

SPECIAL ARTICLE

Impracticability of Informed Consent in the Registry of the Canadian Stroke Network

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ABSTRACT

BACKGROUND

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Government legislators and research ethics boards in some jurisdictions require all patients to give written informed consent before enrollment in clinical registries. However, the effect of such a requirement on the use of clinical registries and the extent to which registry data can be generalized remain uncertain.

METHODS

We examined the effectiveness of a comprehensive attempt to obtain informed consent between June 2001 and December 2002 on the overall participation rate and the characteristics of participating patients in the Registry of the Canadian Stroke Network, a prospective registry based at 20 major stroke centers across Canada.

RESULTS

The overall participation rate (i.e., the consent rate among all potential participants) was 39.3 percent of 4285 eligible patients during phase 1 of the project (June 2001 through February 2002) and 50.6 percent of 2823 eligible patients during phase 2 (June 2002 through December 2002), despite the presence of neurologic research nurse coordinators at each site. Many patients died or left the hospital before they could be approached for consent. Major selection biases were found; the in-hospital mortality rate was much lower among patients who were enrolled (6.9 percent) than among those who were not enrolled (21.7 percent) (relative risk of in-hospital death, 3.13; 95 percent confidence interval, 2.65 to 3.70; $P < 0.001$). We estimate that approximately \$500,000 (Canadian dollars) was spent on consent-related issues during the first two years of the registry.

CONCLUSIONS

Obtaining written informed consent for participation in a stroke registry led to important selection biases, such that registry patients were not representative of the typical patient with stroke at each center. These findings highlight the need for legislation on privacy and policies permitting waivers of informed consent for minimal-risk observational research.

*Other participating site investigators in the Registry of the Canadian Stroke Network are listed in the Appendix.

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EPIDEMIOLOGIC STUDIES BASED ON DATA from clinical registries have contributed to tremendous advances in modern medicine by enhancing our understanding of the natural history of disease and the value of many medical and surgical interventions. Studies using these data bases have increased the use of evidence-based medical therapies and have lowered the mortality rate associated with common conditions.¹⁻⁴ Many clinical data bases have been developed without informed consent from patients. Researchers have argued that informed consent should not be required for participation in clinical data bases because there are large benefits to society from the research conducted and only very small risks to the patients involved, and because it is impracticable and too costly to approach all patients for consent. The strength of many registries lies in their ability to include all patients with a given condition, or at least a representative sample of them, over a defined period of time.

The development of large, electronic health-records systems and technical developments that have facilitated data mining and record linkage have caused increasing concern among the public about the privacy of personal health information. In response, several countries have passed legislation protecting personal information from unauthorized use. Some have argued that overly strict privacy laws will affect the future viability of observational research studies.⁵⁻¹⁰ The passage of privacy legislation mandating informed consent for access to medical records has adversely affected cancer registries in England and Germany and some research studies in Minnesota.^{8,9,11,12} Although most privacy laws, including the Health Insurance Portability and Accountability Act in the United States, do allow waivers of informed consent, some research ethics boards or data holders may interpret the laws very conservatively, virtually mandating that informed consent be obtained before any data are collected.^{6,13}

Ideally, a very high percentage of patients (e.g., more than 95 percent) would be approached and would agree to participate in a clinical registry. We conducted a study to determine the feasibility of obtaining written informed consent for participation in the Registry of the Canadian Stroke Network. The purpose of the registry is to monitor and improve the quality of stroke care in Canada. We attempted a consent-based registry for several reasons: first, there was concern that consent may

become mandatory for registries in Canada through future privacy legislation; second, we intended to contact patients after hospital discharge to collect quality-of-life information; and third, a goal of the Canadian Stroke Network was to share aggregate analyses of the registry data with some commercial organizations developing products such as medications and devices to aid daily living. In this article, we examine the effectiveness of the attempt to obtain consent for participation in the registry during its first two years of operation and describe the challenges and limitations that arose as a result.

