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THE INCIDENCE OF GUILLAIN-BARRÉ SYNDROME
IN ONTARIO AND QUÉBEC

1983 - 1989

USING HOSPITAL-SERVICE DATABASES

by

MARK EDWARD MCLEAN

Thesis submitted to
the School of Graduate Studies and Research
in partial fulfilment of the requirements for the
M.Sc. degree in Epidemiology

University of Ottawa



Mark Edward McLean, Ottawa, Canada, 1992



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ABSTRACT

Background-Guillain-Barré syndrome (GBS) is of public health interest in Canada, as well as the rest of North America, for two main reasons. It is occasionally a vaccine-associated adverse event and is also a differential diagnosis of poliomyelitis.

Ontario hospitals have fully participated in the Hospital Medical Records Institute (HMRI) database since 1978, and since 1981 Québec hospitals have fully contributed to the Med-Écho database. The combined population of these two provinces is approximately 15.5 million persons (1986 census). The availability of hospital admission records for such a large population creates a unique opportunity to study epidemiological aspects of such a rare condition as GBS.

Objectives- 1) To ascertain the incidence of GBS in the Canadian provinces of Ontario and Québec for the years 1983-1989, inclusive. 2) To demonstrate the feasibility of measuring the incidence of GBS through internal record linkage of Canadian hospital-service data.

Design-Internal record linkage study of hospital service records.

Methods-Records containing the ICD-9 code for GBS, or one of the diagnoses most likely to harbour misclassified GBS cases were extracted from both databases. Internal record linkage involving three algorithms programmed in SAS was performed, and incident admissions of GBS were identified. Crude and age-and-sex-standardized mean

annual incidences of GBS were calculated using 1986 provincial census figures as denominators.

Photocopies of a stratified random sample of incident admission charts from each province were examined by two neurologists to detect false positive misclassifications of GBS. Cross linkage of data to the other province's data to detect out-migration of cases, as well as comparison of mortality figures in the Canadian Mortality Database (CMDB) and the hospital service data, and examination of records containing three ICD-9 codes judged to be potential false negative misclassification diagnoses, were all used to investigate the size of the problem of false negative misclassification of GBS.

Results-1,302 and 1,031 records representing GBS incident admissions in Ontario and Québec, respectively, were identified through the record-linkage procedure. The mean annual GBS incidence after age-and-sex-standardization to the 1986 Canadian census population was 2.02 per 100,000 person-years in Ontario and 2.30 in Quebec. The incidence was higher in older age-strata in both provinces (70-80 years), and was higher in males (M:F=1.1). The only apparent geographic influence on the incidence of GBS was that due to migration of cases outside their home province.

Reviews of charts of incident admissions of GBS cases reveal that 26.2%-32.6% of Ontario cases and 21.0%-24.0% of Quebec cases may be false positive diagnoses. No possible false negative cases were identified through chart review. Cross linkage of records belonging to the other province with records from the other dataset revealed 0.5% false negative misclassification of Ontario incident admissions and 1.8% for Quebec. Mortality figures obtained from CMDB were in both provinces less than those

obtained in the hospital service data, indicating that it is unlikely a significant number of GBS cases die before reaching hospital.

Conclusions- 1) It is possible to internally link records in the HMRI and Med-Écho databases into personal histories (cases) of a condition. 2) The GBS incidence, age and sex standardized to the 1986 Canadian census population, obtained through record linkage of hospital service data is 2.02/100,000 person-years in Ontario and 2.30/100,000 person-years in Québec. 3) The high percentage of false positive misclassifications discovered on examination of incident admissions raises concern about the validity of HMRI and Med-Écho data for epidemiological purposes. Verification of diagnoses, through more extensive chart reviews than used in this study, may be necessary for study of some conditions using these databases.

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Although one name appears in the position of author of this thesis, this work would not have been possible without the assistance and support of a number of individuals and institutions.

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The Hospital Medical Records Institute and the 'Ministère de la santé et des services sociaux du Québec' (MSSS) not only provided data for this study, but also acted as liaison between myself and hospitals that had GBS cases for patient-chart reviews. Shelagh Maloney and Christine Proietti at HMRI collected the chart reviews from Ontario hospitals, while on the Québec side of the study, Jeanne Bourdages at the MSSS paved the way for my communications with Québec institutions. Their assistance is gratefully acknowledged.

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Finally, none of these aforementioned persons or institutions can be held responsible for any errors or omissions in this thesis. These are solely the responsibility of the author.

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INTRODUCTION AND LITERATURE REVIEW

Introduction

The condition described by Graves (1843),¹ Landry (1859),² and Guillain, Barré, and Strohl (1916)³ falls under the present day diagnostic category of acute inflammatory demyelinating polyneuropathy⁴. In North America, this entity is commonly referred to by the eponym 'Guillain-Barré syndrome' (GBS), and will be referred to as such in this thesis. A listing of the other common English language designations for this condition is found in Appendix A.

GBS is characterized by (1) relatively symmetric weakness evolving over one to several weeks in the hips and the legs, later the arms, frequently involving the face and respiratory muscles, and less often eye movements; (2) paraesthesias in the toes and fingertips that advance proximally; (3) eventual loss of deep tendon reflexes; (4) spontaneous gradual recovery over several weeks to months; and (5) elevated spinal fluid protein concentration with few white cells in most cases. In addition, there are electrophysiologic abnormalities - particularly conduction block and delayed distal latencies.⁵ The cranial nerves are affected in 25% of cases, and respiratory failure necessitating assisted ventilation occurs in 20%.⁴ Autonomic involvement can cause fatal cardiac dysrhythmias. The illness can occur at any age.

GBS is commonly preceded by a viral or other infection. It has been reported in association with many infectious agents as well as other immunologic stimuli. Those implicated include viruses (herpesviruses,⁶ adenoviruses,⁷ Coxsackie A9⁸), bacteria

(Campylobacter jejuni,⁹ Lyme disease¹⁰), mycoplasmae,¹¹ live-attenuated viral vaccines (OPV),¹² and killed vaccines (influenza A).¹³

Modern theories of the etiology of this condition include: 1) direct infection by wild or attenuated viruses; 2) direct auto-sensitization by myelin antigens in vaccines; and 3) indirect or cross-reactive sensitization by viral or bacterial antigenic determinants (epitopes) having sufficient chemical homology with amino acid sequences in central or peripheral myelin antigens to be recognized as immunological homologies.⁸

The average length of hospitalization for GBS patients has been reported to be 70-75 days,⁴ and the mortality varies from 2-20%,⁴ depending on the setting. Of survivors, 80-90% are ambulatory by 3-6 months, although many require several months to a year or longer for final recovery.

Historical Background

In 1916, Guillain, Barré and Strohl³ described two cases of an acute paralytic syndrome that involved rapidly ascending paralysis with greater involvement of distal than proximal muscles, loss of deep tendon reflexes with preservation of cutaneous reflexes, paraesthesias with only slight disturbances in sensation, and muscle tenderness. Both recovered quickly, suggesting that this condition was both benign and reversible, setting it apart from Landry's paralysis,² a condition that at that time was considered far more serious and disabling and was frequently fatal. Over the next 30 years, numerous reports of various types of polyradiculoneuropathies were grouped under one or the other syndrome, or both.

The discovery by Guillain and Barré that the cerebrospinal fluid (CSF) had increased protein content without an increase in white cell count resulted in the eponym for this condition used today.¹⁴ This distinction, called albuminocytologic dissociation, remains an important diagnostic criterion of GBS. The specificity of the association of albuminocytologic dissociation with GBS has led to inclusion of variant clinical presentations such as ophthalmoplegia, ataxia and areflexia (Miller-Fisher syndrome); sensory loss and areflexia; polyneuritis cranialis; pure pandysautonomia; and sometimes, chronic acquired demyelinating neuropathy.¹⁵

Estimates of the incidence of GBS occurring in the U.S, Australia and various parts of Europe have usually been between 0.6-2.4/100,000/year.¹⁶⁻²³ Data from developing countries is lacking. Apart from differences in age distribution of reference populations, no conclusive ethnic or geographic influence on GBS incidence has ever been observed. GBS occurs at all ages, some studies showing an increase in age-specific incidence with age.^{24,25} Sex distribution in most studies offering this statistic have shown a male predominance.^{13,20,24,26-28}

Most attempts to estimate the incidence of GBS have been performed by examination of case records at referral centre hospitals. Lesser et al²⁸ reviewed medical records and death certificates of all Olmsted county residents presenting to the Mayo Clinic between 1935 and 1968, and having a diagnosis synonymous with GBS. They determined a mean annual incidence of 1.6 per 100,000, based on 29 cases over 34 years. A replication by Kennedy et al,²⁰ for the same population eight years later, found the incidence to be 1.7 per 100,000. Hogg et al¹⁹ reviewed records from all local hospitals serving San Joaquin county, as well as all outpatient records from neurologists caring for

the county's population, for the period 1972-76. They identified 18 cases of GBS, corresponding to an average annual incidence of 1.23 per 100,000. In Norway, Larsen et al²² examined patient files of the department of Neurology at the University Hospital in Bergen for the period 1957-1982 and found an average annual incidence for GBS of 1.2 per 100,000.

These studies all suffer from problems common to the case series method of estimating the incidence of a condition. The denominator for this type of study is usually defined as the population that the referral centre services. If this is well defined (i.e. - few persons from the region seek health care out of the area, and few people from outside the area seek health care inside the region of interest) this method can result in accurate measurement of the incidence for the population in question. However, in the studies described, the populations are small, and therefore subject to significant fluctuations in incidence with only small changes in the number of cases.

The 1976 U.S. Swine Influenza Vaccination Controversy

In the National Influenza Immunization Program of the United States in 1976, 45 million people over the age of 18 received 'swine influenza' vaccine (A/New Jersey/76) between October and December of that year. The program was abruptly ended when it was recognized that more than 500 cases of GBS occurred among the vaccinees, of which 25 died.²⁹ A surveillance system which had been set up to monitor the occurrence of GBS in vaccinees, provided the source of evidence used to halt the immunization program. These data implicated the vaccine as the cause of this GBS 'outbreak'.²⁹⁻³¹

The epidemiological evaluation of this incident remains controversial because the surveillance system was set up on an emergency basis and only began collecting cases 2 months after the immunization campaign had begun. Moreover, the true incidence of GBS in the general population had not been previously determined, making it difficult to compare reported cases in the immunized to the non-immunized population, a methodology much criticized for its strong reporting bias secondary to the publicity surrounding the event.³²⁻³⁴

Poser³⁵ has pointed out that despite the controversy surrounding the 1976 Swine Influenza vaccination campaign, the existence of post-vaccinial GBS or other neurological complications cannot be entirely refuted. He states strongly that the main lesson to be learned from the swine flu incident is that surveillance systems are inadequate to collect data on GBS and other neurological conditions so as to reveal the true occurrence of post-vaccinial complications.^{34, 35}

The publicity surrounding the 1976 swine flu "incident" led also to an awareness of the problems of the nosology of GBS. In response, the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) in the United States formulated 'diagnostic criteria for GBS' to establish uniformity in recognition of the syndrome's diagnostic boundaries (Appendix B).³⁶ These criteria are listed under the categories: 1) Features required for the diagnosis; 2) Features strongly supportive of the diagnosis; 3) Features casting doubt on the diagnosis; and 4) Features ruling out the diagnosis.

The NINCDS developed a definition of GBS that grouped together the clinical signs and symptoms evident in case series but not always present when examining a single case. It is confusing because variants of the condition are clearly in opposition to the features required for, or strongly supportive of, the diagnosis. As well, the list of features casting doubt on, or ruling out the diagnosis is extensive, illustrating the expertise and initiative necessary to correctly exclude differential diagnoses.

The variability of clinical presentation of GBS and the difficulty presented by such a cumbersome case definition makes it easy to see why the clinical diagnosis and subsequent ancillary tests performed can differ among health centers and among cases of GBS. Together these factors can increase the likelihood of misclassification (differential and non-differential) and affect incidence estimates obtained in epidemiological studies.

Increased GBS Incidence During a Nationwide Oral Poliovirus Campaign in Finland - 1985

During a mass oral poliovirus vaccine (OPV) vaccination campaign in Finland in 1985, in which 94% of the population was vaccinated during a 5-week period, 10 cases of GBS were observed.^{12,37} This represented a statistically significant increase above the expected number of cases (3) in the 3 month reporting period in which the vaccination campaign occurred.¹² These observations suggest that live-attenuated polioviruses, like other viruses, may sometimes trigger the onset of GBS. This is especially important for the province of Ontario in light of its recent (1990) change to using OPV in its immunization schedule. It will be important to know whether the GBS incidence has increased since this change in immunization policy.

PAHO's Campaign to Eradicate Poliomyelitis

Poliomyelitis is not only of interest because of the possibility that OPV may cause GBS. On May 14, 1985, the Director of the Pan American Health Organization (PAHO), Dr. Carlyle Guerra de Macedo, announced the goal of eradicating wild poliovirus in the Americas by 1990. One of the three critical areas of action in PAHO's program strategy is enhanced surveillance to document, and to initiate investigation of, each case of acute flaccid paralysis (AFP) that occurs, as well as to certify when cases are not occurring.³⁸

Although the date for eradication has been reset to 1995, progress in the reduction of cases of polio is being achieved. Surveillance for AFP has increased in some Latin American countries where polio remains endemic. GBS is the most important cause of AFP in childhood in the Americas.³⁹ While the two conditions can be objectively differentiated by: a) timely investigation of the stool for polioviruses; b) CSF examination for albuminocytologic dissociation; and/or, c) peripheral nerve electrophysiological studies; if a case presents after the acute phase of illness, the two conditions sometimes may not be differentiated.

PAHO is presently devising a certification process which will enable teams of health experts including epidemiologists to document the elimination of wild polioviruses from each individual nation. Part of this process involves determination of the expected GBS incidence in children.⁴⁰ Determination of the expected GBS incidence in children will contribute to the estimation of expected AFP rates. AFP surveillance can then be performed for certification of nations free of wild poliovirus transmission.

The Importance of GBS in Canada

The descriptive epidemiology of GBS in Canada is not well understood. Bensted and Heffernan⁴¹ reviewed 66 cases of GBS that were admitted to one hospital in Halifax over a period of ten years, but were unable to offer more than a tabulation of the symptoms and signs found in their case series. The age-and-sex-specific incidence as well as the geographic variation in incidence in Canada has not been determined.

The importance of GBS to the Canadian public health lies in the rarely observed temporal association of GBS with vaccination. These events are passively reported to, and entered in the Vaccine-Associated Adverse Events database. However, owing to the small number of GBS cases reported and unreliability in reporting, it is not possible to determine whether these adverse events are caused by vaccination. Compounding the problem, background rates of GBS in Canada are not known. Knowledge of background GBS rates would provide a basis on which to estimate the etiologic fraction of GBS caused by a particular immunizing agent if an outbreak of GBS were to occur, and to better evaluate the risk of temporal association between vaccine administration and GBS.

Canadian Hospital Service Databases

HMRI: The Hospital Medical Records Institute is an independent, non-profit organization maintaining a national database of clinical information pertaining to health-care institution separations. It was created in the 1970's in response to needs for a source of information enabling Canadian Hospitals to demonstrate accountability and measure changes in demand for resources. Since that time it has also been explored for its epidemiological utility.⁴²

HMRI aims to have complete participation of all Canadian health care institutions in submitting hospital separation data. In fiscal 1989/90, the discharges submitted by provinces and territories represented approximately 75% of all acute care discharges (Table 1). Ontario is the only province that has the characteristics required for this study, namely, sufficient population and complete participation of its institutions in the database from fiscal year 1978.

**Table 1: HMRI Participation by Province - 1989/90
(in terms of percentage of acute care discharges)⁴³**

Province/Territory	Participation
Newfoundland	90%
Nova Scotia	30%
Prince Edward Island	85%
New Brunswick	100%
Québec	20%
Ontario	100%
Manitoba	0%
Saskatchewan	80%
Alberta	100%
British Columbia	95%
NWT, Yukon	100%

In 1987, Halliday et al⁴² from the University of Toronto (Dept. of Preventive Medicine and Biostatistics) described a method for estimating "persons" versus "cases" using HMRI data. The authors developed two simple algorithms to estimate the rates of readmission for ten specific diagnoses related to diseases of the liver. One algorithm accurately identified repeat admissions to hospital using the 70% of records which contained health insurance numbers, but pertained only to those selected records. A second algorithm identified patients who were readmitted to the same hospital, using the

institution number in conjunction with the residence code as an identifier. This algorithm was again applied to records having a health insurance number, demonstrating its utility for some HMRI records.

Neither of these methods can be used to ascertain the incidence of GBS. GBS is often first diagnosed in a primary-care institution and requires transfer of the case to a higher-level-of-care institution. For this reason the assumption regarding repeat admissions usually occurring at the same hospital cannot be made. Also, ascertainment of the incidence of GBS would entail examination of all records - not only those records having health insurance numbers.

The HMRI database has been made available to LCDC on CD-ROM with annual submissions corresponding to fiscal years. The relevant variables to which LCDC has been given access are listed in Appendix C; personal identifiers are not available.

Med-Écho: The Med-Écho database is owned and operated by the 'ministère de la santé et du services sociaux du Québec' (MSSS). It evolved in the 1960s out of the interactions of the MSSS with Québec health-care institutions as a means of tabulating services provided by institutions for financial purposes.⁴⁴

Since April of 1981, all acute-care hospitals in Québec have been submitting data to Med-Écho. The database has since been expanded to include a tumour section, coding for long-term care patients occupying short-stay beds, and clientele of chronic care institutions. In spite of the growth of this database and the increase, in Canada, of epidemiological studies using hospital service data, a search of the literature revealed

only one reference to an epidemiological study performed using the Med-Écho database.⁴⁵ A list of the relevant Med-Écho variables for this study is found in Appendix D. It was made available to LCDC, on tape, early in 1991 for epidemiological purposes.

**Public Health Significance of GBS and Justification for the Investigation of its
Incidence Using Hospital-Service Data**

The myriad of etiological agents purported to cause or co-factor in the occurrence of GBS necessitates accurate information about the incidence of this syndrome. Ascertainment of its incidence with attention to age-and-sex-specificity, temporal variation including seasonality, and geographic variation in rates is important. If this is accomplished it will be possible to estimate the etiologic fraction of GBS which might be caused by suspected agents. The changes in GBS occurrence which might be a consequence of certain epidemics, environmental hazards or changes in immunization policy could be monitored if an efficient, reliable and accurate methodology to survey/monitor the incidence of GBS could be developed.

AIMS AND OBJECTIVES OF THE STUDY

AIMS

- 1) To develop a methodology suitable for use in surveillance of vaccine-associated adverse events which will enable future trend analysis of the incidence of GBS using HMRI and Med-Écho data.
- 2) To assess the feasibility of using Canadian hospital service data to study the incidence of GBS. To compare HMRI and Med-Écho data for this purpose.

