ (1–40)	19.1/ (1–48)	

*One IRB did not provide data regarding the number of protocols reviewed.

Table 2 shows the review process by type and annual review volume of IRB. Few university-based IRBs required full-board review of protocols, whereas the two private and Federal IRBs both required full-board reviews. A greater percentage of low volume IRBs required full-board review.

Length of time to obtain approval

For the eight full-board reviews, the mean number of working days that elapsed from the time of the submission of the application to the IRBs until IRB approval was 24.4 days (5–48 days). The mean number of days for the 15 expedited reviews was 18.1 days (1–40 days).

For the 11 hospital sites, the mean number of working days required for IRB approval was only 15.5 days. However, there was great variability in length of time required to obtain these approvals, from 1 to 48 days. The low-volume IRBs required, on average, 14.1 days (1–38) for approval, and the high-volume IRBs required an average of 24.6 days (4–40).

Consent considerations

No patient consents were required by any of the IRBs. Three IRBs did not require clinician or staff consent for the AAFP studies (Table 2). While all ASIPS IRBs required clinician and staff consent, this consent was for an evaluation questionnaire of the reporting system that clinicians and staff were asked to complete. The questionnaire could be tracked back to an individual. Because clinicians and staff had the option of reporting anonymously or not reporting at all, no IRB required consent for the reporting activities.

Application submission requirements

Application submission requirements to the secondary IRBs varied considerably. The least complicated was submission of the primary IRB application only. The most complicated application required a complex 12-page form, a protocol synopsis specifically outlined for the IRB, the primary IRB application, and the primary IRB approval letter. Eighteen unique applications were required by the 23 IRBs (Table 3). These applications covered the participation of 47 sites in the studies. This includes seven ASIPS practices that had more than one site participating in the study. Five IRBs required only the submission of the AAFP or ASIPS application and letter of approval. Local network members supervised only 3 of the 18 secondary IRB submissions, whereas the AAFP or ASIPS staffs oversaw 15 secondary IRB submissions. Table 3 does not include the practices that were not affiliated with an IRB.

An additional 8 legal, risk management, local, and/or hospital resource reviews were required out of 23 submitted protocols (Table 4). Two of these reviews resulted in modification of study participation. As a result of legal reviews, one site was not allowed to participate in the study, even though the site's local IRB had approved the study. A second site decided to limit its employee participation in the protocol, allowing only anonymous reporting of

Table 3. Application preparation requirements by IRB submissions and sites overseen

	Number of IRB submissions (N = 23)	Number of sites (N = 54)
First draft completed by AAFP or ASIPS	15	44
First draft completed by site, with assistance from AAFP or ASIPS	3	3
IRB required copy of AAFP or ASIPS IRB material only (no application required)	5	7

Table 4. Non-IRB approvals required for affiliated institutions by type of approval

Type of approval	Number of affiliated institutions
Legal only	1
Risk management only	1
Legal and risk management	3
Tribal councils	1
Administrative/financial impact	2

events. Two institutions conducted additional administrative/financial reviews of the protocol after the initial IRB review and approval. These institutional reviews, which were conducted after IRB approval was received, delayed the initiation of data collection in several practices.

Number of inquiries and modifications requested

AAFP and ASIPS staff members followed up via e-mail, phone, and fax with IRB chairs and personnel from legal and risk management departments in order to secure protocol approvals and revise consent forms (Table 5). One site requested that the network's attorney and the practice institution's attorney draft a confidentiality agreement. However, after the confidentiality agreement was drafted and agreed upon, the legal department did not allow this site to participate in the project. Another site required documentation of the information technology security audit that was required to establish and maintain the error reporting system used in the study. Several IRBs required phone conversations with the attorney who represented the network.

Estimated network resources required to obtain approvals

AAFP staff and the AAFP attorney spent approximately 40 hours assisting the 14 affiliated sites in securing IRB approval. Of the 40 hours, AAFP staff spent approximately 20 hours writing and revising the first draft of the IRB applications for eight of the practice sites. Fifteen hours were spent on followup of IRB

Table 5. Types of AAFP or ASIPS followup required for IRB and affiliated institutional submissions

Type of followup	Number of IRB and institutional submissions (N = 25)	Percent of IRBs and institutions
Revised consent	8	32%
Revised and signed confidentiality agreement	1	4%
Personnel present at IRB review	3	12%
Phone calls with legal department	3	12%
Phone calls with IRB chair/personnel	8	32%
Phone calls with risk management	2	8%
Documentation of IT security/audit	1	4%
E-mailed and faxed material	10	40%

submissions, including followup on items such as informed consent revisions, answering questions from one site's IRB regarding discoverability concerns, and providing legal documentation ensuring the site's confidentiality while using the AAFP error reporting system. An additional 5 hours were spent on writing, discussions, and followup for a confidentiality agreement requested by one site's IRB. The ASIPS program did not keep records of the time required to obtain approval for their sites to participate in this research study. However, one ASIPS staff person (the department's research coordinator) was designated to prepare, respond to questions, and follow up on all of the IRB submissions.

Discussion

This paper describes the complexity of the IRB process that now challenges researchers who choose to do multisite, office-based research in the United States and describes the added barriers presented by patient safety protocols. Part of the complexity is due to the autonomy given to each IRB by OHRP and the lack of standards provided by this body. Moreover, different IRBs interpret standards in many different ways.