METHODS

PATIENTS AND DATA COLLECTION

The first phase of the registry project took place from June 2001 through February 2002 and involved 20 participating hospitals in eight Canadian provinces. The second phase of the project was conducted from June 2002 through December 2002 and involved the same hospitals. The separate, second phase was not originally planned but became necessary when the participation rates in the first phase were poor and the amount of data collected needed to be reduced. Although registry hospitals constitute only 3 percent of all Canadian hospitals, they admit approximately 20 percent of all Canadian patients with stroke. All the participating hospitals were acute care institutions with specific resources, interest, or expertise in the care of patients with stroke. Approval for the registry project was obtained from the research ethics boards at each participating institution.

A stroke neurologist served as the project leader at each site. Recruitment of patients and data entry were performed by experienced research nurses, the majority of whom had previous experience in obtaining informed consent in clinical trials involving patients with stroke. Each site had either a full-time or a half-time nurse coordinator, depending on the projected volume of patients with stroke at that hospital. Potential registry patients were identified from multiple sources, including emergency department logs, admission lists, and ward census reports. The data collected included comprehensive information about the symptoms at presentation and the in-hospital course of each patient. Encrypted, password-protected data, stripped of personal identifiers, were sent electronically by modem to the Institute for Clinical Evaluative Sciences in Toronto, where the data were securely housed and analyzed.

REGISTRY CONSENT PROCEDURES

The registry coordinators working with the on-site investigators attempted to obtain consent from and to enroll consecutive patients presenting to participating hospitals with acute stroke, transient ischemic attack, or both. A comprehensive brochure (available in both English and French versions) explained the purpose of the registry and the intended uses of the data. Patients or their surrogates reviewed the brochure and the consent form with the nurse coordinator. The consent form, which was written in simple terms, contained a “yes or no” checklist that allowed patients to opt in and consent to any of the four components of the registry, including abstraction of their charts for a full clinical data set; 30-day and 6-month follow-up interviews in which information on quality of life would be gathered; linkage of the registry data to Canadian administrative data bases for long-term follow-up; and release of the aggregate results of analyses of registry data to commercial organizations. Pilot testing and refinement of the consent form were performed before the beginning of the project.

Before phase 1 of the project, the nurse coordinators received standardized training in obtaining

consent from patients, performing chart abstraction, and conducting follow-up interviews. A de-identified minimal data set (including age, sex, and type of stroke) was obtained for all the patients to allow comparison of the basic characteristics of both consenting and nonconsenting patients. Monthly conference calls, led by the principal investigators, were held with all the nurse coordinators to review real-time consent rates at each hospital and to identify barriers to and strategies for maximizing the consent rate at each hospital. The overall participation rate at each hospital was defined as the number of patients who consented divided by the total number of patients who were eligible for the registry. Toward the end of phase 2, data were collected over a two-week period from a random sample of patients to determine the amount of time required by research nurses to obtain patients' consent and to collect data from the patients' charts.

STATISTICAL ANALYSIS

Chi-square tests were used to compare categorical variables; unpaired t-tests were used for continuous variables. All analyses were conducted with the use of SAS software (version 8.2, SAS Institute). All reported P values are two-sided.

Table 1. Overall Participation Rates and Reasons for Nonparticipation among Patients Eligible for Enrollment in Phases 1 and 2 of the Registry of the Canadian Stroke Network.*

Variable	Phase 1 (N=4285)	Phase 2 (N=2823)
	% of patients	
Overall participation rate	39.3	50.6
Consent obtained from patient	27.9	35.9
Consent obtained from surrogate	11.4	14.7
Overall nonparticipation rate	60.7	49.4
Reasons for nonparticipation		
Patient died before could be approached	6.8	4.9
Patient left hospital before could be approached	19.7	4.9
Language barrier	1.4	1.9
Surrogate decision maker unavailable	6.5	5.9
Other reasons†	17.1	20.1
More than three attempts to contact patient unsuccessful	—	10.1
Patient not admitted	—	4.6
Miscellaneous	—	5.4
Patient or surrogate refused consent	9.2	11.8

* Phase 1 took place between June 2001 and February 2002; phase 2 took place between June 2002 and December 2002.

† The “Other reasons” category was expanded in phase 2 to include the subcategories “More than three attempts to contact patient unsuccessful” and “Patient not admitted.”