OBJECTIVES

- 1) To obtain the crude, standardized, age-and-sex-specific incidence rates of GBS in Ontario and Québec during 1983-1989.
- 2) To detect any temporal or geographical patterns in the incidence rates of GBS during 1983-89 within and between these two provinces as well as within and among regions in each of these provinces.

METHODS

Owing to slight methodologic differences in the way data from Ontario and Québec were handled, it is appropriate to consider this study as being composed of two independent studies each conducted to ascertain the incidence of GBS in one of the provinces. To avoid redundancy the methods used in both arms of the study are described once, and differentiating features of the methods are described separately.

Sources of Data

The principal sources of data for this study were the HMRI and Med-Écho databases, from which records of Ontario and Québec hospitalizations for GBS were extracted. Medical records departments from randomly sampled health care institutions in each province provided photocopies of hospital separation sheets, as well as discharge summaries and physician's histories and physical examinations of systematically selected admissions that had occurred within the institution. An additional data source was the Canadian Mortality Database, from which records of all deaths attributable to GBS from 1983 to 1989 were obtained.

Data was provided by HMRI on tape and converted into CD-ROM format, and by the MSSS on tape. Records were extracted from the HMRI database fiscal-year files and downloaded onto a diskette in SAS-readable format. The Med-Écho data tapes were read on a mainframe computer and downloaded to a personal computer, also in SAS-readable format. Both datasets were manipulated using SAS software.

Extracting records of Potential GBS cases

To enable calculation of the incidence rate of GBS using provincial census figures in the denominators, all pertinent records of Ontario and Québec hospital admissions were collected from the time of full participation in the databases. For HMRI the date is 1978. For Med-Écho the date is 1981.

In addition to their representing an admission in the correct province and within the correct time frame, records were extracted only if they also contained selected ICD-9 codes in any of the diagnostic code fields in the database. Diagnostic codes were selected from two of the three-digit categories of ICD-9: 357 - 'Inflammatory and toxic neuropathy'; and, 375 - 'Disorders of lacrimal system'. The specific four-digit subcategories selected for study are found in Table 2.

Table 2: ICD-9 Diagnostic Codes of Interest for GBS Study

ICD-9 Code	Diagnosis
357.0	Acute Inflammatory Polyneuropathy - GBS
357.8	Inflammatory & Toxic Polyneuropathy - other
357.9	Inflammatory & Toxic Polyneuropathy - unspecified
375.0	Dacryoadenitis

The rationale for the selection of records containing the diagnosis 357.0 is as follows. This study aims to find the incidence of GBS, and therefore utilization of hospital admission records having this diagnosis is essential. The other three diagnoses were selected because they are most likely to represent misclassified GBS cases. Specifically, ICD-9 diagnoses 357.8 and 357.9 are two "classifications of exclusion" that are used by medical records departments when a written diagnosis of polyneuropathy does not fit any

of the other 4-digit diagnoses in ICD-9 category 357. The code 375.0 was selected because it is the most likely transposition of the code 357.0. Its use may enable detection of medical records departments transcription errors.

For the HMRI database, selected records were restricted to those in which the diagnoses of interest were classified as being of the type 'main', 'primary' or 'secondary' in the diagnostic-type fields. Similarly, in the Med-Écho database, selected records were restricted to those having the diagnoses of interest located in one of the four 'Final Diagnosis' fields.

An important additional consideration regarding the selection of records from these databases was the time that coding under the International Classification of Diseases - ninth revision - (ICD-9) was implemented. ICD-9 was published in 1978 and implemented immediately by HMRI so that all records pertaining to fiscal year 1978 or later should theoretically contain ICD-9 codes. However, changes in frequencies of the diagnoses of interest in HMRI data for Ontario over the calendar years 1978 to 1989 indicate that 1980 is likely to be the first calendar year during which ICD-9 coding by medical records departments is largely uncontaminated by diagnostic coding from the eighth revision of diagnostic classification (ICD-8). Although not formally evaluated, as can be seen in Table 3, changes occur in the annual frequencies of these diagnostic codes between 1978 and 1980, but thereafter remain fairly constant. This may indicate a period of gradual implementation of ICD-9 coding in institutions across Ontario lasting about two years, after which the new revision of the coding manual was fully implemented as indicated by the more constant frequencies occurring after 1979. Because the earliest year of Med-Écho data used was 1981, fully three years after ICD-9

was published, it was assumed that Québec medical records coding was free from ICD-8 contamination. Therefore, the time frame of data selected for record linkage in this study was 1980-1989 in Ontario and April 1, 1981-1989 in Québec.

Table 3: Number of Occurrences of Selected ICD-9 Codes in HMRI Data for Ontario After ICD-9 Implementation*

Year	Diagnosis			
	357.0	357.8	357.9	375.0
1978§**	159	--	3,174	419
1979	266	8	809	87
1980	306	6	71	--
1981	287	16	59	8
1982	320	14	28	9
1983	366	10	19	9
1984	363	15	19	5
1985	370	18	13	9
1986	410	15	10	4
1987	450	15	8	12
1988	427	31	41	6
1989	484	20	35	5

* Records of these ICD-9 categories were extracted from HMRI data, and are of any diagnostic-type.

§ First year of complete HMRI participation by Ontario hospitals.

** ICD-9 theoretically was implemented in 1978. The corresponding ICD-8 diagnostic categories were as follows: 357 - Other diseases of peripheral nerves except autonomic (including 357.0 - cervical and brachial plexus, 357.9 - other and unspecified), and 375.0 - primary acute glaucoma. 357.8 did not exist in the ICD-8 classification.

Identification of Records Representing Incident GBS Admissions

For this study, a 'case' of GBS represents an occurrence of GBS, comprising one or more 'admissions' to hospital. An incident admission is the first admission of a case. For a case to be included in incidence rate calculations, it must include an incident admission. These definitions are important especially when records of admissions for GBS, occurring within the time period of interest, represent admissions other than the first admission to hospital for an individual, and therefore do not count as a case of GBS.

Ontario: Using the record selection criteria described above, 3,449 records, representing admissions in which a diagnosis of GBS was present, were extracted from the HMRI database. In addition, 134, 267 and 67 records representing admissions in which the diagnostic codes 357.8, 357.9 and 375.0, respectively, were extracted. The selected admissions were further restricted to those having admission dates after December 31, 1979 and before January 1, 1990 in Ontario. The SAS system was used to manipulate the data and tabulate results.

Québec: From the data on tape, 1,889 records having the diagnostic code 357.0 in one of the four 'diagnostic final' fields were extracted. Also extracted were 180, 913, and 47 records representing the diagnoses 357.8, 357.9 and 375.0, respectively.

Québec having fewer records representing GBS cases was due, in part, to its smaller population and shorter time period from which data were selected. The method of selection of records differed from that for HMRI data because of the different structure of these databases, and the author's experience in manipulating the HMRI data beforehand. The decision to exclude cases having an incident admission in a long-term

care or rehabilitation institution was made only after the HMRI data had been manipulated. Specifically, for HMRI data a record was selected if the diagnosis of GBS was found in any diagnostic field (including 'main', 'primary', 'secondary', 'tertiary'), while records were selected from Med-Écho data only if they were found in one of the four 'diagnostic final' fields (and not the 15 'diagnostic' fields). The reason for the high number of 357.9 diagnoses in Québec is unknown.

A modified 'Generalized Iterative Record-Linkage System' (GIRLS), devised for this study, was used to link admissions together into cases of GBS. This was conducted using record linkage theory as described by Newcombe^{46,47} and Fair.^{47, 49} Since this procedure is an essential and innovative part of this study, it will be described in detail.

Record Linkage Procedure

This record linkage procedure was used to link records of hospitalizations together into personalized histories (cases). When records are linked to each other, incident-admissions of GBS can be identified as the first admission within each group. The date of admission of the incident admission in each case will be close to the date of onset of illness in a condition with sudden onset, such as GBS. Record linkage was applied only to records representing admissions having a diagnosis of GBS. The following description is therefore pertinent to only those records.

Pre-sorting Records Before Application of Algorithms: Linkage of records into 'cases' of GBS involved the application of algorithms to record-pairs which had been brought together by pre-sorting records on key variables. Having been used in the pre-sort, these key variables are not involved, or are only marginally involved in the record linkage

algorithm. The variables on which the data were sorted were chosen for their ability to discriminate between matched and unmatched record-pairs. A matched record-pair is two records which are believed to represent the same person. Table 4 lists the variables in each database judged to be the best sorting variables. Factors increasing the chance that a variable would be chosen as a sorting variable included a low frequency of missing values, stability of values among records thought to represent the same person, uniqueness of values, and accuracy of values.

Table 4: Variables Used to Sort Each Database *

Sort	HMRI	Med-Écho §
First Sort:	Birthdate	Birthdate
Second Sort:	Health-care number	Residence code
Third Sort:	Chart number	Chart number

* These variables were used to sort the database prior to applying the algorithm for that step to the dataset. This procedure brings records having the same value for the sorting variable adjacent to one another which increases their chances of being linked by the algorithm.

§ There is no health-care number provided in the Med-Écho database.

In each step of the record-linkage procedure the records were initially sorted using one of these key variables as well as the admission date and discharge date, in decreasing order of priority. Sorting the dataset in this way greatly increases the probability that two adjacent records will match. The admission and discharge dates are included as sorting variables to ensure that the records brought together into groups having the same value of the key sorting variable are ordered chronologically within each group. The algorithms then function as a logical decision making process, giving a score to adjacent

records (record-pairs) based on the similarity of specified variables. A record-pair given a high score is more likely to represent two records which match, that is, they represent two records from the same case of GBS.

Algorithms: The algorithms were programmed in SAS and compared values of specific variables in adjacent records giving a weight to this comparison. The value of the weight of each variable comparison was based upon the probability that the variable would match in both matched and unmatched record-pairs. The likelihood of a match between two records depends upon the number of compared variables which have matching, and unmatched values, accounting for the weight given to each outcome of variable comparisons.

Calculation of Weights: Calculation of weights given to various outcomes of variable comparisons required tabulation of these outcomes in a smaller subset of the data in which the matched and unmatched record-pairs had already been identified. This requires that the record-pairs in the subset be subjectively judged as to whether they are, or are not matched. Five hundred records each from the HMRI and Med-Écho GBS datasets were selected, as described next, to calculate weights for the record linkage procedure. The data were sorted by birthdate, after which, the first record of the 500 was identified through a random process. The rest of the records in each of these subsets of data followed the first consecutively. The selected records were sorted by birthdate, admission date and discharge date and subsequently were manually examined to determine the similarity of identifiers between adjacent record-pairs. Within this subset, record-pairs were grouped into 3 groups:

1. record-pairs considered to represent one person (truly linked).
2. record-pairs considered to represent two persons (truly unlinked).
3. record-pairs which are unable to be placed into either groups 1 or 2 (indeterminate).

Categorization of record-pairs from the HMRI data resulted in 228 record-pairs falling into group one and 282 record-pairs falling into group two, while 3 record-pairs were indeterminate. Corresponding numbers of record-pairs from Med-Écho data were 122 in group-one, 354 in group-two and 25 in group-three. The difference between the two sets of data may be attributed to the randomness of the selection of the 500 records and the variability in the number of admissions occurring in persons afflicted with GBS. However, the larger number of indeterminate record-pairs in the Med-Écho data subset may indicate greater difficulty in manual linkage of Med-Écho records.

Once the record-pairs were classified into these three groups, each variable to be used in the record-linkage algorithm was compared between adjacent records to tabulate the frequency of matches and non-matches on the variable in question, or outcomes, for both linked record-pairs and unlinked record-pairs. An odds ratio (OR) pertaining to each outcome was then obtained:

$$\text{OR} = \frac{\text{probability of the outcome in truly linked pairs}}{\text{probability of the outcome in truly unlinked pairs}}$$

An odds ratio for an entire record comparison can then be obtained by multiplying the odds ratios of each of the variable comparison outcome odds ratios. However, it is more convenient (and it has become the convention in record-linkage studies)^{48,49} to take the logarithm to the base 2 of these ORs and add them to obtain the total weight, or score of the entire record comparison. This logarithm, called the 'binit weight', is defined as:

$$\text{WEIGHT} = \text{LOG}_2(\text{ODDS RATIO})$$

The weights of outcomes were incorporated into the first algorithm. For further ease in computation of total weight, each weight was multiplied by ten and rounded off to a whole number to eliminate the need to deal with decimals. Algorithm variables were selected by the criterion of having the largest difference between the weight given to a match versus that given to a non-match. The sorting variable in each step had its weights reduced towards neutrality (0) because the sorting procedure already greatly increased the probability of a match on this variable and, therefore, simultaneously increased the probability that a record-pair would be linked. The weights given to each variable comparison outcome for each set of data are listed in Tables 5 and 6. The first algorithm for each dataset can be found in Appendices F and G.

Other considerations for record-linkage are missing-values, extreme weights, splitting variables into more than one field - each with a separate weight, and, value-specific weights. For this study, when one or both records in a pair had a missing value for a particular variable in the algorithm, the weight assigned to this outcome was zero. If in the calculation of the odds-ratio the numerator or the denominator was zero, the resultant logarithm would be negative or positive infinity, respectively. These outcomes were

given smaller weights as shown in Tables 5 and 6. Split-variables included birthdate - which was split into the two digit fields of birth-year, birth-month and birth-day; postal code - which for the HMRI part of the study was split into two three-character fields (the Med-Écho database contains only a three character postal code); and, residence code - which is a variable devised by the Ontario Ministry of Health having four digits, the first two of which represent the census division within Ontario and the last two the municipality of the person's residence. Value-specific weights were considered for both Toronto and Montreal residence codes, but since these did not add to the efficiency of the record linkage algorithms, they were not implemented.

Table 5: Weights Given to Outcomes of Variable Comparisons: HMRI

Variable	Outcome Comparison	Odds Ratio	Weight
Algorithm 1			
Birthdate	month and day agree	22.2	+45
	day disagrees	0.03	-55
Postal-code	characters 1-3 agree	∞	+50
	characters 1-3 disagree	0.161	-25
	characters 4-6 agree	∞	+40
	characters 4-6 disagree	0.19	-25
	characters 1-6 agree	∞	+250
	missing	1	0
Sex	agree	1.98	+10
	disagree	0.02	-60
Institution	agree	18.6	+40
	disagree	0.70	-5
Health-care number	agree	∞	+500
	disagree	0.006	-200
	missing	1	0
Chart number	agree	∞	+500
	disagree	0.575	-8
Residence Code	characters 1-2 agree	14.1	+40
	characters 1-2 disagree	7.4	-50
	characters 3-4 agree	0.04	+30
	characters 3-4 disagree	0.09	-35
	missing	1	0
Second admit date - first discharge date (number of days between admissions) *	days \leq -10	0.04	-50
	-10 < days < 0	0.6	-10
	days=0	∞	+300
	days=1	∞	+200
	days \leq 5	∞	+100
	days \leq 20	7.4	+50
	days \leq 90	5.5	+20
	days > 90	0.43	-10
Algorithms 2 and 3 **			
Birth-year	agree	73.0	+60
	disagree	0.5	-40
Birth-month	agree	11.4	+35
	disagree	0.06	-40
Birth-day	agree	28.8	+50
	disagree	0.05	-40

* Subtraction of the first record's discharge date from the admission date of the second.

** Only these weights changed in algorithms 2 and 3.

Table 6: Weights Given to Outcomes of Variable Comparisons: Med-Écho

Variable	Outcome Comparison	Odds Ratio	Weight
Algorithm 1			
Birthdate	month agrees	2.2	+10
	month disagrees	∞	-500
	day agrees	176.0	+75
	day disagrees	0.008	-70
Postal-code	characters 1-3 agree	∞	+200
	characters 1-3 disagree	0.17	-25
	missing	1	0
Sex	agree	2.0	+10
	disagree	1	-500
Institution	agree	13.3	+40
	disagree	0.75	-5
Chart number	agree	∞	+500
	disagree	0.76	-5
Residence Code	characters 1-3 agree	35.0	+50
	characters 1-3 disagree	0.1	-30
	missing	1	0
Second admit date - first discharge date (number of days between admissions) *	days ≤ -10	0.02	-50
	$-10 < \text{days} < 0$	0.5	-10
	days=0	∞	+300
	days=1	∞	+200
	days ≤ 5	∞	+100
	days ≤ 20	10.2	+50
	days ≤ 90	5.2	+20
	days > 90	0.08	-10
Destination § (institution)	agrees with institution	235.0	+100
	disagrees	0.35	-15
	missing	1	0
Algorithms 2 and 3 **			
Birth-year	agree	46.0	+55
	disagree	0.02	-55
Birth-month	agree	11.3	+35
	disagree	0.4	-10
Birth-day	agree	46.9	+55
	disagree	0	-40

* Subtraction of the discharge date of the first record from the admission date of the second.

** Only these weights changed in algorithms 2 and 3.

§ Institution to which the person was transferred, if any.

Application of the Algorithms: The GBS data were sorted by birthdate, admission date and discharge date, and the first algorithm was applied. The total weight of each record-pair was then plotted in a frequency distribution, resulting in the distribution presented in Figure 1. Within this distribution of scores, two separate distributions of weights can be identified. These are the distributions of linked and unlinked record-pairs. At this point the record-pairs and their corresponding scores were examined manually to determine the score above which a record-pair was certain to be linked. This score is termed the 'upper threshold'. Similarly, the records were again examined to determine the score below which two records were certain to be unlinked; this score being the lower threshold. After this manual examination, the algorithm was finely tuned by adjusting weights to aid in differentiation of both truly-linked record-pairs from falsely-linked record-pairs, and truly-unlinked record-pairs from falsely-unlinked record-pairs.

The first algorithm was run again and the total weight distribution was plotted to verify improved separation of the two distributions. These steps were reiterated until adjustment of the weights created more errors in classification than corrections.

A final upper threshold was then selected which was placed sufficiently high to exclude linkage of any truly-unlinked record-pairs. Record-pairs with scores greater than this threshold were permanently linked into the same 'person' or 'case of GBS'. Record-pairs with scores that were between the upper and lower threshold values were then manually examined to correct any misclassification of falsely-unlinked record-pairs. This procedure involved identification of record-pairs which would have had a weight surpassing the upper threshold, but were separated from each other by one or more records missing data. In this way, manual record linkage increased the efficiency of the computerized record linkage procedure.

