EXPERIENCES AND PROBLEMS IN DEVELOPING A SAMPLING METHODOLOGY FOR A SURVEY OF PATIENTS WITH MULTIPLE SCLEROSIS AND RELATED DISORDERS

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INTRODUCTION

The purpose of today's paper is to discuss some of the major problems in surveying the incidence, prevalence, and costs of multiple sclerosis. The findings for this paper come from the data gathered to date in the pilot study.

Let me begin by describing the nature of the disease and some of the problems it presents to the epidemiological researcher. A working medical definition of multiple sclerosis is that it is a demyelinating disease of the central nervous system characterized by periods of exacerbations and remissions. In layman's terms, the myelin, or protective fatty coating, of the nerve sheath breaks down. This breakdown, or lesion, may cause a variety of symptoms, depending on where in the nervous system it occurs. Periods in which the symptoms are extant are called exacerbations. As the myelin is rebuilt or scars over, the symptoms will partially or completely disappear. The patient enters a symptom-free period called remission.

Sometimes, the symptoms are so mild that they go virtually unnoticed or unattended, making MS very difficult to diagnose. The recurrent pattern of exacerbations and remissions contributes to the clinical diagnosis of MS.

The difficulty of diagnosis presents us with our first set of problems. Onset of the first symptoms and the ultimate diagnosis may be years apart. Physicians may have suspected cases which they will not confirm until after the patient has several exacerbations.

Even if a diagnosis of MS is confirmed, physicians sometimes withhold this information from the patient and/or members of the family. Therefore, any attempt at deriving information from these uninformed patients must deal with the thorny problem of gathering information on multiple sclerosis without mentioning the disease by name or even hinting that there may be a single disease underlying their symptoms.

As if these problems were not enough, the research is further complicated by the similarity between MS symptoms and other disorders of the central nervous system. "The great imitator," as MS has been called, can be mistakenly diagnosed as one of several other demyelinating diseases. Not all physicians are equally able by training to make these distinctions. Neurologists and physicians in related specialties generally are the most accurate diagnosticians. They are less likely than other physicians to see patients experiencing their earliest symptoms. If we are to determine accurately incidence and prevalence from physicians' records, we are faced with the problem of how most efficiently to sample the medical specialties.

OVERALL RESEARCH DESIGN

The research design we have chosen is similar to the one we successfully employed several years ago with a study of hemophilia. It is adapted here to take account of those problems which are unique to the study of MS. We have two distinct sources of information:

- The health care provider sample, and
- The patient sample.

The health care provider sample is intended to yield an unduplicated count of all the MS patients seen during a given period of time. These data will serve as the major inputs into the incidence and prevalence rates. They will also constitute the list of names from which we will draw the patient sample. The personal interviews with MS patients or their families will focus on medical expenses associated with the disease and the impact of the disease on employment pat-terns and lifestyle. These data will be used in the analysis of the cost of the disease. In the interest of time, only the health care provider sample will be discussed.

Our procedures for this sample begin by requesting:

- An institution or physician to report any MS patient seen since January 1, 1970. Both confirmed and suspected cases will be reported. By studying a time period extending back five years we intend that enough time will pass for patients to present a pattern of exacerbations and remissions from which a more clear-cut diagnosis is possible.
- All health care providers to identify MS patients by first name and last initial, thus maintaining the confidentiality of the provider/patient relationship. In addition, we are requesting certain basic demographic data such as date of birth, sex and race.

The patient identification information then will be computer-matched to eliminate duplicate mentions of the same individual by more than one source. From this unduplicated list, a sample of patients will be drawn. The sources identifying patients in that sample will then be asked to provide us with full name and address of those individuals, being urged, first, to obtain permission for release of this information to us.

HEALTH CARE PROVIDER DESIGN

In regard to the health care provider sample, the purpose of the pilot study is two-fold:

- To test the case finding techniques just described, and
- To compare alternative methods of contact with health care providers, particularly physicians, to determine which is the most cost-efficient means of obtaining cooperation.

Our pilot study is being conducted in ten counties, with matching sets of five control and five experimental counties. Each set is composed of two rural Alabama counties, two small SMSA Illinois counties, and one larger SMSA Pennsylvania county.

Four health care provider universes have been delineated: physicians, hospitals, neurological out-patient clinics, and nursing homes. All four universes are being sampled and surveyed in half of the ten counties.

Let's look first at hospitals, neurological out-patient clinics and nursing homes. OMB clearance for relevant documents was obtained in time to begin field work at the end of June.