RESULTS**PHASE 1**

Early in phase 1 of the registry project, the nurse coordinators reported that they were having difficulty obtaining consent from all the patients and that the time required for the consent process was limiting the time available for data collection, leading to an overwhelming workload. Various elements, such as the collection of information from patients with a transient ischemic attack who were not admitted to the hospital and the 30-day follow-up interview on quality of life, were eliminated to decrease the workload. Analyses of data gathered during phase 1 (June 2001 to February 2002) confirmed poor participation rates and difficulties keeping up with data entry, resulting in much missing data. Overall, 39.3 percent of 4285 patients who were eligible for the registry consented to full chart abstraction. Many barriers to obtaining consent were identified (Table 1).

PHASE 2

Because of the poor participation rate during phase 1 and the coordinators' heavy workload, a number

of steps were taken to streamline processes and to decrease the workload. The number of data elements collected in the full chart abstraction was reduced, and the six-month follow-up interview was substantially shortened. A two-day national training workshop, held at the beginning of phase 2, included instruction on strategies to increase the consent rate.

The results of phase 2 of the registry project are shown in Table 1. Overall, after seven months of data collection, 50.6 percent of 2823 eligible patients were enrolled, a moderate improvement over phase 1. Barriers to the consent process that were identified in phase 1 persisted; consent could not be sought in the case of patients who died before they could be approached for participation, were not admitted or left the hospital before a coordinator could meet with them, or were away from their hospital bed (e.g., while undergoing diagnostic tests or rehabilitative therapy) when the coordinator went to interview them. Improvements were noted in these outcomes in phase 2. However, considerable variation among the hospitals in overall participation rates was observed in both phases 1 and 2 (Fig. 1).

COMPARISON OF PARTICIPATING AND NONPARTICIPATING PATIENTS

Although improvements were noted over time, the overall consent rate during both phases was moderate, resulting in a data base that was not representative of the overall population of patients with stroke at each hospital. Table 2 compares the characteristics of the patients who participated in either phase with those who did not participate. In general, patients who participated in the registry were younger, more likely to be alert at admission, and more likely to be alive at discharge, and their preferred language was more likely to be English or French. The in-hospital mortality rates differed significantly between patients who were enrolled (6.9 percent) and those who were not enrolled (21.7 percent) (relative risk, 3.13; 95 percent confidence interval, 2.65 to 3.70; $P < 0.001$). Selection biases in outcomes were seen at both hospitals with high participation rates and those with low participation rates (Fig. 2 and Table 3). Of the 50.6 percent of patients who did agree to participate during phase 2, 94.0 percent agreed to participate in all four subcomponents of the registry. Of the 6.0 percent who agreed to some but not all subcomponents, 3.5 percent (50 patients)