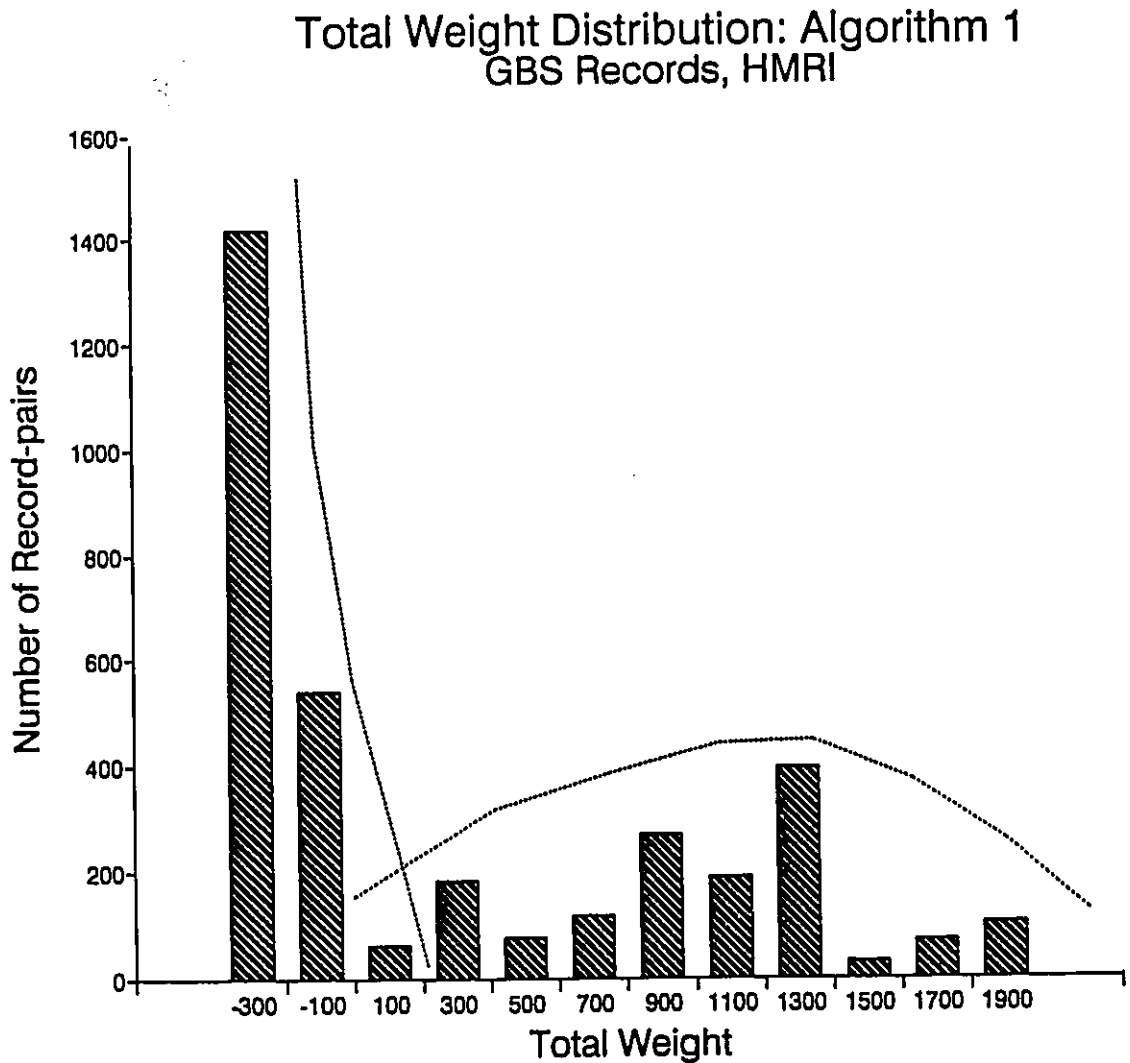


Figure 1: Example of the distribution of total-weight found after the application of Algorithm 1 to HMRI data. The 3,449 record-pairs representing GBS admissions received total-weights ranging from less than -300 to greater than 1900. This graph helps determine the upper and lower thresholds for linkage by displaying two distributions (truly-linked record-pairs having higher total-weights and truly-unlinked record-pairs with lower total-weights). Where these two distributions overlap indicates total-weights of record-pairs that were examined manually before the application of the second algorithm

The database was then resorted by health-care number, admission date and discharge date in preparation for application of the second algorithm to the dataset. This procedure was sufficiently similar to the application of the first algorithm so that only differences are described here. The test database was sorted by health-care number before recalculation of the binit weights for outcomes of variable comparisons. All weights remained the same except for the weights determined for birth-year, birth-month, and birth-day, which were the sorting variable in the first step (Tables 5 and 6). Again, the variable specific weights were adjusted to separate, as much as possible, the distributions of truly-linked and truly-unlinked record-pairs. The weight given to the health-care number was unchanged. Records not having a health-care number were excluded from this step, although the new linkages created by this step sometimes involved them.

The third algorithm was run after sorting the database on chart-number, admission date and discharge date. Weights used were not different from step two. This step was not sufficiently different from the first two to justify a separate description.

Grouping Records into Cases of GBS: The records were then sorted by 'Case Number', a variable created to group linked records together into cases of GBS, as well as admission date and discharge date. The first record in each case was then selected for entry into a separate dataset to be used to examine various aspects of the hospitalizations of 'incident-admissions'. The dataset containing all of the admissions (both incident and non-incident) was retained for examination of various other aspects of cases of GBS.

Review of Hospital Chart Information to Verify Diagnoses

Misclassification of the diagnosis of GBS can result in both false-positive and false-negative outcomes. Working with hospital service data alone might not give an accurate picture of the incidence of GBS if there is significant misclassification. The algorithm presented in the previous section of the methods provides a way to exclude non-incident-admissions of GBS, but does not tell us whether the incident-admissions which remain are truly cases of GBS; nor does it tell us how many cases of GBS were missed.

Detection of False-positive Diagnoses

Reference to information recorded in the hospital chart of identified incident-admissions of GBS should be an efficient way to examine the validity of the diagnosis of a case of GBS. A sample of charts corresponding to records of GBS incident-admissions was obtained in order that the rate of false-positive diagnosis of GBS could be measured.

Measurement of the false-positive diagnosis rate included the following steps:

1. Selection of a sample of records from those records having a diagnosis of GBS and identified as an incident-admission.
2. A photocopy of essential information in the hospital chart was obtained from the institution where the patient was admitted. This information included:
 - i) physician's history and physical exam
 - ii) discharge summary
 - iii) discharge diagnoses as written by the attending physician

3. The information in these photocopied materials was compared by two neurologists (Pierre Jacob and Peter Humphrey, both of the Children's Hospital of Eastern Ontario) against the case definition to determine whether the case in question was a true case of GBS.
4. The rate found in the sample was generalized to the entire group of incident-admissions.

Case Definition of GBS

The case definition for this study is adapted from that devised by the expert neurology group of a Centers for Disease Control study.⁵⁰

Definite:

1. Absence of fever at onset of neurologic symptoms unless due to coexisting illness.
2. Progressive weakness of legs and arms.
3. Areflexia or marked hyporeflexia in legs and arms.
4. Deficit relatively symmetric.
5. CSF protein raised during or after first week of illness; or, electrophysiological or EMG abnormalities consistent with a demyelinating polyneuropathy.
6. CSF cells (mononuclear) < 10/ml.
7. No evidence that another illness could have caused the neuropathy.

Probable:

1. Clinical findings as in definite category, except progressive weakness of arms is not necessary.
2. CSF and EMG results normal or not performed.

Possible:

1. Clinical findings are compatible with GBS except that deep tendon reflexes were not recorded.

Chart Selection Process

To select a representative sample of records representing incident-admissions of GBS from each database a multistage sampling process was used to first obtain a sample of hospitals from within each province, and second, to identify separations from each of these hospitals. As described below, stratified random sampling of hospitals was performed to ensure representation of both primary care institutions and tertiary care institutions. This was followed by systematic sampling of admissions having a diagnosis of GBS within each hospital.

1. After determination of the number of incident-admissions reported by each hospital, hospitals were grouped into 2 strata. Each stratum accounted for as close to 50% of the admissions as possible with stratum-one containing hospitals having more admissions.
2. The sample size of records for chart review was calculated by the method described by Lemeshow and Hosmer for stratified random sampling.⁵¹

The estimated proportions for false-positive GBS cases were 0.02 for stratum-one and 0.05 for stratum-two institutions. These proportions were chosen based on the assumptions that the error rate would be higher in primary care institutions and that overall the error rate is less than ten percent (Personal communication - Karp H., Emory University, 1990. Personal communication Jacob P. - Children's Hospital of Eastern Ontario, 1990.).

3. Because there was still a large range of admissions per institution in stratum-one, this stratum was further divided into 3 substrata of equal numbers of institutions (seven each in Ontario and 4 each in Québec) in order to ensure representation from all classes of institutions. One institution was randomly selected from each of these substrata using random number tables.⁵² From each selected institution, every fourth chart, chronologically, was selected, beginning with the any of the first four charts decided by two consecutive coin tosses.

In stratum-two, institutions were chosen by the same random process and all records from a chosen institution were selected until the desired sample size was obtained.

The calculation was done to obtain a result within 5 percentage points of the true value and was inflated by a factor of 1.25 to protect against non-response. The numbers of charts requested from Ontario and Québec were 64 and 76, respectively.

The examination of the hospital separation sheet, physician's admission history and physical exam, and, discharge summary was performed by a panel of two neurologists (P. Jacob, P. Humphrey). Cases were classified into five categories based upon the information provided by the institution. The five categories are listed below. The definition of GBS is according to that listed in the methods.

1. **Definitely not GBS:** Cases not called GBS and not having clinical findings compatible with GBS. Also, cases called GBS (either by the physician or the medical records transcriber) that give a clinical description of another condition.
2. **Probably not GBS:** Cases in which there are some clinical findings compatible with GBS but there are also some findings not compatible. The information available is not extensive, so GBS cannot be totally ruled out.
3. **Unknown:** Information is insufficient to grade the case.
4. **GBS compatible:** Clinical findings are generally compatible with GBS or there is reference in the discharge summary to a consult or transfer in which the diagnosis of GBS was corroborated. There is no reference to CSF or nerve conduction studies supporting the diagnosis of GBS.
5. **Definitely GBS:** Clinical findings are generally compatible with GBS and CSF and/or EMG findings secure the diagnosis. Reference in the discharge summary to a referral where electrophysiological tests, or, EMG or CSF findings are confirmatory, is acceptable.

The panelists independently judged the cases to be in one of the above five categories, discussing cases that each had graded differently (unless the difference was between category 1 and 2, or category 4 and 5) to arrive at a mutually agreed upon category for the case. Only two such cases from each province's sample required discussion between the neurologists before it could be categorized.

Detection of False-negative Diagnoses

Cases of GBS which are misclassified under another diagnostic code pose a difficult problem of error measurement. Any search for false-negative cases cannot possibly be exhaustive because, theoretically, they could be given any diagnosis, or might be missed altogether if the afflicted person is not admitted to hospital, or less likely, does not present to a physician. This renders attempts to measure the "global false-negative rate" (that is, the discoverable plus undiscoverable false-negative rate), futile. This study can only measure that rate of false-negative diagnosis that is identifiable using the restricted data available for the study. Consequently, the false-negatives investigated were those verifiable through searches of records submitted with specific ICD-9 codes.

The specific ICD-9 codes chosen to assess the false-negative rate included those believed to be most nosologically similar to GBS - that is, 357.8 and 357.9, which are the diagnostic codes for 'Inflammatory and Toxic Polyneuropathy - Other' and '...- Unspecified', respectively. Another diagnosis was chosen because it is a transposition of the diagnostic code for GBS, 'Dacryoadenitis' (375.0), an ophthalmological condition clinically dissimilar from GBS. The purpose of using 357.8 and 357.9 was to obtain an estimate of the accuracy with which medical records departments translate written diagnoses into ICD-9 codes. A search of these diagnoses would not be an exhaustive

investigation of all diagnoses harbouring misclassified cases of GBS, but because these diagnoses are the least specific codes for polyneuropathy in the ICD-9 system, they are probably the two diagnoses under which more cases of GBS would be misclassified, if such a problem exists (Personal communication - Jacob P, 1990). The time and expense involved in an exhaustive search of all diagnoses which actually could represent case of GBS would render this study infeasible. The diagnostic code 375.0 was examined to estimate another aspect of medical records coding, that of transcription error of the part of medical records personnel leading to transposition of digits within the ICD-9 code.

Separation sheets were requested from those sampled institutions to be searched for false-negative GBS diagnoses. A written diagnosis suggestive of a case of GBS was defined as a false-negative.

Chart Sampling Procedure for Detection of False-negative Diagnoses

From the formula by Lemeshow and Hosmer,⁵¹ the number of records having diagnostic codes 357.8, 357.9 and 375.0 to be sampled from each stratum was determined. The expected proportion of records in each diagnostic category that are misclassified GBS cases were obtained in a way similar to the proportions for estimation of false-positive diagnoses (Table 7). Cases in each diagnostic category were divided into two strata having as close to equal numbers of cases in each stratum as possible. Stratified random sampling was then performed.

Table 7: Expected Proportions of Diagnostic Error

Diagnosis	Strata Expected Proportions *
357.8	0.01
	0.02
357.9	0.02
	0.05
375.0	0.01

* These values represent the proportion of records representing admissions of each diagnosis listed that is expected to be a misclassified GBS case.

The margin of error of this sample size calculation is 5 percentage points. The result obtained was multiplied by a factor of 1.25 to protect against anticipated losses occurring through non-response of institutions. For 357.8, 357.9 and 375.0 cases, the number of written diagnoses for each province sampled was 31, 56 and 16 for Ontario; and, 45, 52 and 16 for Québec, respectively.

Cross-Linking Out-of-Province Records to Assess Migration Error

When "Ontario" HMRI records were selected, obtained records pertained to GBS hospitalizations occurring in Ontario, as opposed to GBS hospitalizations of Ontario residents. Fifty-six of these records represented Ontario hospitalizations of Québec residents. Internal record linkage was performed manually on this subset of the dataset to detect incident admissions, followed by exclusion of records outside the seven years covered by this study. This left 27 records of GBS admissions of Québec residents hospitalized in Ontario.

The Med-Écho database was searched for records representing GBS admissions of Ontario residents and 11 were found. Eight of these were unaccounted for after exclusion of non-incident-admissions found through manual internal linkage and two records from before 1983.

Because these remaining records may represent cases of GBS which are not recorded in the home province's database, they were manually cross-linked to the other database to determine the number admitted at some time, within the province of the person's residence. Those records that matched another in the opposite dataset would represent cases that did contribute to the tabulation of each province's cases in this study. The remaining records would likely represent GBS cases that received health-care only outside of the person's home province. Such a person would be misclassified as a non-GBS case. As described in the next chapter, the final number of outmigrated cases was small, and therefore was not used to adjust the incidence rate of either province.

Denominators Used in Rate Calculations

The complete participation of all health-care institutions from both provinces in the databases allows utilization of provincial population figures for the calculation of the incidence rate of GBS. Provincial population data from the 1986 Canadian census were obtained as well as population estimates from study years prior to 1986 and population projections for study years after 1986. These were used as denominators in the calculation of annual provincial rates. Canadian population data from the 1986 census was used in the direct standardization of the average annual provincial incidence rates of GBS.

The 1986 census gives a breakdown of the population for each province by age, sex, and geographical region. Figures for five-year age groups up to the age of 90, as well as one age group for those over 90 years were used in the age-specific calculations. Census divisions were the unit of geographical breakdown of the provincial figures.

Calculations of GBS Incidence

The identification of incident-admissions of GBS produced a dataset of records representing persons having had a diagnosis of GBS. This dataset also contains variables that were used in the calculation of rates: age, sex and census district. These variables were used to breakdown the number of cases. Similarly, appropriate denominators were selected from 1986 Canadian census data. In this way, age-specific, sex-specific and census district rates, as well as crude rates, were determined.

Rates were calculated annually for seven calendar years, 1983-1989, as well as calculation of an average annual incidence rate for this time period. This seven-year time period was chosen for two reasons. The first reason is that the initial year of data for each province contains readmissions from previous years that were not linked to earlier admissions because these data were not obtained; therefore, the first complete calendar year of each province's data was excluded - 1980 for Ontario and 1982 for Québec. Data from Ontario in 1981 and 1982 were also excluded to facilitate the comparison of Ontario and Québec.

The crude frequencies of GBS by month were tabulated and monthly incidence rates were calculated in order to detect any seasonality in the occurrence of GBS. These frequencies were standardized to a 30-day month. Ninety-five percent confidence limits based on the

variance of case frequencies occurring in each month over the 7 years were calculated.

The mean annual incidence rate was calculated for each census district.

Data Analysis

Those results better appreciated pictorially can be found in Figures 2 through 20. Wherever possible, provincial data from both provinces were placed on the same graph to enable comparison. Incidence rate by census district was mapped to show the geographical variation in GBS incidence.

A chi-square test was used to compare mean annual provincial incidence rates after standardization to the 1986 Canadian population. Ninety-five percent confidence intervals of cumulative mean monthly incidence rates were calculated for each province. A coefficient of correlation (least squares method) was used to determine whether the frequency of cases per month, in both provinces, was correlated.

The mortality attributed to GBS was investigated as another validity check on these data. A count of the number of deaths of residents in each province, by sex, for each year, having GBS listed as the principal cause of death, was requested from the Canadian Mortality Database. These figures were compared to the number recorded in the Med-Écho and HMRI databases occurring during incident-admissions of GBS as well as during subsequent admissions of GBS.

RESULTS

Because this thesis is both methodological and descriptive, results will be presented in sections. These sections relate to: the record linkage procedure; incidence rate determinations; and, error determinations obtained through review of hospital charts.

Record Linkage Procedure

The record linkage procedure for each of the databases was sufficiently different to present results separately for each database.

Ontario: A list of the variables in the HMRI database that were judged to have sufficient discriminating value for use in the record linkage algorithms is presented in Table 5. Logarithms (to the base 2) of odds ratios of field comparison outcomes were calculated to obtain the binit weights also shown.

Application of Algorithm-1 to the 3,449 HMRI records containing a diagnosis of 357.0 was performed three times, after which the distribution of scores of truly linked record-pairs could not be further separated from that of truly unlinked record-pairs without increasing the contamination of either distribution with false-positive and false-negative linked record-pairs, respectively. An upper threshold of 200 (total weight) was then set which resulted in grouping the records into 1,981 'persons', or cases of GBS when the algorithm was run for the final time.

Manual inspection of the algorithmic variables in the dataset sorted by birthdate, admission date and discharge date enabled manual linkage of 15 records to other records.

or cases that met criteria for linkage but missed being linked by the algorithm. Most of these were not linked by Algorithm-1 because of separation of two or more records matching on key variables by one or more records with missing or unmatched fields of the same key variables occurred. After these linkages were performed, 1,966 cases existed ("linkage groups") prior to the application of Algorithm-2.

In Algorithm-2, only the weights for birth-year, birth-month and birth-day were changed from Algorithm-1. These are listed along with their calculated odds ratios and binit weights in Table 5. Application of the second algorithm was required twice before adequate separation of the two distributions of scores had occurred. Running this algorithm with its upper threshold score of 100 resulted in capturing 62 more linkages, decreasing the number of cases to 1,904. No further links could be established upon manual inspection of records at this point.