The case study presented here shows that most IRBs have their own application and approval processes. For the most part, the secondary IRBs were not able or willing to say, "The primary ASIPS or AAFP IRB has already approved this protocol, so I will accept that approval." Instead, most secondary IRBs required that staff take several hours to complete a unique, generally complicated IRB application. In addition, it took anywhere from a few days to more than a month to receive final approval for study participation.

Beyond the complicated process of IRB approval, these highly sensitive safety studies also were required to undergo several secondary reviews. These reviews added months to the process and resulted in a loss of considerable data. The two

legal reviews required 3 months or more to complete, and both resulted in changes to site participation in the research activities, including disallowing confidential data in one instance and a 10-week cutback from the data collection period for one site in the second instance. Secondary reviews are becoming more common as health care systems are divided between multiple stakeholders. The addition of these secondary layers of approval not only further complicate the research process, but also may lead to additional protocol modifications and erosion of the integrity of the final product. PBRNs that limit themselves to stand-alone practices can avoid these problems, but restricting the practices involved in the research process erodes the generalizability of results.

There was an interesting dichotomy between university- and hospital-based IRBs. University IRBs required fewer full-board reviews than the hospital IRBs, but that process did not shorten the time for approval. Chairs of the low-volume hospital-affiliated IRBs may not have felt comfortable making decisions on highly sensitive patient safety research based on the chairs' reviews only. These chairs may not have been experienced researchers, and the hospital-based IRBs may be more attuned to potential negative consequences of medical errors. In contrast, the more active university IRBs were more likely to have chairs with personal research experience and, consequently, felt more comfortable with their personal decisions. In addition, the university-based IRBs may not have been as sensitive to the potential negative effects of patient safety research, as there is typically greater separation between research and clinical care in university settings. This said, it appeared that the low-volume hospital-affiliated IRBs pushed the protocols through faster than the high-volume academic-affiliated or private IRBs. In addition, the ASIPS protocol required less time for approval than the AAFP protocols. The ASIPS program has designated a single staff member to work with the IRB staff at the secondary IRB sites. In addition, the ASIPS program has been working with the secondary IRBs for a much longer period of time than the AAFP staff and has formed personal relationships with the IRB chairs and coordinators. Both of these strategies have apparently cut down on required approval time.

Nonetheless, the IRB challenge has created a significant barrier to the work of PRBNs. Some researchers have considered the inclusion of only unaffiliated investigators in their research studies. Others have asked their affiliated investigators to complete a FWA and designate the network's primary IRB as the IRB of record for PBRN studies. However, many institutions will not allow their practices or clinicians to be affiliated with another IRB. Thus, all protocols carried out within the institution must be approved by the institution's IRB, regardless of the level of risk involved. In addition, the review of low-risk studies is not necessarily less complicated or less time-consuming than reviews of high-risk studies.

PBRNs must find better solutions to the IRB dilemma if they are to fulfill their potential of providing quality and generalizable research at the point of care that will subsequently result in enhanced health care delivery and health status of patients and communities. These solutions also will be necessary to keep the interest of both investigators and practice participants. One possible solution is the

creation of a central IRB for a given PBRN or even a central IRB for several primary care PBRNs in a given discipline (e.g., family medicine). This concept has been required in a recent call for the development of dental research networks by the National Institute for Dental and Craniofacial Research (Grant RFA DE 05-006).[16]

A central IRB model has been developed in the United States for the conduct of oncology clinical trials. "A large percentage of oncology clinical trials are coordinated through the National Cancer Institute's (NCI) system of cooperative groups" allowing for centralized scientific review.[17, 18] What is possible with oncology clinical trials seems entirely reasonable and persuasive for PBRNs, especially since the risks to human subjects associated with most PBRN research pale in comparison to that of oncology clinical trials. Thus, "there is a tremendous opportunity to employ a centralized mechanism to provide ethical review by highly trained IRB members, allowing local IRBs to take advantage of the financial and time efficiencies that central review provides. Centralized review boards (CRBs) would also contribute consistency and efficiency to the process."[16] This possible solution has also been recognized by others.[5, 14] Such a solution portends benefits to investigators and practices associated within PBRNs and also to the multiple local IRBs that have authority over these practices. It would resolve what Burman et al. refer to as the "crisis in local IRB function" brought on by the administrative burden of multicenter clinical research.[8]

Another possible solution that would improve—though not totally resolve—the problems of multiple IRB approvals would be the use of a generic application form. This solution is not as helpful as the creation of a central IRB, but at least this would cut down on the time and resources required for IRB application preparation.

Conclusion

The IRB approval process presents a formidable barrier to carrying out quality research in practice-based research networks in the United States. To meet the need for high quality primary care research, PBRNs need to expand their research into sensitive areas, at the patient or institutional level. This study suggests that a move in this direction will further highlight IRB inconsistencies. This paper presents a case study of three patient safety research studies coordinated by the University of Colorado Department of Family Medicine and by the American Academy of Family Physicians' National Research Network. The staffs of both networks closely facilitated, whenever possible, the approval process for all IRBs involved in these three studies. However, even with these staff resources, the IRB approval process was very complex and required extensive preparation time for this mandatory regulatory work before study initiation. A better solution must be found to alleviate this barrier so that PBRNs can advance in their quest to improve health care delivery.

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