All short-term hospitals, neurological out-patient clinics and nursing homes in the control counties were drawn into the sample, yielding 20 hospitals, one outpatient clinic, and 44 nursing homes.

Hospitals and Neurological Out-Patient Clinics (Procedures)

Hospitals were contacted first by mail and then by telephone and asked to provide the basic demographic information about patients hospitalized on or after January 1, 1970 for whom a primary or secondary diagnosis of MS had been recorded. Hospitals were offered assistance or reimbursement for their personnel in order to obtain this information. The one hospital with an out-patient neurological clinic is keeping a prospective log recording visits by patients with a primary or secondary diagnosis of MS.

Nursing Homes (Procedures)

Nursing homes were sent a letter of introduction, followed by a phone call, in which they were asked to provide comparable information about MS patients in their care since January 1, 1970.

Hospitals (Results)

Of the 20 hospitals in our sample, one was declared ineligible (dental patients only). We have obtained cooperation from 17 of the 19 remaining hospitals. Three have had no MS patients in the time period under consideration. Completed records have been received from two, and the remaining twelve are still in the process of conducting a search of their files. (See Table A)

Nursing Homes (Results)

Of the 44 nursing homes drawn into the sample, one has gone out of business, three have refused to cooperate, and two have not yet decided whether they will comply. Twenty-one of the remaining 38 nursing homes indicated that they have had no MS patients during the time period under discussion, while 17 had such patients and provided us with the information requested. (See Table B)

Physicians (Procedures)

Now, let's turn to our procedures and experiences with physicians.

Based on our understanding of the disease and of the probability that physicians in any given specialty would have contact with MS patients, physicians were divided into two strata. The first, or the certainty stratum, consists of all neurologists, neurosurgeons, and ophthalmologists, in the pilot counties, whether medical or osteopathic doctors. This stratum provides 108 physicians.

All remaining physicians in active practice are in the second, or non-certainty, stratum. These physicians were aggregated into six groups, and were sampled at varying rates based on the anticipated likelihood of their seeing MS cases. The groupings and the rates were delineated in order to observe "treater"/"nontreater" status and cooperation rates by area of specialization. (We have, incidentally, used the terms "treater" and "non-treater" to indicate physicians who have or who have not seen MS patients for any reason, whether in consultation for an MS-related symptom or not. In the strict sense there is no treatment for MS.) The six non-certainty sample groups are:

Physical Medicine	3
Internal Medicine	36
General Practice	36
Family Practice	36
Other Strata "1" and "2"	
Remainder expected treater	
specialists	23
Remainder low expected treater	
specialists	23

for a total of 150 physicians.

The total number of physicians selected is, therefore, 258. Their distribution by control/experimental county, certainty/non-certainty designation, and population density is detailed in Table C.

Now let us consider our findings to date. Actual field efforts were begun on June 30, when the first mailings were received by physicians. Thus field efforts are still on-going and the findings reported here represent six weeks, or less than half of our projected time in the field. Moreover, these results derive from relatively small samples.

IDENTIFICATION OF "TREATERS"

As expected, the results of the physician sample show that there are more "treaters" among those in the certainty sample than in the non-certainty group. Seventyone percent of the certainty sample treat as opposed to 52% in the non-certainty group. (See Table D)

Data for the certainty sample reveal approximately 81% of the neurologists and neurosurgeons who have responded to date are treaters, whereas only 66% of the ophthalmologists say they treat.

Essentially our expectations concerning the non-certainty sample were confirmed. The data for the six specialty groups in the non-certainty sample show a range of "treater" rates from 100%-17%. The 100% "treater" rate is based on the three specialists in physical medicine in our sample. The 17% is based on the "other 2" stratum. (See Table D)

The general practitioners turned out to be the most interesting group. Even though GP's as a group yield a "treater" rate of just 30%, those GP's in the southern, rural point (Alabama) had a "treater" rate of 38%, compared to 25% in the two urban areas combined.

While epidemiologists believe that MS may be more prevalent in the northern latitudes, our finding of a higher treater rate among Southern GP's may reflect the relative absence of neurological specialists in the rural South, and this suggests that in the national study differential sampling rates should be used within the GP group based on degree of urbanization. (See Table E)

The preceding data suggest the following modifications for the national survey:

- Specialists in physical medicine be considered part of the certainty sample.
- 2. Ophthalmologists be moved to the noncertainty sample.
- 3. All specialists in internal medicine, all family practitioners, and <u>rural</u> general practitioners each be <u>sampled</u> at the same rate.
- 4. Other specialists and the <u>urban</u> general practitioners should be sampled at a lower rate than the former non-certainty group.