Application of the third algorithm revealed seven new linkages. Two of these were judged to be false-positive links after manual inspection. These false-positive links probably occurred because the record-pairs involved had four-digit chart numbers, increasing the probability that a match on this field would occur by chance. Five of the 7 links created in this step were therefore accepted as true linkages. The distribution of scores after this step was well separated into two distributions so that manual inspection of the database after application of this algorithm was not performed. The final number of cases determined to be in this dataset was 1,899.

Of the 1899 cases, 1809 were identified to be from institutions providing active treatment. The 90 cases having first admissions within institutions not providing active

treatment consisted of 24 from rehabilitation hospitals, 16 from chronic-care institutions, 9 from 'other' institutions which are unlikely to be acute-care institutions (Personal communication - Maloney S, HMRI, 1991), 32 from special rehabilitation institutions and 9 from same day surgery hospitals. These 90 cases were not counted in the calculations of the incidence rate of GBS.

Exclusion of cases having a date of first admission before 1983 left a final total of 1,302 GBS cases occurring in Ontario between 1983-1989.

Québec: Variables in the Med-Écho database having sufficient discriminating power for use in record linkage algorithms are presented in Table 6 along with odds ratios of field comparison outcomes and calculations of binit weights.

Application of Algorithm-1 to the 1,847 extracted Med-Écho records having a diagnosis of GBS was performed three times. This step resulted in grouping these records into 1,312 'persons', or cases of GBS. Manual inspection of the algorithmic variables in the dataset sorted by birthdate, admission date and discharge date enabled manual linkage of 15 additional records. Therefore, there were 1,297 cases prior to the application of Algorithm-2.

In Algorithm-2 the weights for birth-year, birth-month and birth-day were changed from Algorithm-1 (Table 6). Application of Algorithm-2 was performed twice before adequate separation of the two distributions of scores had occurred. Running this algorithm resulted in capturing 9 more linkages, decreasing the number of cases to 1,288. No further links could be established upon manual inspection of records at this point.

Algorithm-3 did not reveal any new linkages. As well, manual inspection of the dataset which was now sorted by chart number, admission date and discharge date did not result in any new linkages. The final number of cases determined to be in this dataset was 1,288.

Exclusion of cases having incident admissions before 1983 left 1,040 incident admissions in Québec over the seven years of interest. A search for incident admissions occurring in non-acute-care institutions revealed 9 records. Deletion of these from calculations of GBS incidence rate left a final number of 1,031 records representing incident-admissions of GBS.

For each dataset, the three algorithms were run in reverse order and the results were found to be unchanged.

Results of Cross-Linkage of Out-of-Province Records

Eight of 27 HMRI records representing possible incident admissions of Québec residents in Ontario were linked to records in the Med-Écho database having the same birthdate and sex, and having an admission date or discharge date within one month of the opposite date in the corresponding record. This leaves 19 records that could represent Québec GBS cases not accounted for by this study. Taken as being representative of true cases, the mean number of Québec GBS cases per year missed through this out-migration to Ontario is therefore 2.7 cases per year or 1.8% of the mean annual number of cases in this province.

Of the 8 Med-Écho records of Ontario residents hospitalized with a diagnosis of GBS, 6 could not be cross-linked to HMRI records by the above method. This could mean that 0.9 Ontario GBS cases per year were not accounted for by this study because of out-migration of these cases to Québec. This number represents only 0.5% of the mean annual number of GBS cases in Ontario.

Descriptive Epidemiology of GBS in Ontario and Québec

The 1,302 and 1,031 incident admissions in Ontario and Québec, respectively, from the years 1983-1989 inclusive were used to calculate incidence rate figures. Figure 2 shows the number of incident admissions per year in each province, with Ontario having a mean of 186 incident admissions per year, and Québec, 147.3. The yearly annual incidence rates of GBS in each province is displayed in Figure 3. These data were age-and-sex-standardized to the 1986 Canadian census population. The mean of these annual incidence rates is 2.07/100,000 for Ontario and 2.25/100,000 for Québec. The difference in frequency of incident admissions for the seven years is statistically significant (chi-square = 5.48; $p < 0.05$; 1 d.f.).

The mean annual number of GBS cases occurring in each 5-year age stratum is illustrated in Figure 4. This figure shows the often mentioned bimodal distribution of GBS cases across age-groups. The peak frequencies occur in the 65-69 year-old group in both provinces with lesser peaks occurring in the 30-34 year-old group and the 25-29 year-old group in Ontario and Québec, respectively. When these frequencies are used to calculate mean annual age-specific GBS incidence rates (Figure 5), the peak incidence rate of 6.5/100,000 and 6.6/100,000 are found in the 75-79 year-old group in Ontario and in the

70-74 year-old group in Québec, respectively. Lesser peaks occurring in the young adult age-groups in these distributions are not as evident in this graph as in Figure 4.

The mean annual age-and-sex-specific incidence rates of GBS in both provinces from 1983-1989 for males and females, respectively, are found in Figures 6 and 7. The peak rate in Ontario males of 8.2/100,000 in those aged 75-79 is slightly less than the rate of 8.3/100,000 which occurs in the same age-group in Québec. However, both of these rates are less than the rate of 14.4/100,000 which occurs in Québec males aged 90 years or more. In females of both provinces the peak rates are smaller. In Ontario the peak incidence rate of 5.4/100,000 occurs in those aged 75-79, while in Québec the highest incidence rate is 5.8/100,000, occurring in those aged 70-74.

The cumulative mean monthly GBS incidence rate for each province is shown in Figures 8 and 9. The rate of 0.22 incident admissions per 100,000 per month in August in Ontario and 0.26 per 100,000 per month in March in Québec are the highest cumulative mean monthly rates for each province. October and July saw the lowest rates in each province - 0.15/100,000 per month for both Ontario in October and Québec in July. The mean cumulative mean monthly GBS incidence rate in each province is 0.17/100,000 in Ontario and 0.19/100,000 in Québec. Error bars shown on these two graphs indicate 95% confidence intervals (CIs) calculated based on the standard deviation of the cumulative mean monthly incidence rate. Figure 10 displays the two provincial cumulative mean monthly incidence rate graphs together without CIs to enable visual comparison of these data. These data have been standardized to a 30-day month.

The seven-year (1983-1989) picture of the frequency of incident-admissions per individual month for each province is presented in Figure 11. A simple linear regression of these data was performed, by taking the average of the preceding and following months as well as the month for which a value is plotted. The data from each province also were compared for correlation of case frequencies per month, revealing a correlation coefficient of $(r=) 0.093$ ($p > 0.05$).

Sex Ratio of GBS Cases

The male to female ratio of GBS cases and of crude GBS incidence rate in each province is shown in Table 8. Both provinces exhibit a male to female ratio of case frequency and of mean annual sex-specific incidence rate greater than one.

Table 8: Male to Female Ratio of GBS Cases and Incidence rates

Province	Ontario		Québec	
	Male	Female	Male	Female
Sex				
Mean Number of Cases per Year	97.9	88.1	76.4	70.9
Mean Annual Incidence rate	2.19	1.90	2.39	2.13
Male:Female (Number of Cases)	1.11		1.08	
Male:Female (Incidence rate)	1.15		1.12	

The number of hospital days per GBS case in Ontario and Québec, for the period of interest, are shown in Figures 12 and 13, respectively. The mean number of hospital days per case in Ontario was 54.5 and in Québec was 42.6. The range is from one to 1,196 days in Ontario and from one to 1,135 in Québec. The number of hospital days in the incident admission of each case is shown in Figures 14 and 15. In Ontario, the

range of hospital days per incident admission is from one to 536 with a mean value of 24.7 days. In Québec, the range of days per incident admission is from one to 754 with a mean of 29.8. The number of hospital admissions per case of GBS in each province is found in Figures 16 and 17. The range of admissions per case in Ontario is from one to 33 with a mean of 1.8 admissions per case. In Québec, the range of admissions per case is from one to 12 with a mean of 1.4.

The 1983-1989 mean annual GBS incidence rate in Ontario, age-and-sex-standardized to the 1986 Canadian Census population is 2.02 per 100,000 person-years. This is close to the unstandardized rate of 2.04 per 100,000 person-years (using the 1986 Ontario census population as the catchment population). The same calculation pertaining to Québec is 2.30 per 100,000 person-years, differing only slightly from the unstandardized mean annual incidence rate in Québec of 2.25 per 100,000 person-years.

Regional Incidence rates

The mean annual crude incidence rate by census district (county, district, regional municipality) in Ontario is mapped in Figure 18. The range of incidence among these geographical divisions is from zero in Kenora to 3.85 per 100,000 person-years in Bruce county. An analogous map for Québec is shown in Figure 19, with an enlarged view of the Québec eastern townships in Figure 20. The range of incidence among these regions is from zero in Iles de la Madeleine and Napierville to 4.75 per 100,000 person-years in Brome.

Two Ontario regions have an incidence rate less than 1.0 - Kenora district (0), and Prescott and Russell county (0.99). Three Ontario regions have an incidence rate greater

than 3.0 - Sudbury Regional Municipality (3.33), Grey county (3.44) and Bruce county (3.85).

Those CDs in Québec having a mean annual GBS incidence rate less than 1.0/100,000 include Iles de la Madeleine (0) and Napierville (0), as well as Dorchester (0.42), Drummond (0.59), Berthier (0.89), Joliette (0.68), Papineau (0.71), Gatineau (0.50) and Pontiac (0.72). Census districts with an incidence rate greater than 3.0 but less than 4.0 are Gaspé-ouest (3.02), Rimouski (3.47), Ste. Hyacinthe (3.51) and Vaudreuil (3.21). And lastly, CDs with a mean crude annual GBS incidence rate greater than 4.0 are Matane (4.39), Montmorency No.2 (4.22), Compton (4.26), Bagot (4.06) and Brome (4.75).

A complete list of CDs for both provinces and their respective crude GBS incidence rates may be found in Appendices H and I.

ANNUAL GBS INCIDENT ADMISSIONS ONTARIO AND QUEBEC, 1983-1989

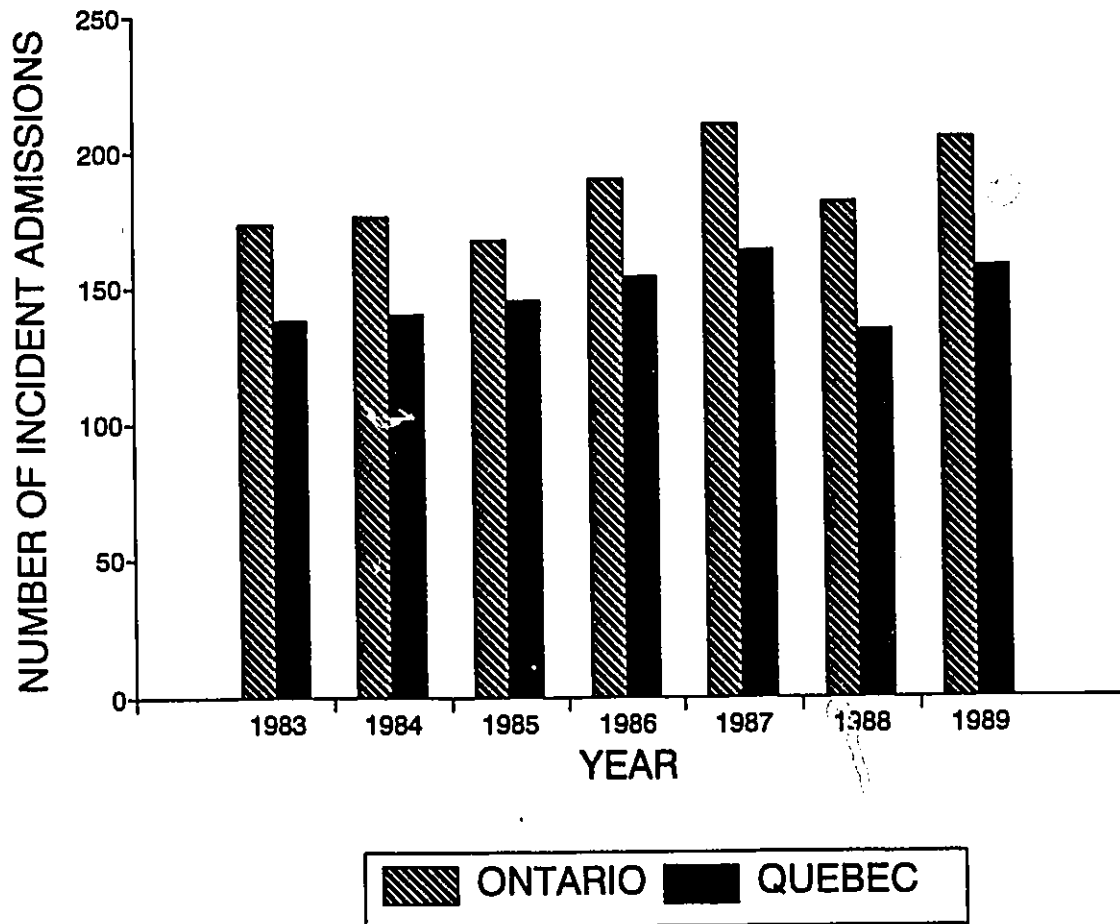


Figure 2: Number of annual incident admissions in Ontario and Québec from 1983-1989. There were 1,302 and 1,031 incident admissions of GBS to acute-care institutions in Ontario and Québec, respectively, during this time-period. The mean number of annual incident admissions is 186.0 for Ontario and 147.3 for Québec.

ANNUAL INCIDENCE RATE OF GBS AGE AND SEX STANDARDIZED

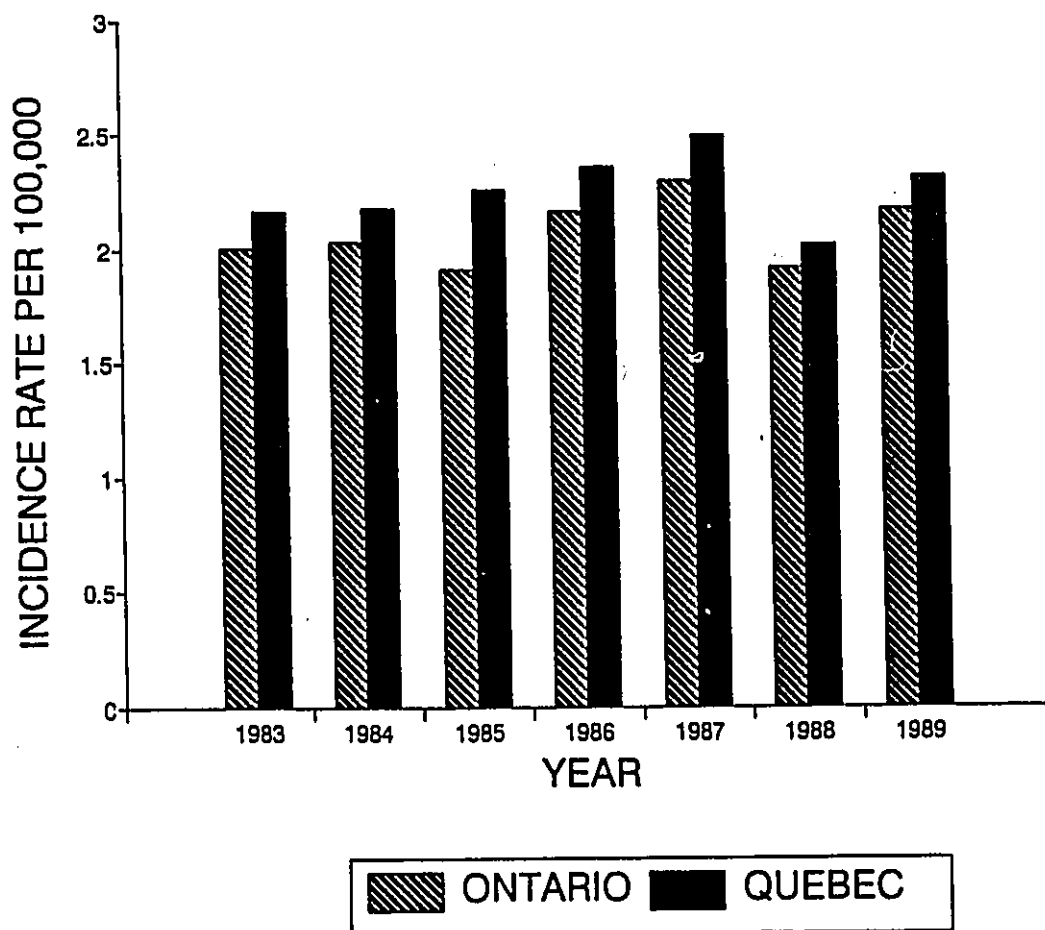


Figure 3: Annual incidence rates of GBS in Ontario and Québec from 1983-1989. Each incidence rate was calculated using the appropriate provincial population estimate (1983-1986) or projection (1987-1989) based on the 1986 census, and then was age-and-sex-standardized to the 1986 Canadian census population, direct method. The mean of these annual incidence rates is 2.07/100,000 person-years for Ontario and 2.25/100,000 person-years for Québec. The difference between these mean values is statistically significant ($p < 0.05$). Note that both provinces had their highest incidence rate in 1987 and their lowest in 1988.

MEAN ANNUAL GBS CASES BY AGE-GROUP ONTARIO AND QUEBEC 1983-1989

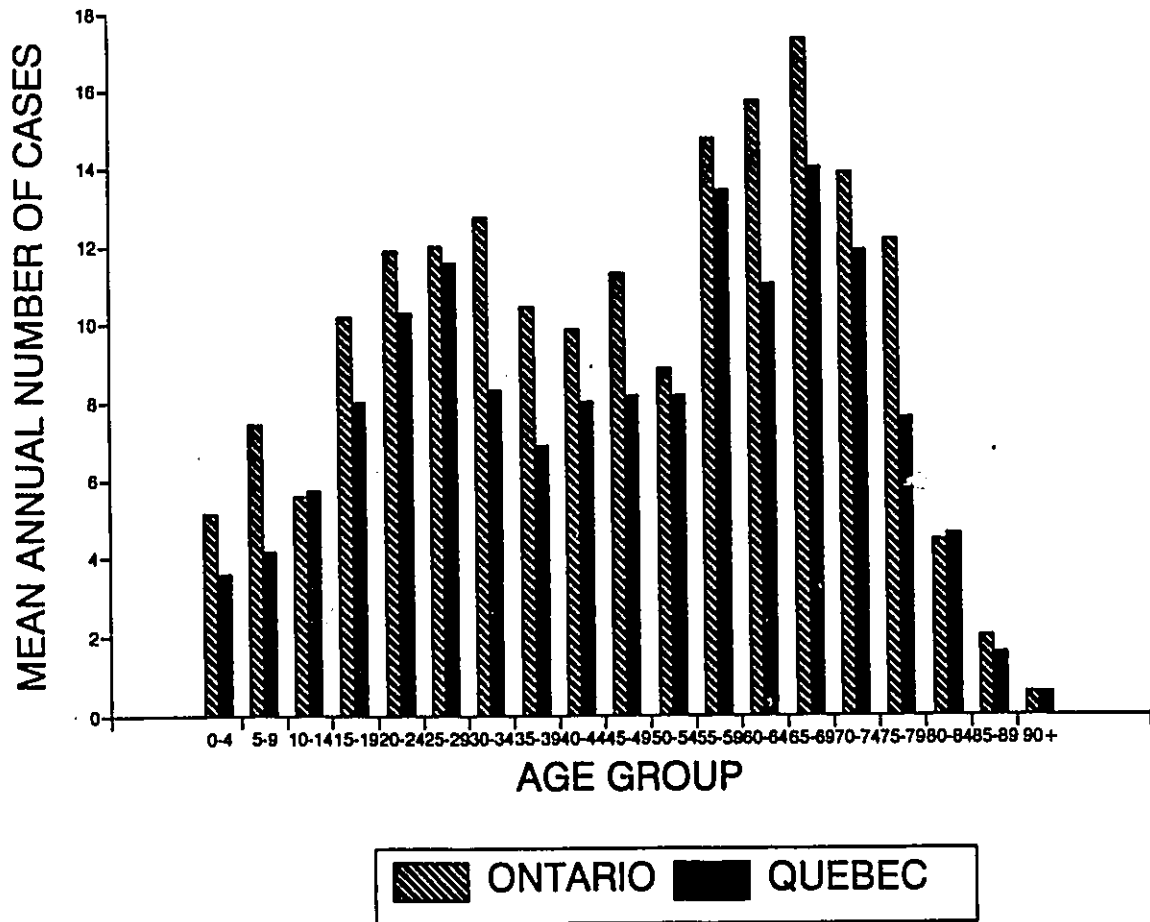


Figure 4: Mean annual number of GBS cases occurring in each province by 5-year age-groups. Both provinces have a major peak at the 65-69 year age-group, and each also have a minor peak - at 30-34 for Ontario and 25-29 for Québec.