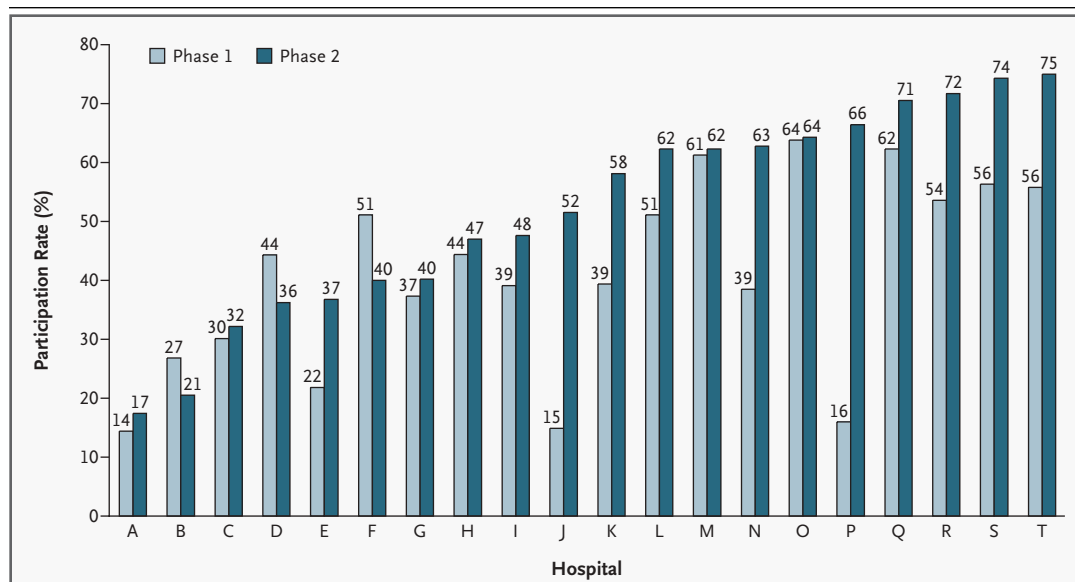


Figure 1. Overall Participation Rates during Phases 1 and 2 of the Registry of the Canadian Stroke Network, According to Hospital.

The hospitals (denoted by letter code) are shown along the horizontal axis, sorted by their overall participation rate in phase 2, from the lowest rate (Hospital A) to the highest rate (Hospital T). The participation rate is the percentage of patients who consented to participate relative to the total number of patients who were eligible for the registry (including both those who could and those who could not be approached).

Table 2. Characteristics of the Patients Who Consented to Participate and Those Who Did Not Participate in the Registry of the Canadian Stroke Network.

Variable	Phase 1			Phase 2		
	Participating	Not Participating	P Value	Participating	Not Participating	P Value
Median age (yr)	69	72	<0.001	72	73	0.09
Male sex (%)	53.3	51.1	0.17	54.7	48.7	0.002
Alive at discharge (%)	94.3	84.3	<0.001	93.6	84.4	<0.001
Level of consciousness on admission (%)						
Alert	78.5	65.7	<0.001	88.1	79.9	<0.001
Confused*	7.7	12.6		—	—	
Drowsy	4.3	8.2		9.1	13.0	
Unconscious	9.5	13.5		2.8	7.1	
Race or ethnic group (%)						
Asian	4.0	15.7	<0.001	2.4	8.1	<0.001
White	91.3	77.3		85.0	63.2	
Other	4.7	7.0		12.6	28.7	
Preferred language (%)						
English	59.9	55.9	0.002	75.5	65.0	<0.001
French	30.3	28.4		14.5	10.1	
Other	9.8	15.7		6.1	12.1	
Unable to determine				3.9	12.8	
Median length of stay (days)	10	3	<0.001	11	9	<0.001

* The “confused” subcategory was eliminated in phase 2 of the registry.

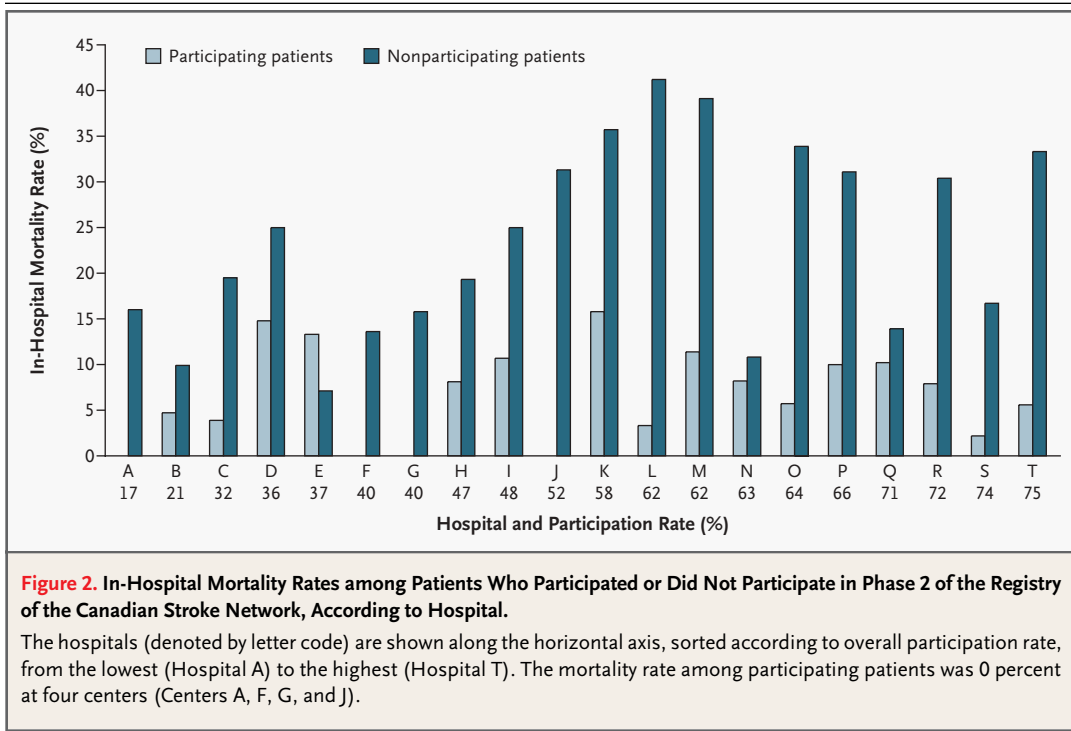
refused the follow-up interview, 3.0 percent (43 patients) did not consent to linkage to administrative data, and 2.7 percent (38 patients) did not consent to the sharing of data with commercial organizations.