EXPERIMENTAL METHODOLOGY AND RESULTS

In order to determine the most effective and cost-efficient way to approach physicians, we varied procedures to obtain cooperation and patient information both between and within the certainty and non-certainty strata as well as between and within control and experimental counties. These variations are detailed in Exhibits 1 and 2. The approach to the certainty strata physicians is outlined in Exhibit 1. In essence, the procedures provide for contact with all certainty sample physicians by both mail and telephone. Contact with non-certainty physicians, as outlined in Exhibit 2, is by mail only until it has been established that those in this stratum are treaters, when mail/telephone procedures to obtain patient information are instituted. Physicians in the experimental counties are offered assistance or reimbursement for search of their records at an earlier point in our contact with them; those in the control counties are made that offer only if it appears necessary to gain cooperation.

Our findings with the certainty sample, to date, indicate an overall cooperation rate of 79%. Physicians receiving a letter of announcement followed by a telephone call (that is, Condition A) show no difference in cooperation from physicians in Conditions B and C, where request for cooperation was initiated by mail. Moreover, offer of assistance or reimbursement in the initial mail contact does not produce a higher cooperation rate. (See Table F) Our findings with physicians in the noncertainty stratum to date show a 50% first stage cooperation rate, significantly lower at the 95% confidence level than the 79% completion rate achieved with physicians in the certainty stratum. We believe that this difference is not as much reflective of differences in our approach to this stratum as it is of the respondent's interest in the disease being studied. As with the certainty sample, the experimental conditions did not affect cooperation rates. (See Table G)

The second stage completion rate -- that is, the proportion of physicians we identify as treaters who submit completed logs -- will, of course, constitute the correct test of the different experimental conditions imposed on this stratum. This rate has, however, not been computed. The time delay inherent in first establishing treater status puts non-certainty physicians at least two weeks behind the others. Returns to date, therefore, do not warrant such computation, nor any comment on whether or not the offer of assistance or reimbursement has different implications for the two strata.

Our experiences in attempting to establish treater/non-treater status with noncertainty physicians in the pilot phase suggest that our methodology for the national study should be revised to provide for telephone contact with at least a sub-sample of non-cooperators in this stratum.

On the other hand, while we are confining this report to the health care provider sample, we feel we should mention that an initial analysis of the data collected from patients indicates that most have consulted at least five physicians during the time period under consideration and most have seen one or more specialists included in our certainty stratum. Thus, there appears to be a strong possibility that completion rates among physicians may be less critical than we initially anticipated, since, if we "lose" a patient by the non-cooperation of one physician, we have a strong possibility of that patient's still being mentioned by another physician.

In conclusion, we feel that, to date, our pilot methodology demonstrates that:

- We have devised a sampling plan which will enable us to estimate, with known probability of error, the number of MS patients in the United States

- Physicians will cooperate with us in providing the information required to make these estimates
- Physicians should be divided into certainty and non-certainty strata, with different sampling rates applied by specialty and urbanization to the non-certainty stratum
- The certainty stratum should consist of neurologists, neurosurgeons and specialists in physical medicine. Ophthalmologists should be moved to the non-certainty stratum.

TABLE A: HOSPITAL AND NEUROLOGICAL OUT-PATIENT CLINIC SAMPLE	
Total hospitals in sample Ineligible Base	20 1 19
Cooperators Non-cooperators	17 2
Cooperation rate	89%
Logs received to date	2
Have neurological out-patient clinic	1
Cooperators	1

TABLE B: NURSING HOME SAMPLE

Total nursing homes in sample	44
No longer in business	1
Base	43
Cooperators	38
Non-cooperators	3
Undecided	2
Cooperation rate	888
Have had MS patients	17
No MS patients	21
Patient rate	40%

TABLE C:	NUMBER	OF	PHYSICIANS	IN	PILOT	STUDY

	Control	Counties	Experime Count:	ental ies
	Certainty	Non- certainty	Certainty	Non- certainty
Alabama (rural)	1	14		11
Illinois (small SMSA)	19	33	30	29
Pennsylvania (large SMSA)	29	33	29	30
Total	49	80	59	70