MEAN ANNUAL AGE-SPECIFIC GBS INCIDENCE
ONTARIO AND QUEBEC 1983-1989

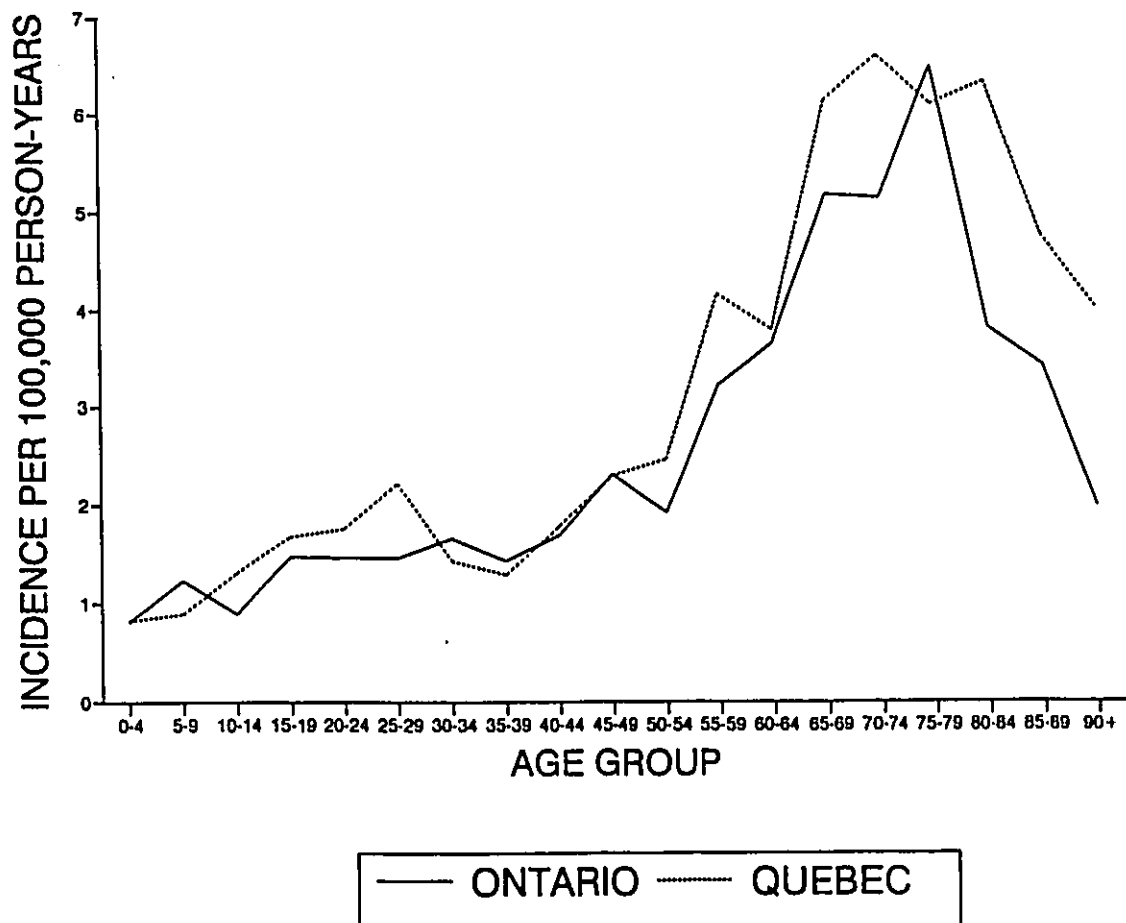


Figure 5: Mean annual age-specific GBS incidence rates in Ontario and Québec from 1983-1989, inclusive. The peak incidence rates of 6.5/100,000 for Ontario and 6.6/100,000 for Québec are found in the 75-79 year and 70-74 year age-strata, respectively. A minor peak in the Québec graph at 25-29 years is less pronounced than the analogous minor peak in Figure 3, and does not have a counterpart in the Ontario graph.

MEAN ANNUAL AGE SPECIFIC GBS INCIDENCE ONTARIO AND QUEBEC MALES 1983-1989

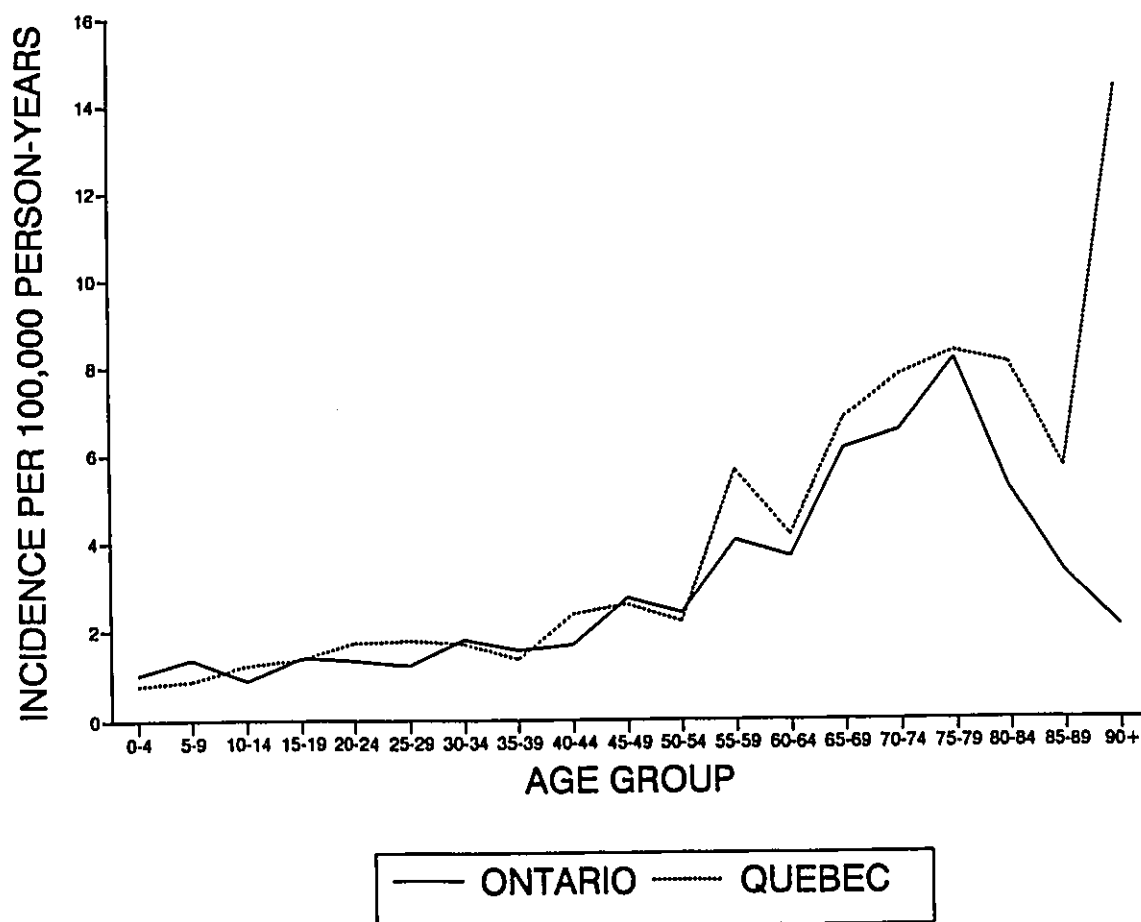


Figure 6: Mean annual age-and-sex-specific GBS incidence rates: Ontario and Québec males, 1983-1989. The peak rate for Ontario of 8.2/100,000 occurs in males aged 75-79 years, and is only slightly less than the rate of 8.3/100,000 occurring in the same age-group in Québec. Both of these rates are less than the incidence of 14.4/100,000 which occurs in Québec males aged 90 years or more. This latter rate is likely due to a small numbers effect, reflecting both the small Québec population in this age-group and the variability that can occur in a small number of cases.

MEAN ANNUAL AGE-SPECIFIC GBS INCIDENCE
ONTARIO AND QUEBEC FEMALES 1983-1989

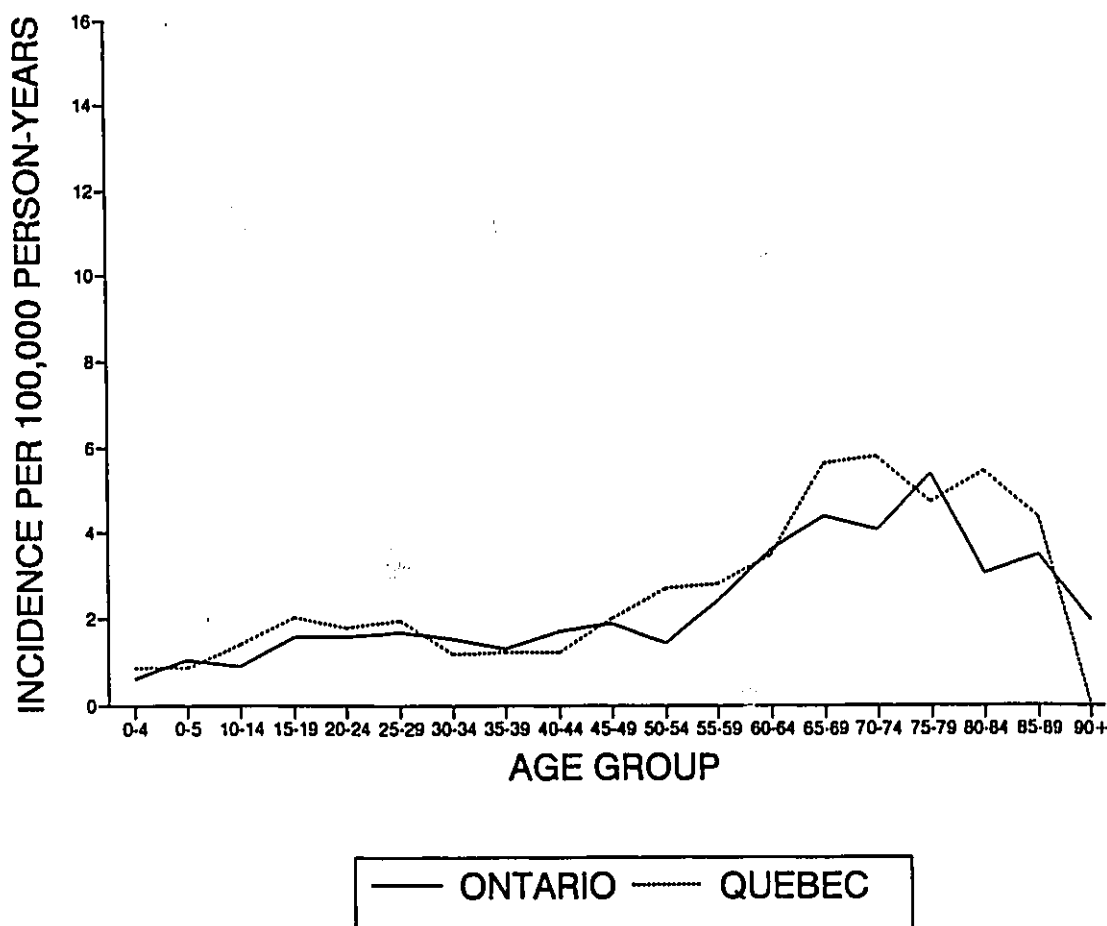


Figure 7: Mean annual age-and-sex-specific GBS incidence rates: Ontario and Québec females, 1983-1989. In Ontario the peak incidence rate of 5.4/100,000 occurs in those aged 75-79 years; while, in Québec, the highest incidence rate occurs in those aged 70-74 years old at 5.8/100,000. Both of these rates are less than the peak male rates seen in Figure 5.

CUMULATIVE MEAN MONTHLY GBS INCIDENCE ONTARIO 1983-1989

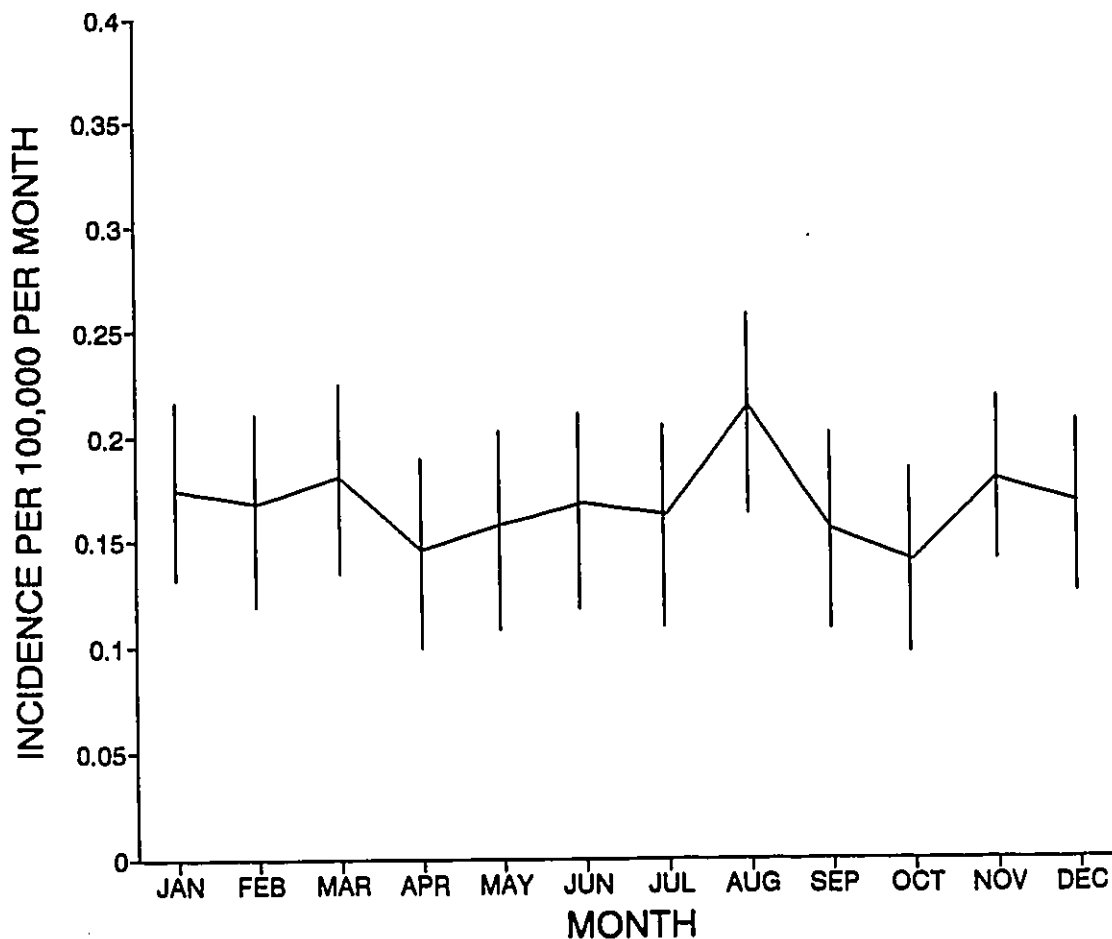


Figure 8: Cumulative mean monthly GBS incidence rates in Ontario, 1983-1989. These data are standardized to a 30-day month. August has the highest number of incident-admissions per 100,000 population per month (0.22), while October has the lowest (0.15). The mean cumulative mean monthly incidence rate is 0.168/100,000. The error bars represent 95% confidence intervals for the true mean of each cumulative monthly value calculated based on the standard deviation of each mean.

