Institutional Variability in a Minimal Risk, Population-Based Study: Recognizing Policy Barriers to Health Services Research

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Objective. To describe (1) the institutional variability in study approval and willingness to obtain federal assurance documents for a federally supported, minimal risk health services research project conducted during the implementation of the Privacy Rule and federalwide assurances, and (2) the potential impact of such policy on selection of research subjects and generalizability of study results.

Data Sources. Primary data collection from 2001 to 2004.

Study Design. We provide a descriptive analysis of a prospective, observational, out-of-hospital study.

Study Setting. Twenty-seven pediatric receiving hospitals were approached for participation in a study validating a decision rule to identify seriously injured children involved in motor vehicle crashes in Los Angeles County. Two federal research policies, the Privacy Rule and the requirement for federalwide assurances, were implemented during the project.

Data Collection. All 27 hospitals were sent an identical research protocol requesting approval to review charts of children transported to their facility. The research protocol included strict confidentiality protections, was noninterventional, did not alter the standard of care at the scene or at the hospital, and met requirements for waivers of both informed consent and the Health Insurance Portability and Accountability Act. Because the project was federally supported, all participating hospitals were required to have a federalwide assurance. The hospitals receiving the research protocol were the unit of analysis and outcomes included: approval of the research protocol, total number of days to study approval, and successfully obtaining a federalwide assurance.

Principle Findings. Overall, 6 of 27 (22 percent) hospitals refused to participate in the study, all of which were community hospitals. The median time from submitting an application to study approval was 118 days (interquartile range 34–254, range 12–960 days) and time to study approval differed when hospitals were categorized by type and the presence of an institutional review board ($p = .053$). No institutional review resulted in a change in the basic study protocol, although one hospital required paramedic consent. Following intensive efforts to secure federalwide assurances, 12 of 27 hospitals

(44 percent) possessed the necessary assurance to conduct the study. If all patients transported to hospitals that failed to obtain such an assurance were omitted, the sample size would have been reduced by 62 percent and would have excluded all children transported to community hospitals.

Conclusions. There is substantial institutional variability in approval of a minimal risk observational study and in willingness to obtain a federalwide assurance, particularly among community hospitals. Federal research policy involving patient privacy and institutional assurances may be contributing to this variability, which can adversely affect selection of research subjects, disrupt population-based study design, and threaten the generalizability of study results.

Key Words. Federalwide assurance, HIPAA, institutional review board, privacy rule

Federal rules and regulations exist to ensure the protection of human subjects involved in research (Belmont Report 1979; Title 45, Code of Federal Regulations, part 46 2001); but it is the institutional review board (IRB) that interprets, implements, and applies these guidelines in a given health care or research facility (Moreno, Caplan, and Wolpe 1998; Title 45, Code of Federal Regulations, part 46 2001). Additional federal research regulations, the Health Insurance Portability and Accountability Act (HIPAA) "Privacy Rule," and the requirement for federalwide assurances have recently been implemented with the intent of further protecting patient privacy and standardizing institutional research standards (Title 45, Code of Federal Regulations, part 46 2001; Title 45, Code of Federal Regulations, parts 160 and 164 2002).

The Privacy Rule, as applied to research, requires strict confidentiality and limited access to individual protected health information unless informed consent is provided or the research qualifies for a waiver. Federalwide assurances serve as a document or agreement that defines an institutional obligation to comply with federal research regulations (Newgard and Lewis 2002). Such

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“assurances” have existed for many years, being provided to centers for multiple studies or for a single study after central (i.e., federal) review of a given research protocol. In 1998, the Office for Human Research Protections began a paradigm shift of decentralizing responsibility for protocol review, changing accountability, “simplifying” assurances, and promoting the concept of accreditation and education with a single, broadly applicable federal assurance (i.e., the federalwide assurance) for all institutions participating in federally supported or federally conducted research (Newgard and Lewis 2002). While the Privacy Rule and federalwide assurances are only strictly applicable to federally supported or federally conducted research and to hospitals receiving federal funds, they have been broadly applied throughout the health care system.

Whether these regulations confer any additional protection for human subjects involved in research is unclear, and concerns have been raised about the potentially negative effect of these regulations on research, particularly on population-based health services research (Kulynych and Korn 2002). In the case of federalwide assurances, there is no evidence to suggest that such an assurance further improves the protection of human subjects, particularly for minimal risk research conducted in nonacademic institutions where the individual tasked with obtaining and signing the assurance often has no involvement in or direct supervision over such research activities.