An audit performed toward the end of phase 2 revealed that the nurse coordinators spent a median of 40 minutes (including time spent arranging interviews, answering stroke-related questions, and obtaining consent) with each patient or surrogate. A median of two visits per patient were necessary to arrange an interview in order to seek consent. Nurse coordinators spent a median of 15 minutes abstracting chart data for the minimal data set and 40 minutes abstracting additional data for the full clinical data set.

Approximately \$2 million (Canadian dollars) was spent on the registry from June 2001 through May 2003. Calculating the amount of time spent obtaining consent (approximately one third of each nurse coordinator’s time), we estimate that approximately \$500,000 (Canadian dollars) of the registry’s budget was spent on consent-related issues alone.

DISCUSSION

The Registry of the Canadian Stroke Network represented an opportunity for the Canadian neurologic community to develop a data base that could potentially improve the quality of care for patients with stroke in Canada. The key step was abstraction of the records of the in-hospital course for each patient. However, despite a concerted effort to obtain written consent for participation, the overall participation rate never exceeded half of the eligible patients. Patients who could be enrolled in the registry were different from those who could not — a phenomenon that has been termed “authorization bias.”⁷ The registry data will be useful for some research projects, but because of the selection biases introduced by the consent process, the full potential of the registry will not be realized. The data are similar to those in clinical-trial data bases, in that certain observational inferences can be made about risk factors and outcomes, but the extent to which the findings can be generalized to the overall population of patients with stroke is uncertain. In



addition, the usefulness of the data for the monitoring and planning of health care delivery is limited.

Approximately one of every six eligible patients who could be approached refused to participate. However, a number of other barriers were observed that cumulatively had a large effect on the overall participation rate. Nurse coordinators understandably reported having difficulty approaching the families of patients who were critically ill or who had died, while the family members were in the midst of the grieving process. Consequently, the in-hospital mortality rate among the enrolled patients was only 6.9 percent, which is much lower than the true mortality rate among all patients with stroke in Canada.¹⁴ In many cases, patients could neither give nor refuse to give consent because they were cognitively impaired and because a surrogate decision maker was not available. Many of the potentially eligible patients could not be approached for consent, even though most of the participating hospitals had a dedicated, full-time nurse coordinator whose primary responsibility was to approach patients and collect data for the registry.

The wide variation in participation rates across centers suggests that the overall consent rate might have improved at some centers with additional training and experience. However, large selection biases

in outcomes were still observed even after the analyses were restricted to the hospitals with the highest participation rates, suggesting that additional attempts to improve the participation rate at other hospitals would probably not adequately solve the selection-bias problem. In the light of these considerations, the registry's executive committee decided to end phase 2 of the registry project after seven months. The committee believed that proceeding with a consent-based registry was futile, since the sample would never be useful for monitoring the delivery of stroke care at each hospital, which was a major objective of the project.