CUMULATIVE MEAN MONTHLY GBS INCIDENCE QUEBEC 1983-1989

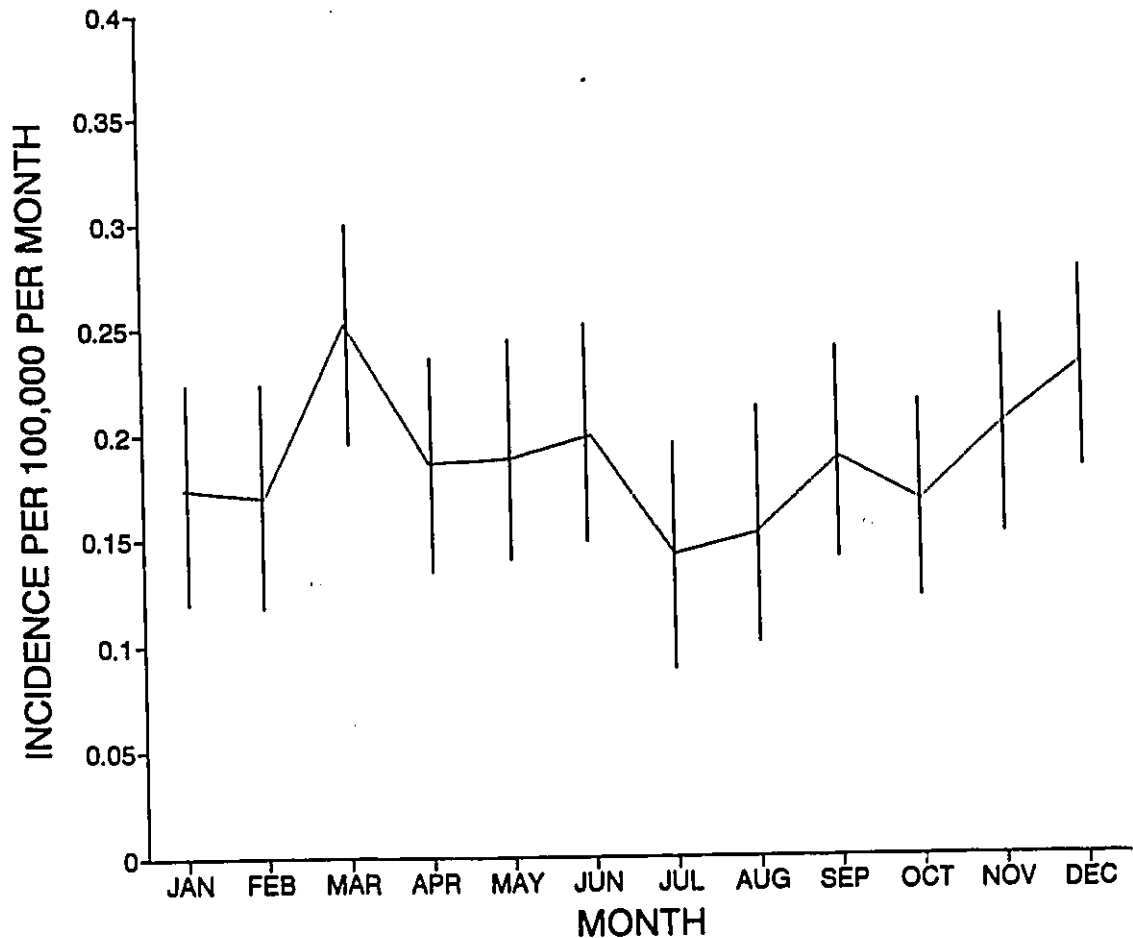


Figure 9: Cumulative mean monthly GBS incidence rate in Québec, 1983-1989. Values are standardized to a 30-day month. March has the highest number of incident-admissions per 100,000 population per month (0.26), while July has the lowest (0.15). The mean cumulative mean monthly incidence rate is 0.188/100,000. The error bars represent 95% confidence intervals for the true mean of each cumulative monthly value calculated based on the standard deviation of each mean.

CUMULATIVE MEAN MONTHLY GBS INCIDENCE ONTARIO AND QUEBEC, 1983-1989

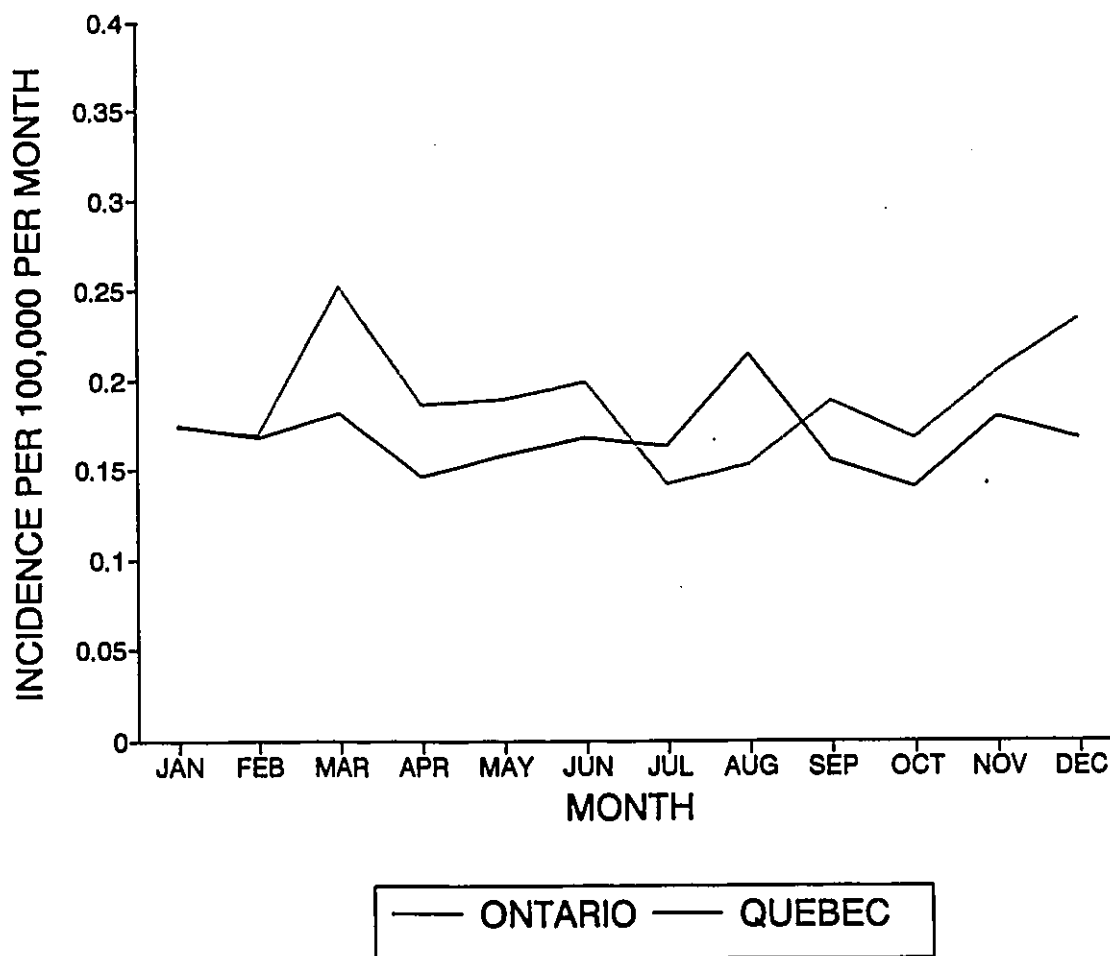


Figure 10: Comparison of cumulative mean monthly incidence rates between Ontario and Québec, 1983-1989. These data have been standardized to a 30-day month. The mean cumulative mean monthly incidence rates are 0.168 and 0.188 for Ontario and Québec, respectively.

GBS INCIDENT-ADMISSIONS BY MONTH ONTARIO AND QUEBEC 1983-1989

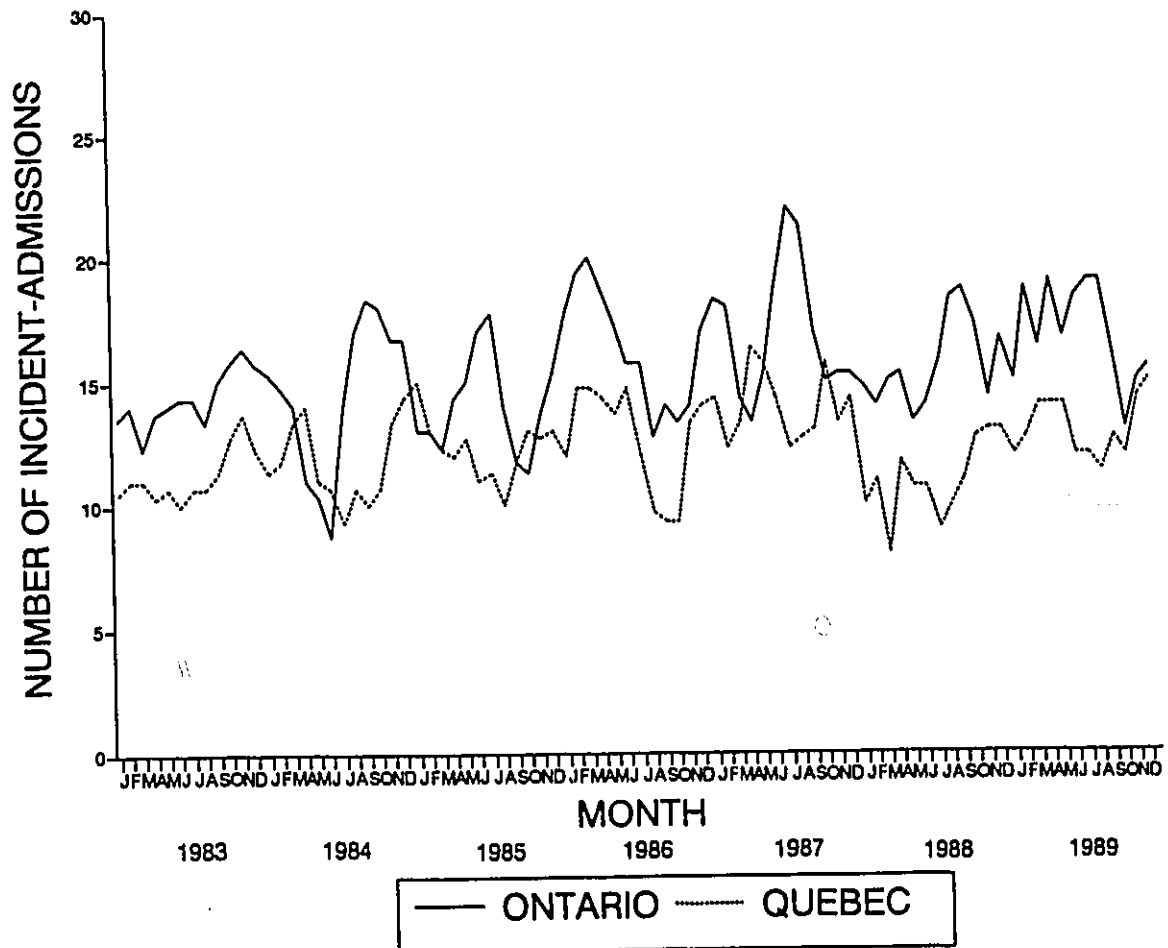


Figure 11: Monthly GBS incident-admissions in Ontario and Québec, 1983-1989. The plotted value for each month is the mean of the month it represents as well as the previous and following months. These data were compared for correlation of case frequencies per month, revealing a correlation coefficient of $(r=)$ 0.093.

NUMBER OF HOSPITAL DAYS PER GBS CASE
ONTARIO, 1983-1989, HMRI DATA

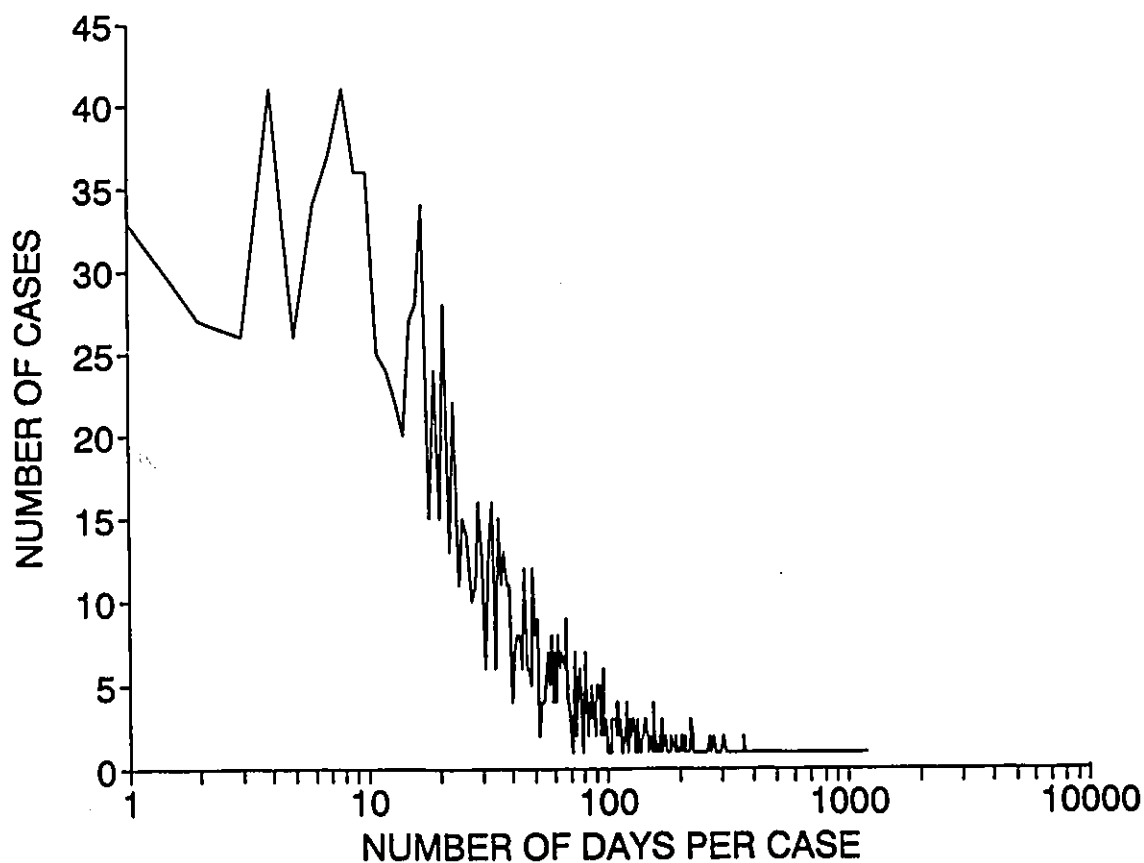


Figure 12: Number of hospital bed-days per GBS case in Ontario, 1983-1989. The number of bed-days per case is placed on a logarithmic axis in order to appreciate the low-end of this Poisson distribution. The range of bed-days per case is from one to 1,196. The mean number of bed-days per case is 54.5.

NUMBER OF HOSPITAL DAYS PER GBS CASE
 QUEBEC, 1983-1989, MED-ECHO DATA

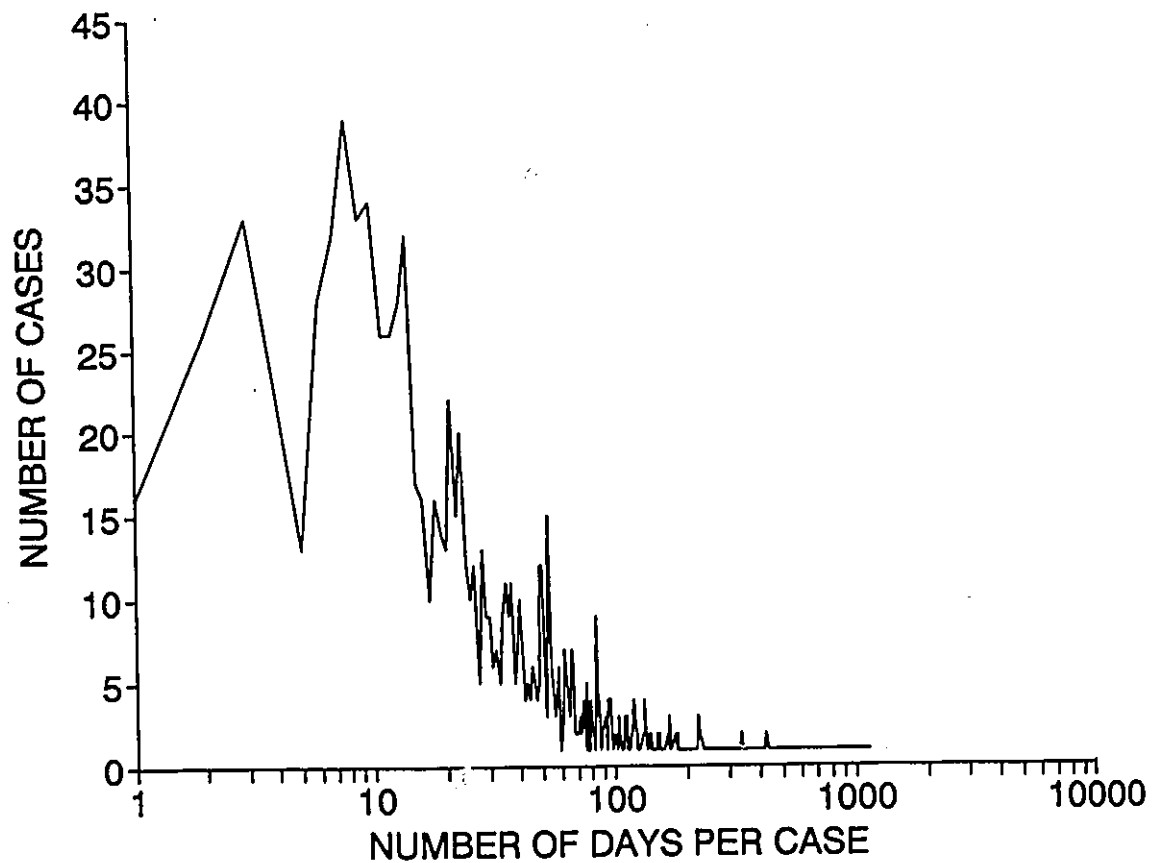


Figure 13: Number of hospital bed-days per GBS case in Québec, 1983-1989. The number of bed-days per case is placed on a logarithmic axis in order to appreciate the low-end of this Poisson distribution. The range of bed-days per case is from one to 1,135. The mean number of bed-days per case is 42.6.

HOSPITAL-DAYS IN FIRST GBS ADMISSION ONTARIO, 1983-1989, HMRI DATA

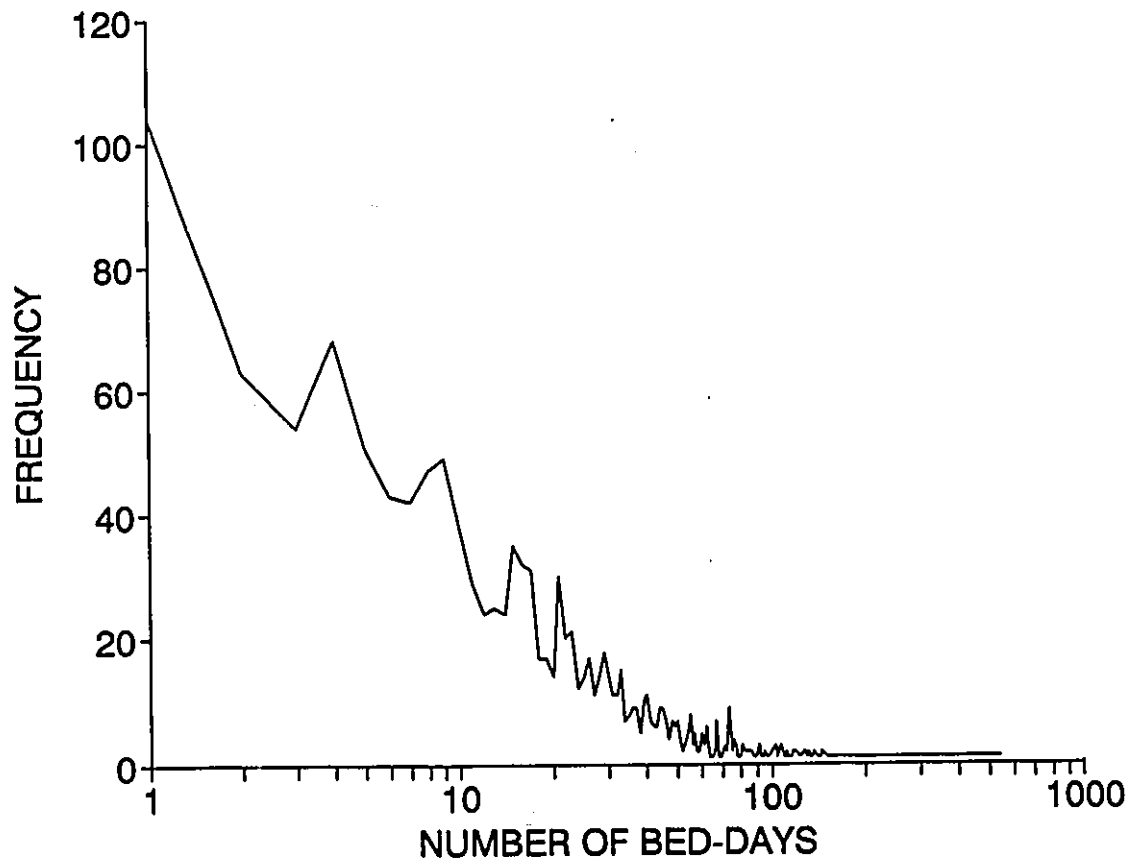


Figure 14: Number of hospital bed-days in incident-admissions of GBS; Ontario, 1983-1989. The range of bed-days is from one to 536; the mean number of bed-days is 24.7. One-hundred and three incident-admissions are of one day.