Including patients from many different practice settings (e.g., academic, tertiary, and community) in health services research is important to produce valid results with broad generalizability. Regulatory burden may threaten broad participation (Kulynych and Korn 2002), especially among centers that would rarely, if ever, participate in research activities. Policies that effectively restrict the selection of research subjects to those in academic centers may have the unintentional result of reducing the generalizability of subsequent study results and raise concerns about whether important findings truly apply to the vast majority of patients who receive care in nonacademic centers. Finally, such restricted selection of research subjects potentially violates the principle of justice in research (Belmont Report 1979).

The objective of this study was to describe (1) the institutional variability in study approval and willingness to obtain federalwide assurance documents for a federally supported, minimal risk health services research project conducted during the implementation of the Privacy Rule and federalwide assurances, and (2) the potential impact of such policy on selection of research subjects and generalizability of study results.

MATERIALS AND METHODS

Study Design

This is a descriptive analysis of data from a prospective, observational research study.

Study Setting

From 2001 to 2004, we conducted a federally supported, prospective, multicenter, emergency medical services (EMS) study to validate a previously derived clinical decision rule intended to identify children seriously injured during motor vehicle crashes (Newgard, Lewis, and Jolly 2002). We selected 20 fire stations in Los Angeles County, California, and identified 27 pediatric receiving hospitals that received pediatric patients from these squads during the previous year. These 27 hospitals represented 47 percent of the pediatric receiving hospitals in Los Angeles County.

Data Collection

In July 2001, all 27 potential receiving hospitals were sent an identical research protocol requesting approval of a retrospective chart review to determine outcome information (i.e., injury severity and hospital resource use) for children transported to their facility by participating EMS personnel. Fire fighters and paramedics prospectively identified children at the scene of a crash, and completed a standardized data form. The research protocol included strict confidentiality protections, was noninterventional, did not alter the standard of care either at the scene or at the hospital, and met requirements for waivers of both informed consent and HIPAA regulations (the Privacy Rule).

Because the project was federally supported, we were required to obtain federalwide assurances at all participating hospitals. Seven of the hospitals, all tertiary care centers, had an assurance in place or were in the process of acquiring one at the start of the study. We undertook a major educational and facilitative effort to assist the additional 20 hospitals in obtaining these documents. This effort has been previously described (Newgard and Lewis 2002), and consisted of: phone calls and e-mails to all IRB chairs or hospital chief administrative officers (for hospitals without an IRB) explaining the concept of federalwide assurances and the need to obtain such assurances for this (and future) projects, coordinated sequential mailings detailing a step-by-step instructional guide to securing a federalwide assurance, and personnel to assist in the process of securing an assurance.

Our local hospital IRB agreed to oversee the out-of-hospital portion of the project and approved this study. External hospitals and/or their IRBs were asked to approve the retrospective chart review required at their institution.

Data Analysis

We use descriptive statistics (proportion, median, and interquartile range [IQR]) and the Kruskal–Wallis test to describe differences among the hospitals and the variation in total number of days from protocol submission to approval by hospital academic status and presence of an IRB. Hospitals serve as the unit of analysis and were stratified into four groups: (1) academic hospital with an IRB (level I trauma center, pediatric critical care center, university affiliation, and full spectrum of residency training programs); (2) part-academic hospital with an IRB (level II trauma center, pediatric critical care center, possible university affiliation, and at least one residency training program); (3) community hospital (nontrauma center, no pediatric critical care availability, and no university affiliation) with an IRB; and (4) community hospital without an IRB.

RESULTS

Institutional Variability in Study Approval

Overall, six of 27 hospitals (22 percent) refused to participate in the study. Figure 1 illustrates the proportion of hospitals approving the protocol, stratified by type of facility. Of the hospitals approving the study protocol, the median time from submitting an application to study approval was 118 days (IQR 34–254, range 12–960 days). There were significant differences in time to study approval when hospitals were categorized by type and the presence of an IRB ($p = .053$) (Figure 2). No institutional review resulted in a change in the basic study protocol, although one hospital required paramedic consent. Of the 123 children transported to a hospital by EMS personnel, eight (7 percent) were excluded solely because of the refusal of institutional approval, all from community hospitals. If the hospitals requiring >12 months to review and approve the request were dropped from the study, 21 of 123 children (17 percent) would have been excluded, all from community hospitals.