TABLE D: "TREATER" STATUS BY MEDICAL SPECIALTY

	Certa	aint	y Sti	atum		Non-Certaint				y Stratum			
	Ophthalmologists	Neurologists	Neurosurgeons	Total Certainty Sample	Physical Medicine		General Practitioners		Internal Medicine	Family Practice	Other "1"	Other "2"	Total Non- Certainty Sample
						Rural	<u>Urban</u>	Total					
Number of "treaters"	35	17	8	60	3	3	3	6	12	13	7	1	42
Number of "non-treaters"	18	4	2	24	_	5	9	14	4	5	5	5	33
Total physicians responding	53	21	10	84	3	8	12	20	16	18	12	6	75
Percent treating	66%	81%	80%	71%	100%	38%	25%	30%	75%	72%	58%	17%	56%

TABLE E: "TREATER" STATUS BY DEGREE OF URBANIZATION

		Rural South Alabama	Urban Illinois	Urban Penńsylvania	Total Sample
T	Number of "treaters"	8	50	44	102
t	Number of "non-treaters"	8	19	30	57
	Total physicians responding	16	69	74	159
	Percent treating	50%	72%	60%	64%

TABLE	F:	CERTAINTY	SAMPLE	RESULTS

	Condition A Introductory Letter Followed by Phone Call	Condition B Explanatory Letter with Offer of Assistance/ Reimbursement	Condition C Explanatory Letter, No Offer of Assistance/ Reimbursement	Total Sample
Physician is a treater	19	12	29	60
Physician is a non-treater	4	9	11	24
Number answering	23	21	40	84
Treater rate	83%	57%	72%	71%
Non-cooperators	6	8	8	20
Other reasons	1	-	1	2
Total Sample	30	29	49	106
Cooperation rate	75%	72%	82%	79%

TABLE G: FIRST STAGE RESULTS NON-CERTAINTY SAMPLE BY COLLAPSED STRATA

	Condition D			Condit	ͲΟͲΔΤ.		
	PM/GP/IM/FP*	°1′°2**	Total	PM/GP/IM/FP*	0 ₁ /0 ₂ **	Total	SAMPLE
		5					
Physician is a treater	16	5	21	18	3	21	42
Physician is a							
non-treater	12	3	15	11	7	18	33
Number answering	28	8	36	29	10	39	75
Treater rate	57%	62%	58%	62%	30%	54%	56%
Non-cooperators	22	9	31	28	12	40	71
Other reasons		-	2				, 1
· · · ·	3	-	3	L	-	L _	4
Total sample	53	17	70	58	22	80	15
Cooperation rate	53%	47%	51%	50%	45%	49%	50%

*Physical medicine, general practice, internal medicine, family practice. **<u>Other 1</u>, including: hand surgery, obstetrics and gynecology, occupational medicine, orthopedic surgery, otolaryngology, psychiatry, rheumatology and urology. <u>Other 2</u>, including: allergy, abdominal surgery, anesthesiology, cardiovascular disease, child psychiatry, clinical pathology, dermatology, emergency medicine, endocrinology, gastroenterology, geriatrics, general surgery, hemotology, infectious disease, nuclear medicine, pediatrics, pathology, pulmonary diseases, radiology, thorasic surgery, are other specialties.

EXHIBIT 1

Certainty Sample: Experimental Methodologies for Obtaining Physician Cooperation

Condition A - Experimental Counties

- Letter announcing a phone call to explain the study
- Telephone call to secure cooperation, with promise of assistance or reimbursement for records search
- Mailing of patient inquiry logs to cooperating treaters
- Remail in two weeks if logs not received

Condition B - Experimental Counties

- Logs mailed with letter offering assistance/reimbursement
- Telephone call after two weeks if
- logs not returned
- Remail, if necessary, to cooperating treaters
- Second remail in two weeks if logs not received

Condition C - Control Counties

- Logs mailed with letter which makes no reference to assistance/ reimbursement
- Telephone call after two weeks if logs not returned. Assistance/ reimbursement offered if necessary to obtain cooperation
- Remail, if necessary, to cooperating treaters
- Second remail in two weeks if logs not received

EXHIBIT 2

Non-Certainty Sample: Experimental Methodologies for Assessing Treater Status and Obtaining Physician Cooperation

Experimental and Control Counties

- 1/2 of sample mailed letter and selfenumerative questionnaire asking "Did you treat"; 1/2 mailed same letter and self-enumerative questionnaire asking "How many did you treat"
- Remail of initial forms to non-respondents after two weeks
- Second remail of initial forms to non-respondents two weeks after first remail

Upon identification as a treater

- Experimental Counties Same procedures as Condition A, Certainty Sample
- Control Counties Same procedures as Condition C, Certainty Sample