HOSPITAL DAYS IN FIRST GBS ADMISSION QUEBEC, 1983-1989, MED-ECHO DATA

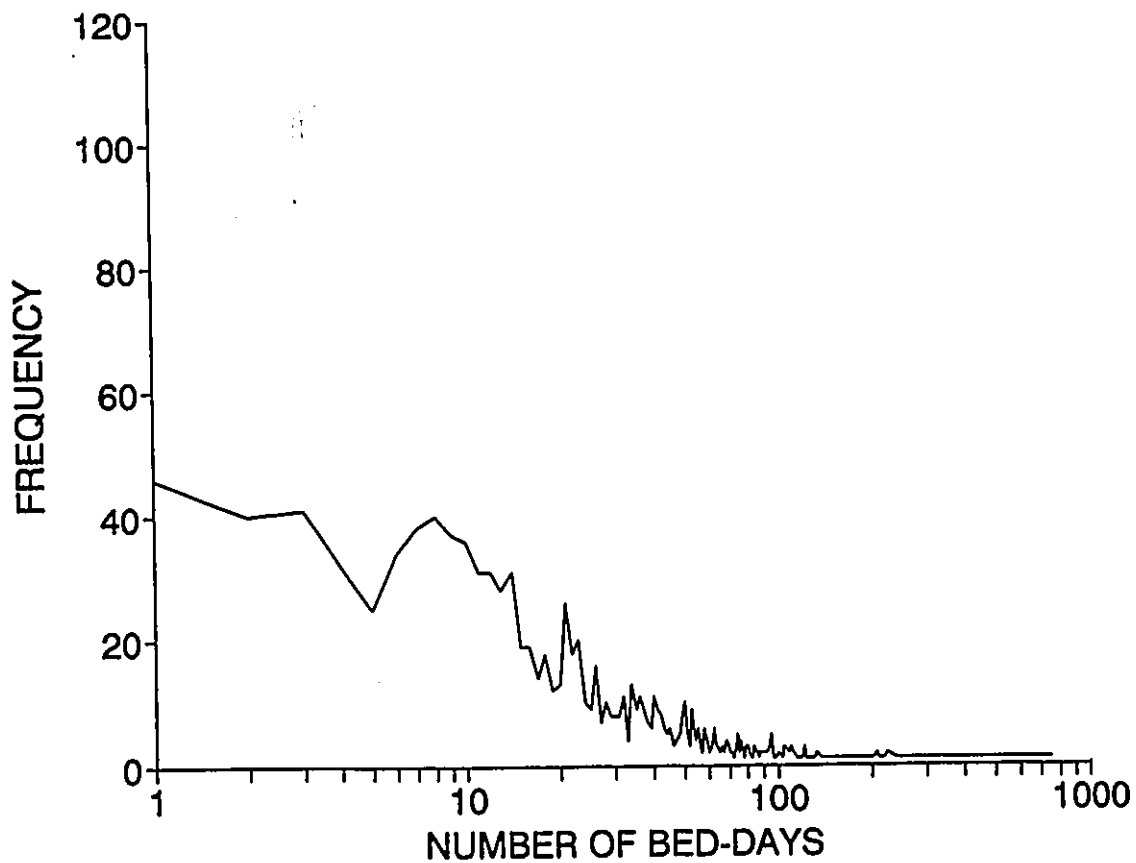


Figure 15: Number of hospital bed-days in incident-admissions of GBS; Québec, 1983-1989. The range of bed-days is from one to 754; the mean number of bed-days is 29.8. Forty-six incident-admissions are of one day.

NUMBER OF ADMISSIONS PER GBS CASE
ONTARIO, 1983-1989, HMRI DATA

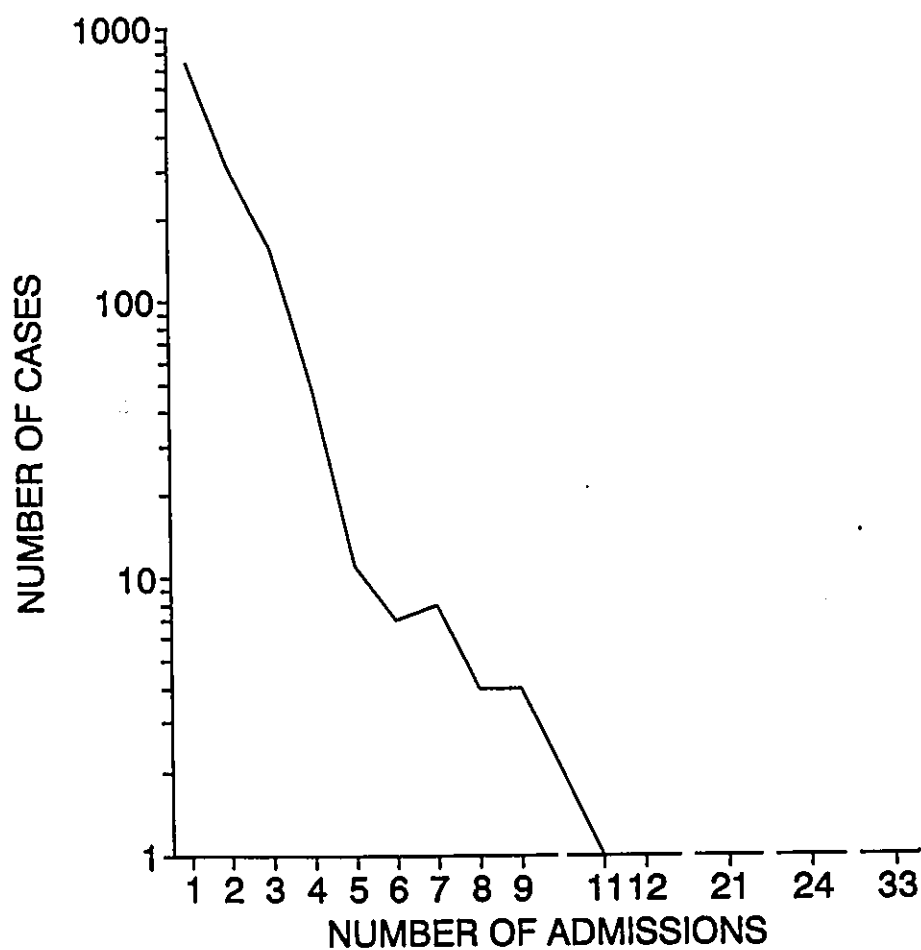


Figure 16: Number of admissions per case of GBS, Ontario, 1983-1989. The range of admissions per case is from one to 33, with by far the most cases having one admission, and, five single admissions of 11, 12, 21, 24, and 33 occurring at the other extreme. The mean number of admissions per case in Ontario is 1.8.

NUMBER OF ADMISSIONS PER GBS CASE
QUEBEC, 1983-1989, MED-ECHO DATA

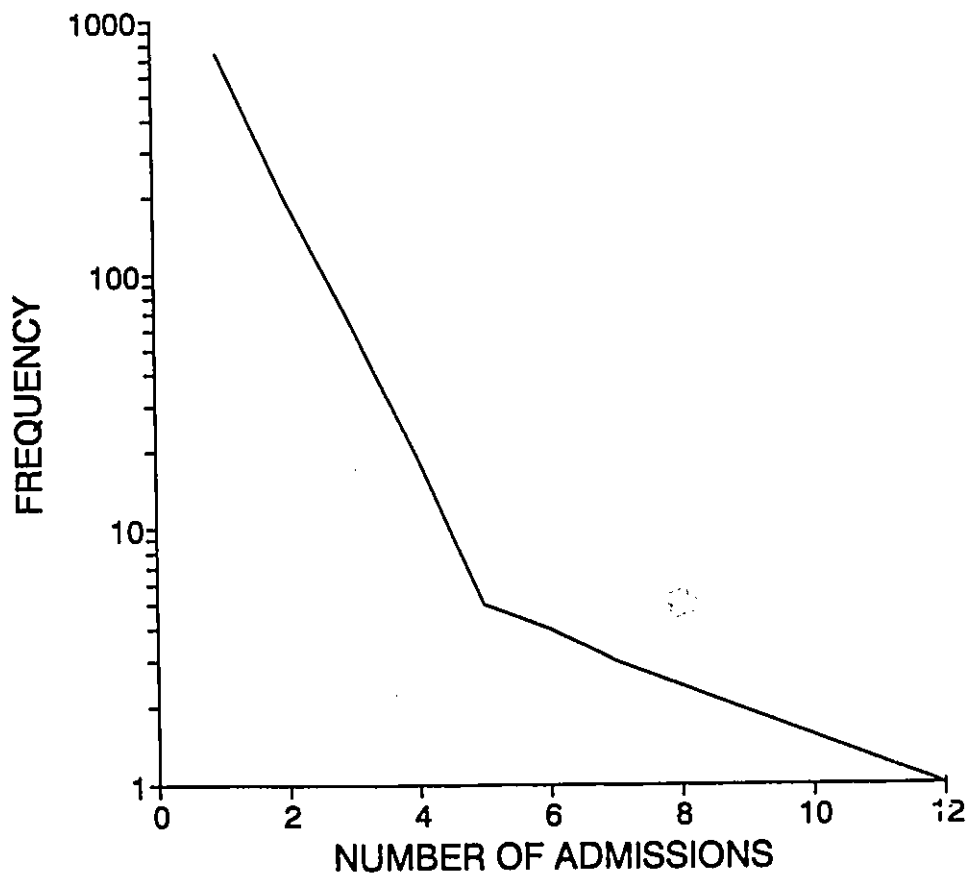


Figure 17: Number of admissions per case of GBS, Québec, 1983-1989. The range of admissions per case is from one to 12, with most cases having one admission and one case having 12 admissions. The mean number of admissions per case in Québec is 1.4.

GBS IN ONTARIO BY CENSUS DISTRICT: 1983-1989

Crude Incidence per 100,000 Population

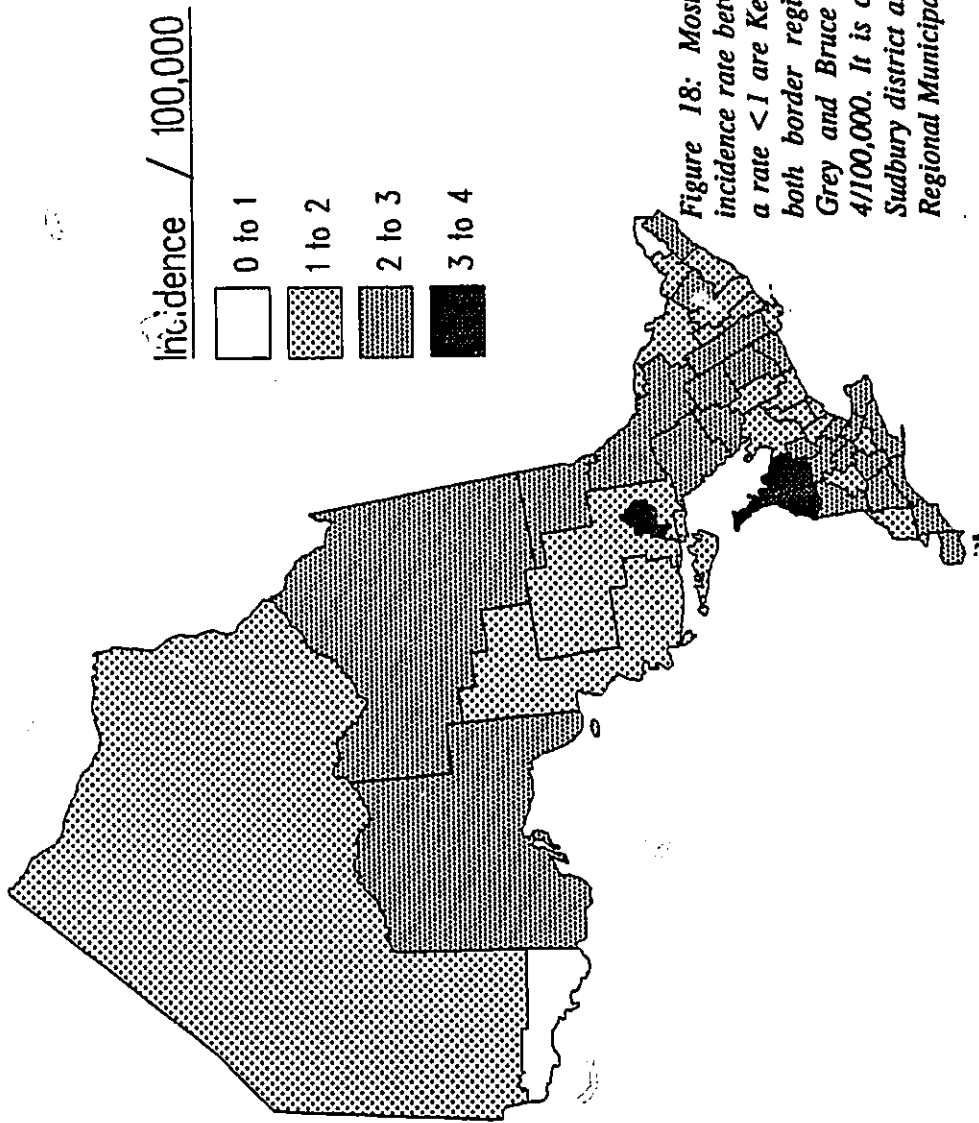


Figure 18: Most Ontario census districts have an incidence rate between 1 and 3 per 100,000. Those with a rate <1 are Kenora and Prescott & Russell which are both border regions. Sudbury Regional Municipality, Grey and Bruce counties have rates between 3 and 4/100,000. It is conceivable that some GBS cases from Sudbury district are misclassified as being from Sudbury Regional Municipality, accounting for its high incidence.

GBS IN QUEBEC BY CENSUS DISTRICT: 1983-1989

Crude incidence per 100,000 Population

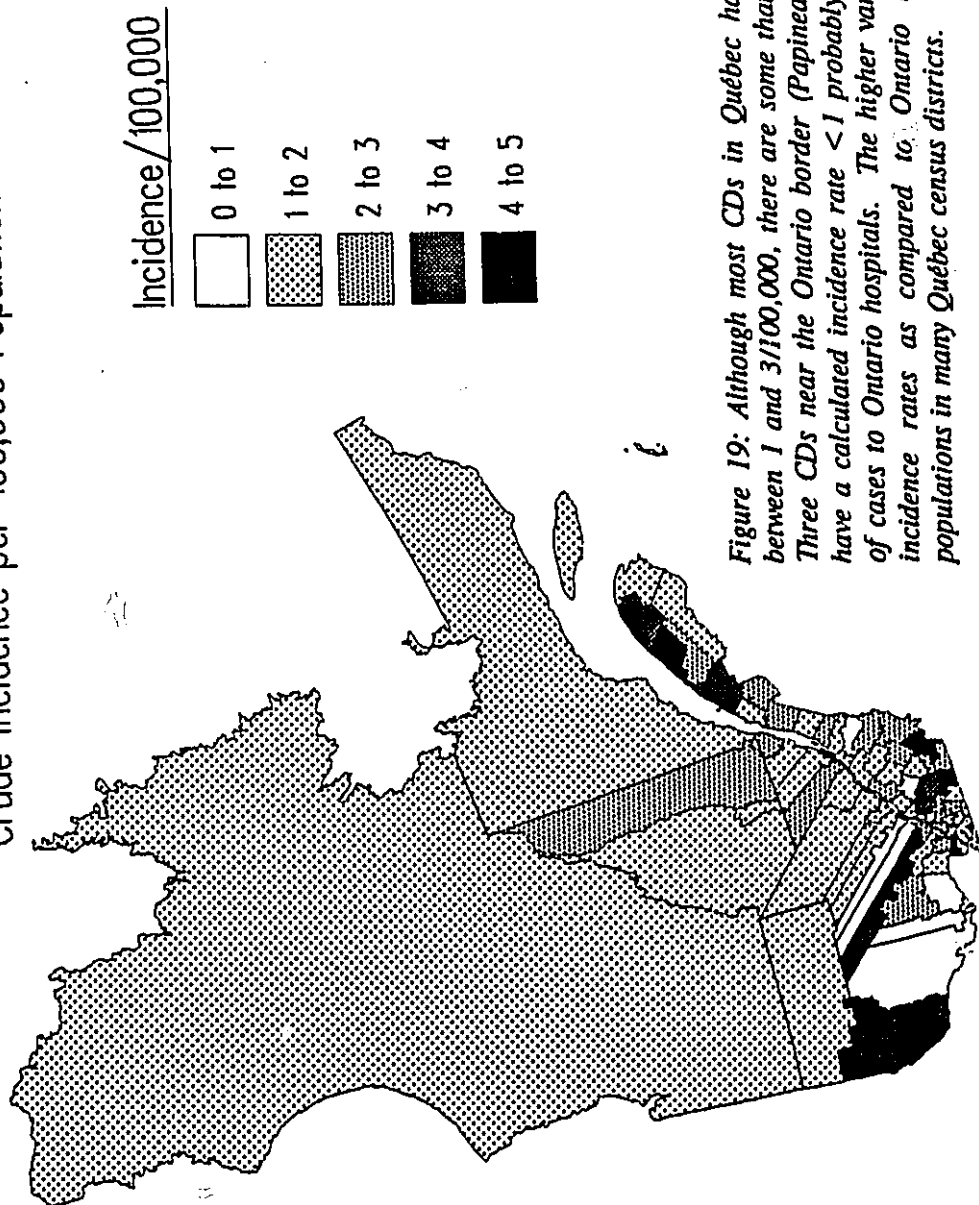


Figure 19: Although most CDs in Québec have a GBS incidence rate between 1 and 3/100,000, there are some that lie outside of this range. Three CDs near the Ontario border (Papineau, Gatineau and Pontiac) have a calculated incidence rate <1 probably because of out-migration of cases to Ontario hospitals. The higher variation in Québec regional incidence rates as compared to Ontario may be due to smaller populations in many Québec census districts.