Institutional Variability in Federalwide Assurances

Seven hospitals (26 percent) had a federalwide assurance in place or had taken steps to secure an assurance before the study began. All of these hospitals

Figure 1: Hospitals Approving the Protocol, Hospitals Possessing a Federalwide Assurance after an Intensive Countywide Campaign, and the Absolute Number of Transported Patients, by Type of Hospital and Presence of an IRB*

*For study approval and federalwide assurances, the maximum proportion of hospitals within each stratum is 100 percent (primary axis). For transported patients ($n = 123$), the vertical bars represent the absolute number of transported patients taken to each hospital type (secondary axis).

were tertiary care centers with a relatively high volume of research. Of the remaining 20 hospitals, five facilities obtained an assurance following intensive countywide efforts, resulting in 12 of 27 of the hospitals (44 percent) originally targeted for the study having or acquiring the necessary assurance to conduct the study (Figure 1).

After extensive discussion with the Office for Human Research Protections and demonstration of the study's strict confidentiality protections and minimal risk nature, we were granted a conditional waiver from securing a federalwide assurance at every hospital in order to perform a chart review and the study was allowed to proceed. If we had been forced to omit all patients transported to hospitals that had failed to obtain an assurance, the sample size would have been reduced to 47 patients (62 percent reduction in enrolled children transported to a hospital), and would have excluded all 46 patients (37 percent) that were transported to community hospitals (Figure 1).

Figure 2: Days to Protocol Approval by Type of Hospital and Presence of an IRB ($n = 27$)*

*The six hospitals that did not approve the protocol are included in the “no approval” area. These hospitals were included in the Kruskal–Wallis analysis of differences in days to study approval by assigning values from the date study materials were mailed until completion of the project (1,095 days).

DISCUSSION

In this minimal risk, multicenter, health services research study, there was substantial institutional variability in study approval, time to approval, and willingness to obtain a federalwide assurance when stratified by type of institution and presence of an IRB. The potential for selection bias in minimal risk, observational research requiring informed consent (Tu et al. 2004) and variability in IRB review (Bennett et al. 2001; Silverman, Hull, and Sugarman 2001; Stair et al. 2001; Hirshon et al. 2002) have been previously described. However, there has not been previous research assessing the potential impact of federal research policy (i.e., the Privacy Rule and need for federalwide assurances) on health services research.

While the current study does not necessarily demonstrate a causal relationship between federal research regulations and the lack of hospital

participation, it is our perception, through hundreds of phone calls, mailings, and e-mail communications, that community hospitals with little or no research volume increasingly perceive participation in such research as a liability rather than as a means to improve the care of their patients. This concern has been raised before (Kulynych and Korn 2002; Newgard and Lewis 2002). A previous study conducted in Los Angeles County (including the same 27 hospitals approached for the current project) before implementation of the Privacy Rule and federalwide assurances may serve as a basis for comparison. From 1993 to 1995, institutional approval was obtained from all pediatric receiving hospitals in Los Angeles County to conduct an out-of-hospital, randomized, controlled, interventional trial for emergent airway management in children with waiver of consent (Gausche et al. 2000). All 27 hospitals involved in the current cohort previously approved the Gausche protocol and participated in the airway study, however, only 21 of these 27 hospitals (all community hospitals) were willing to approve a request for a minimal risk, observational study at their institutions after implementation of the Privacy Rule and federalwide assurances. Although other factors could have changed over this time period (e.g., hospital management, IRB personnel, risk management, etc.), we believe the implementation of more complex federal research policy during this time period and a resulting perception of increased institutional risk associated with research cannot be ignored as a potential reason for lack of participation.