We believe that a reasonable alternative way of obtaining data from a representative sample of patients with stroke is to collect de-identified data from all patients' medical records without obtaining consent but with appropriate confidentiality safeguards in place. This position has been supported by others, who have argued that in a publicly funded health care system, patients have a social obligation to permit their de-identified health care data to be used without their consent so that the health care system can be monitored and improved for the benefit of all.^{5,7} However, we believe that for certain subcomponents of a registry (e.g., direct patient interviews and collection of biologic samples),

consent should be obtained, and we recognize that in our registry project the request for a follow-up interview may have limited the achievable consent rate. Furthermore, we suggest that the decision to grant waivers of informed consent for clinical registries must be made carefully and should be based on the judgment of an independent research ethics board.

For phase 3 of the registry project, we plan to collect de-identified data from patients' medical records without obtaining consent but also with-

out conducting follow-up interviews with the patients. Although some may question whether it is appropriate to obtain access to patients' charts without first seeking permission, one needs to balance this consideration against the potential for harm if patients are given misleading prognostic information on the basis of data from a consent-based registry or if the frequency and reasons for adverse events in representative samples of patients with stroke are not tracked in multiple institutions.¹⁵⁻¹⁷ The Personal Information Protection and Electronic Documents Act, which took full effect on January 1, 2004, in Canada, allows waivers of informed consent for scholarly research when it is impracticable to obtain consent. The Canadian Institutes of Health Research has offered guidance on factors to be considered in determining the practicability of obtaining informed consent (Table 4).¹³

This study has important limitations. First, we cannot be certain about the extent to which our experience with an informed-consent process can be generalized to other clinical registries. However, published data suggest that requirements regarding informed consent have led to selection biases in retrospective studies based on chart review^{12,18} and to decreased enrollment in cancer registries.⁸ Second, consent-based registries might be feasible in the case of chronic conditions for which, in comparison with cases of acute stroke, there is more time to contact patients, the prevalence is lower, and patients are less sick or cognitively impaired. Third, we could not systematically collect data pertaining to the reasons some patients did not wish to participate in the registry. One possible reason is that patients were focused on trying to recover from an acutely stressful and debilitating event and did not perceive any benefits of participating in an observational research study.

In summary, we found significant sampling biases in our attempt to obtain informed consent from patients with stroke in Canada. Our findings highlight the importance of developing privacy legislation and policies allowing waivers of informed consent for minimal-risk observational research on grounds of impracticability. Determining the right balance between the need for both individual privacy in a society and the benefits gained from a limited loss of privacy in observational studies will pose a difficult challenge in the years ahead. We hope that our experiences will assist legislators and research ethics boards in identifying some of the circumstances in which it may be impracticable to obtain

Table 3. In-Hospital Mortality Rates among Patients Who Participated and Those Who Did Not Participate during Phase 2 of the Registry Project, According to the Hospitals' Participation Rank.

Hospital and Participation Rank*	Mean Participation Rate	Mortality Rate		P Value
		Participating Patients	Nonparticipating Patients	
		percent of patients		
P-T (top 5 hospitals)	71.6	7.2	25.1	0.006
K-T (top 10 hospitals)	66.8	8.0	28.6	<0.001
A-T (all hospitals)	51.9	6.8	23.4	<0.001

* The hospitals are denoted by letter codes (which correspond to those shown in Fig. 1). The hospitals were ranked according to their overall rate of patient participation during phase 2 and were grouped into the categories shown.

Table 4. Factors Affecting the Practicability of Obtaining Informed Consent from Research Subjects.*

Size of the population to be studied
Proportion of subjects likely to have relocated or died since the personal information was originally collected
Risk of introducing bias into the research, thereby affecting the validity of the results and the extent to which they can be generalized
Risk of creating additional threats to privacy by having to link otherwise de-identified data to nominal identifiers in order to contact patients or their surrogates to obtain consent
Risk of inflicting psychological, social, or other harm by contacting patients with particular conditions or families in certain circumstances
Difficulty of contacting patients or their surrogates directly when there is no existing or continuing relationship with them
Difficulty of contacting patients or their surrogates through public means, such as advertisements and notices
Requirements for additional financial, material, human, organizational, and other resources in order to obtain consent, imposing an undue hardship on the research team or organization

* The information is based on recommendations from the Canadian Institutes of Health Research.¹³

informed consent for participation in clinical registries. Clinical registries play a vital role in disease surveillance, quality improvement, and patient safety and must continue to do so if patients are going to receive the best possible care.

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APPENDIX

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