The majority of hospitals failing to obtain a federalwide assurance and/or refusing to approve the protocol were unwilling to discuss their reasons for inaction. However, one IRB specifically cited the need for a federalwide assurance as a reason *not* to approve the protocol and several other hospitals suggested that after implementation of the Privacy Rule, we could no longer review charts without obtaining informed consent from patients, despite qualifying for a waiver from these regulations. For many community hospitals, there was little incentive to obtain a federalwide assurance or to approve a research protocol that forced administrators to understand the nuances of performing minimal risk research with a waiver from the Privacy Rule. It was much easier to simply refuse to participate. The mechanism allowing one IRB to serve as a surrogate for another IRB (or institution) did little to persuade most of the hospitals refusing to participate in the project, despite the seemingly simple nature of the retrospective chart review and strict confidentiality protections.

If we had been prevented from following up patients transported to hospitals not possessing an assurance, the sample would have been severely

skewed towards children transported to academic or part-academic centers (i.e., selection bias), threatening the population-based study design and generalizability of study results. Only four of the 17 community hospitals pursued for this project ultimately obtained a federalwide assurance. Without the negotiated waiver through the Office for Human Research Protections, enrollment in this study would have been very limited, excluding all patients transported to community hospitals. Based on these results, we believe there is a real potential for the current federalwide assurance policy to adversely affect the selection of research subjects (i.e., selection bias), to disrupt population-based study design, and to reduce the generalizability of subsequent study results (Kulynych and Korn 2002; Newgard and Lewis 2002).

The requirement for federalwide assurances and the stringent nature of the Privacy Rule provide a strong disincentive for nonacademic hospitals to participate in research, despite caring for the majority of patients in the United States. We cannot assume that patients presenting to academic medical centers (or centers possessing federalwide assurances) are similar to patients presenting to community hospitals (or hospitals not willing to obtain such an assurance), and yet our current research climate is to assume such results can be generalized to all practice settings. Without evidence of additional human subjects protection from these regulations in minimal risk research, such policy may ultimately hurt the same persons these regulations are designed to protect by excluding them from studies and by reducing the value of study results to those populations. As a result, current federal research policy may serve as an impediment to improving the health of the vast number of patients cared for outside the setting of academic medical centers. While the number of subjects in this study was modest, if these results are indicative of national multicenter health services research efforts, the impact could be far-reaching.

Any potential solution to these issues must maintain the current high standards for the protection of human subjects in research, while appropriately accounting for the risk of a given study. A large portion of health services research is observational and very low risk. Requiring federalwide assurances at all institutions involved in minimal risk, population-based research neither guarantees increased human subjects protection nor the standardization of research at these institutions, as many of the persons charged with obtaining these assurances have little or no involvement in such research studies (e.g., the chief administrative officer at a community hospital). The requirement for assurances and the strict enforcement of the Privacy Rule among all institutions participating in multicenter health services research places further

burden on a system that is already under considerable stress (Moreno, Caplan, and Wolpe 1998; Phillips 2000; Burman et al. 2001; Levine 2001; Steinbrook 2002).

Applying the concept of a central IRB (Christian et al. 2002) to multicenter, observational, minimal risk research may provide a balance between high research standards and catalyzing research designed to improve health outcomes in the community setting. Experienced academic IRBs may serve as regional IRBs for hospitals within specified regions. Regional sites could provide study review, oversight, federalwide assurance of research standards, and informed interpretations of the Privacy Rule, with expedited review by each of the smaller participating centers. All institutions would maintain the right to withhold approval for a given protocol, but the efforts, expertise, and oversight from the central IRB would allow more efficient and less burdensome review by centers with less experience in reviewing such protocols. Even without the establishment of regional IRBs, the requirement for federalwide assurances for minimal risk research could be eliminated without adversely impacting the protection of human research subjects. This type of template, if formalized by federal research policy, would remove the need for every institution to obtain a federalwide assurance in minimal risk research, may reduce the perception of liability among community hospitals and other facilities not traditionally involved in research, and may facilitate achieving the National Institutes of Health Roadmap objectives (Zerhouni 2003) by removing some of the current barriers to creating a collaborative clinical research network among community centers and academic centers. If such an arrangement was acceptable to federal agencies, several of the current obstacles to population-based, minimal risk research could be removed without compromise in the protection of human subjects.

CONCLUSIONS

There is substantial institutional variability in study approval and willingness to obtain a federalwide assurance among hospitals presented with a protocol for minimal risk health services research, particularly among community hospitals. Federal research policy involving patient privacy and institutional assurances may be contributing to this variability, which can adversely affect selection of research subjects, disrupt population-based study design, and threaten the generalizability of study results.

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