GBS IN QUEBEC BY CENSUS DISTRICT: 1983-1989

(Eastern Townships)

Crude Incidence per 100,000 Population

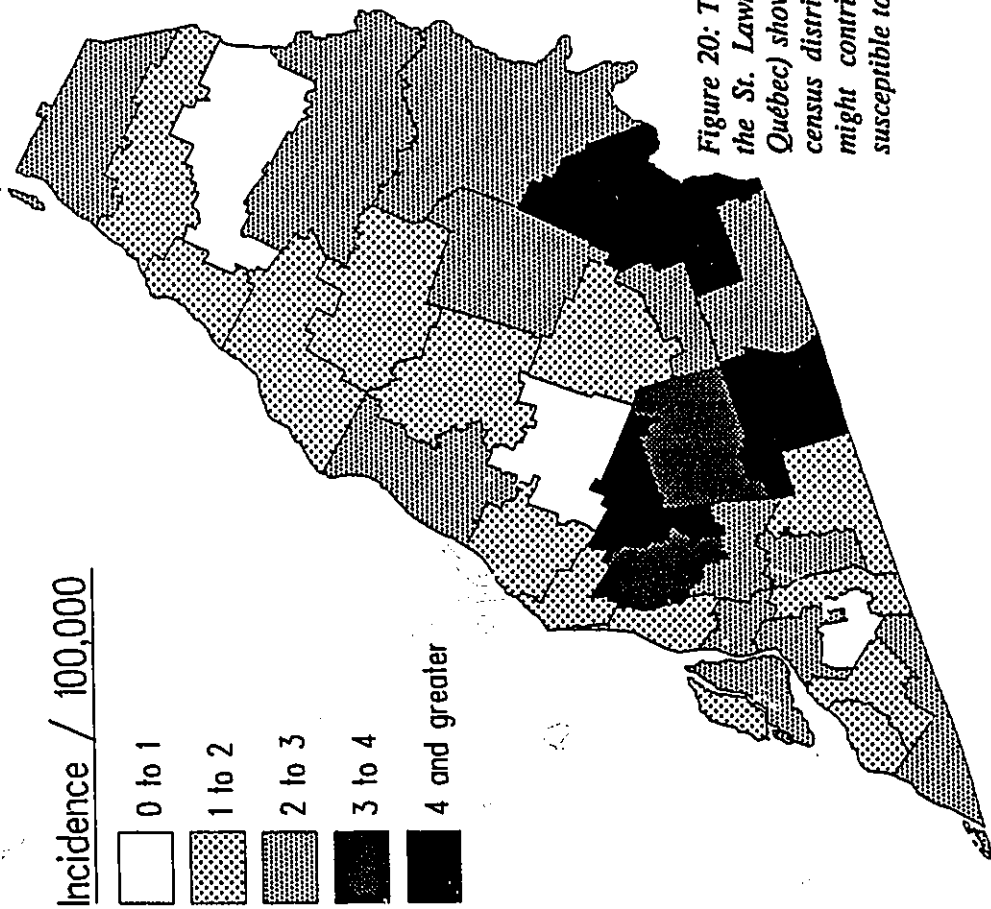


Figure 20: This enlarged view of the southern portion of Québec east of the St. Lawrence River (commonly called "the eastern townships" of Québec) shows the variation of GBS incidence rates in this sector. Many census districts in this part of Québec have small populations which might contribute to the variability in the incidence rate by being susceptible to a small change in number of GBS cases.

Mortality

The number of deaths due to GBS is shown in Table 9. Figures from the CMDB show the number of deaths in each province during the years 1983-1989 that were attributed to GBS. The number of deaths shown for the HMRI and Med-Écho databases are deaths occurring in hospital during any admission of a case of GBS. The number of deaths in 1983-1989 found occurring during incident admissions of GBS in Ontario (not in the table) are 16 for males and 20 for females (for a total of 36), and in Québec are 23 for males and 21 for females (for a total of 44).

Table 9: GBS Mortality in Ontario and Québec, 1983-1989

Province	Ontario		Québec	
Source	CMDB*	HMRI**	CMDB*	Med-Écho**
Number by sex	M:18 F:16	M:28 F:27	M:10 F:11	M:36 F:29
Total	34	55	21	65

* Number of deaths attributed to GBS in this database.

** Number of recorded deaths occurring during an admission in which GBS was listed as a significant diagnosis.

Results of Patient-Chart Reviews

The number of chart reviews requested for each diagnosis is listed in Table 10 along with the number of charts returned for that category. In all, 366 charts were requested and 263 were returned, a returned rate of 72%.

Table 10: Charts Requested and Returned in GBS Study

Province	Diagnosis*	Requested**	Returned
Ontario	357.0	74	60
	357.8	31	24
	357.9	56	41
	375.0	16	8
Québec	357.0	76	62
	357.8	45	19
	357.9	52	40
	375.0	16	9

* ICD-9 diagnostic codes for GBS (357.0), Toxic and inflammatory neuropathy - other (357.8), Toxic and inflammatory - unspecified (357.9), and Dacryoadenitis (375.0).

** Sample size required as calculated using the formula by Lemeshow and Hosmer⁵¹ for stratified random sampling, and inflated by 25%. The requested number of charts was often greater than the number required because the number in the last hospital sampled was more than required.

The final results of the chart reviews are shown in Tables 11 and 12. In the analysis of these results, categories 4 and 5 were considered to be true GBS cases; categories 1 and 2 were considered to be false-positive GBS cases; and, category 3 cases were indeterminate.

Table 11: Panelist agreement on Categorization of GBS cases

Ontario		Québec	
Categorization*	Frequency	Categorization	Frequency
1,1	9	1,1	8
1,2	2	1,2	1
2,2	5	2,2	4
3,3	12	3,3	8
4,4	19	4,4	19
4,5	9	4,5	12
5,5	5	5,5	10

* These numbers indicate the categorization combinations of the neurologists on the panel.

Table 12: GBS Chart Review Case Categorization

Category *	Ontario	Québec
1-2	16 (8A, 8B)**	13 (6A, 7B)
3	12 (2A, 10B)	8 (4A, 4B)
4-5	33 (23A, 10B)	41 (29A, 12B)
Total	61 (33A, 28B)	62 (39A, 23B)

* Charts were categorized by the panelists based upon how these compared to the case definition of GBS.

** The letters 'A' and 'B' refer to the institutional stratum from which a record was selected.

Sixteen of the total of 61 Ontario cases (26.2%), or 16 of 49 cases (32.6%) having enough information available to judge the validity of a case were found to be false-positive GBS cases. For Québec cases, 13 of 62 cases (21.0%), or 13 of 54 cases (24.0%) if cases without enough information were excluded from the analysis, were judged to be false-positive.

The odds ratio pertaining to the likelihood that a false-positive case is from a "stratum B institution" is 1.3 or 2.3 in Ontario, depending on whether indeterminate cases are included in, or excluded from, the calculation, respectively. Corresponding odds ratios for Québec are 2.4 or 2.8, respectively.

Only 4 Ontario and 2 Québec GBS cases that were categorized as '1-2' (not GBS) had an incident admission length of less than 4 days. Half of each province's cases fitting this description were from institutional stratum B.

Measurement of False-negative GBS Diagnoses

Of the 141 returned separation sheets corresponding to records of admissions having the diagnostic codes 357.8, 357.9 or 375.0 attached, there were none with written diagnoses compatible with GBS. No false-negative diagnoses were found by this method.

Compensation for False-positive Diagnosis Rate

If the false-positive cases of GBS are accounted for in the calculation of the mean age-and-sex-standardized GBS incidence rate in each province the incidence will decrease. The mean annual number of incident admissions in Ontario from 1983-1989 was 186.0. If the false-positive fraction of these cases is taken to be 0.262, then the mean annual number of incident admissions of true cases of GBS is $186.0(1-0.262) = 137.3$. Recalculating the incidence rate for Ontario results in a new value of 1.51 GBS cases per 100,000 person-years.

For Québec, the mean annual number of incident admissions within the time period of interest is 147.3. If the fraction of false-positive cases within these is considered to be

0.21, then the mean annual number of true cases of GBS in Québec is $147.3(1-0.21) = 116.4$. The incidence rate of GBS in Québec would be 1.78 GBS cases per 100,000 person-years based on this new frequency.

DISCUSSION

Utility of Hospital Service Data for Disease Surveillance

Canadian hospital service data is not collected for the purpose of health research, but for administrative and financial evaluations. Despite this, the Med-Écho and HMRI databases are amenable to community health research. The databases with which we are concerned record only hospital admissions and not visits to emergency departments or clinics within the health-care institution. Therefore, a condition which is studied through these databases should have a degree of morbidity or potential mortality that would require hospitalization. Epidemiological insights into conditions meeting these criteria are possible through access to, and manipulation of, these data.

The type of information collected within databases and made available to researchers both enables and dictates the limitations of the research. The presence of a unique identifier or of relatively unique identifiers (e.g. - social insurance number, name, address) in a database would facilitate many epidemiological studies, but this information might also enable identification of persons whose admissions have been recorded in the database. This situation would create ethical problems; and therefore, these types of variables are not available to researchers that have access to HMRI and Med-Écho data. While this may hinder the progress of research, it no doubt reassures our society about matters of privacy, ultimately enabling the conduction of health research using these data. Absence of unique identifiers makes record linkage a more complex procedure. Variables that describe individuals, such as age, sex and place of residence, are instrumental in probabilistically determining whether the identity of an individual in two records is the same. These variables are more useful if they are accurate and precise.

Validity of the Data

The validity of HMRI and Med-Écho data is an important concern for both of these relatively epidemiologically untried databases. Issues here include the completeness and accuracy of data entry as well as the accuracy of diagnosis and of coding diagnoses and procedures. A detailed analysis of data quality was not performed; however, some issues that became evident during this study will be outlined.

The most unique variable in the HMRI database is the health-care number. In Ontario, up to the end of 1989, theoretically one number was issued to each family (Med-Écho did not provide a health-care number variable in its database). This valuable identifier could have been more useful than it was in this study if it were present in more than the 81% of records in which it was found. This rendered it less useful for record linkage purposes than other less unique variables, e.g. - birthdate.

Birthdate and sex were completely entered in both databases, increasing the utility of these variables for record linkage. However, if one accepts that the health-care number acts as a unique variable for this study, and is reliably entered, then it can be used to evaluate the accuracy with which the birthdate variable is entered into the HMRI database. Sixty of 62 record-pairs linked in the second algorithmic step (which had been brought together because of their identical health-care numbers) had birthdates that differed either by one digit or by a rearrangement of the year, month and/or day fields. These likely are data entry errors; thus, the HMRI data used in this study had birthdate entered incorrectly in at least 60 of 3,449 (1.7%) records representing admissions of GBS. The same problem was not found in the Med-Écho database; however, Med-Écho did not provide a variable with the specificity of a health-care number. Therefore, we

cannot say with certainty whether the lack of detection of birthdate errors in Med-Écho data means that data entry was superior in this database. Sex appeared to be miscoded in a few HMRI records (but not to as much degree as in the case of birthdate), and appeared not to be miscoded in the Med-Écho database.

Postal-code was essentially a different variable in each database. The data provided by HMRI contained six-character codes while Med-Écho contained only three, making this variable potentially a better tool with which to link HMRI records. Because values were present in only 54% of HMRI records compared to 94% for Med-Écho, this potentially useful six-character HMRI variable may have been less useful than the three-character Med-Écho variable.

Residence codes were present in close to 100% of records in both databases. These were of slightly different composition in each database - in Ontario the four-digit code has two digits each representing census division and municipality, while for Québec the five-digit code (code municipale du bénéficiaire) has two digits for census division and three for municipality. In each database a match on this variable increased the probability that record-pairs represented the same person, but the weight given to outcomes of comparing this variable was not as great as one might expect because of the frequency of true change in the value of residence code.

The validity of diagnostic codes present in these data is dependent upon the accuracy of the physician's diagnosis, including the use of correct ICD-9 nomenclature, and upon the accuracy with which medical records departments translate and transcribe physician's written diagnoses into ICD-9 codes, as well as the accuracy with which these codes are

entered into the database. The chart review that was performed addressed all of these steps when the validity of GBS cases was concerned - i.e. - the detection of false-positive cases. The search for false-negative cases of GBS did not include a complete check on the validity of the diagnosis as written by the physician. By only examining the written diagnosis of the physician along with the diagnostic code into which it was translated, we might have found cases which had been diagnosed by a physician who had written the name of a condition accepted by many as being a synonym for GBS, but which had an ICD-9 code other than 357.0. No such false-negative translation errors were found. Unfortunately, this does not rule out the possibility that the physician had misdiagnosed the case. Our search for false-negatives was therefore incomplete; however, it should be remembered that a physician probably would not record much information that is relevant to GBS in the medical record if she/he suspects a different diagnosis. Also, no search for false-negative cases could ever be complete because of the multitude of diagnostic codes under which a case of GBS theoretically could be hidden, and, the impossibility of accounting for cases that are not admitted to hospital.

Migration of GBS Cases Across Borders

Migration of a province's residents across borders to obtain health services leads to an incidence rate measurement problem because of the differential misclassification (of the diagnosis) of a province's residents. Error in the number of cases within a province due to in-migration of cases was eliminated in this study through access to a variable representing the person's place of residence. Out-migration is another story. In this study, out-migration of GBS cases to the other province in the study was measured; however, out-migration to other Canadian provinces or territories, and to other countries was not evaluated.

Although the entire effect of out-migration of GBS cases across provincial borders is not known for this study, the 19 cases of Québec residents that are present in HMRI data and cannot be linked to records in Med-Écho data, and the 6 records of Ontario residents found in Med-Écho data which could not be linked to records in HMRI data would seem to indicate that the amount of cross-border migration of GBS cases is small. These findings are compatible with what is known about the rapid clinical progression, and the severity of GBS; any person afflicted by this condition would not likely seek health-care outside of their home province unless they were outside of the province at the time of its onset, or lived in a border city/town that is serviced largely by health services outside the province.

The small number of cases exchanged between Ontario and Québec therefore are probably, in the worst scenario, representative of the number of cases being exchanged across other provincial boundaries. Extraction, from all provinces, of records having a diagnosis of GBS from HMRI data would likely decrease the number of false negatives lost to out-migration; however, the incomplete participation of some provinces' institutions in HMRI might prevent the capture of all cases. The number of cases out-migrating to the United States or other nations is likely even smaller than the number exchanged between provinces. Finding cases admitted outside Canada might be possible if records of provincial payments for insured health services performed outside the province are examined.

Mortality

The number of deaths attributed to GBS in the CMDB was not more than the number of deaths occurring during cases of GBS as recorded in each database. Therefore, it seems

that the principal cause of death in some of these GBS cases was not attributed to GBS. The number of deaths occurring during only incident admissions of GBS is alone greater than the number of deaths attributed to GBS in the CMDDB for Québec persons of both sexes and for Ontario females. This is an important finding if one believes that in incident admissions of GBS death is more likely to be attributed to GBS. These data suggest that the number of persons dying before reaching hospital and therefore not having a chance of being entered into the appropriate hospital-service database is minimal, if this in fact occurs at all. These findings concur with what has been stated by Arnason,⁴ concerning the progression of GBS to respiratory paralysis. He states that respiratory paralysis does not occur faster than 72 hours, which, in Ontario and Québec, should allow enough time for an afflicted person to get to hospital. Here, if a diagnosis is correctly made, the admission will be entered into the database.

Nosologic and Clinical Considerations of GBS

The term 'syndrome' is defined as a set of signs and symptoms which occur together.⁵³ GBS is a syndrome because it lacks a specific etiologic agent or mechanism. It is important to note that for any one individual afflicted with GBS some of the signs and symptoms that make up its definition may be missing; as well, some others may be present which do not fit the definition. The physician making a diagnosis on an individual whose illness does not clearly match the case definition of GBS may have a difficult classification to make.

This task is not made easier by the complexity of variant forms of GBS and the controversy surrounding their inclusion in its definition. Separate definitions for each of these variants have recently been described,⁵⁴ but for the time-period of this study

these were not clearly laid-out for physicians nor uncritically accepted as variants of GBS. In modern practice the strongest evidence for GBS is provided by electrophysiologic changes consistent with a demyelinating polyneuropathy.⁵⁵ This will improve the classification in those centers having the technology available to perform these tests. A problem presented by this situation is that primary care centers may be unable to make the diagnosis if it is dependent upon these electrophysiologic tests.

In this study, I restricted the number of times that a person can have GBS to one. Recurrent GBS has been described,⁵⁶ but the debate about the differentiation between this condition and CIDP continues. Therefore, if a person was readmitted with a diagnosis of GBS in this study, it is considered an extension of the same GBS episode rather than a new event. Furthermore, assuming that there is no increased risk of a subsequent case of GBS from a primary case, the risk for a person to get GBS a second time would be extremely low, and would likely represent less than one case overall.

Record Linkage

Record linkage studies commonly involve two separate databases. This study differs from the classical conception of record linkage in that it involves internal linkage of records within each of the HMRI and Med-Écho databases. It also differs because of the type of variables present in each database. Neither of these databases have variables for patient-name or address. This eliminates two relatively unique identifiers as well as some of the process of record linkage, particularly the need for dealing with soundex codes of names.⁵⁷ As a result, the theory behind record linkage in this study is simple.

The gold standard for record linkage is intuition (personal communication - Joan Lindsay, 1990), because only an exhaustive review of every hospital chart represented by each record in a case of GBS could evaluate the accuracy of this procedure. A complete review of charts would require either travel to a large number of institutions to review the charts, or acquisition of a copy of each chart. Each of these options would create immense logistical and ethical problems.

The record linkage performed in this study had several unique characteristics. The use of three sorting variables to sort the datasets (used in conjunction with admission date and discharge date) before the application of an algorithm brought records having the same value for the sorting variable to adjacent positions in the dataset. This allowed only adjacent records to have a chance of being linked by the algorithm - a property of these simple algorithms that differs from GIRLS, which compares all record-pairs within a block (blocked by the sorting variable). Although comparison of adjacent records only sometimes prevents two records with the same value for a relatively unique variable from being linked (if an intervening record has a different or missing value), our method worked because of the number of other variables on which the records could match; because of the manual linkage steps; and, also because there were three algorithms used in each record linkage procedure.

The number of records from which weights were calculated for each dataset (500) was determined arbitrarily. Newcombe⁵⁷ recommends that about 10,000 records be used; but, clearly this suggestion is not helpful when one is dealing with datasets of the size used in this study. It may be that the weights obtained by using such a small number of records are not as accurate as they might be if a larger number of records were used for

these calculations, but the record linkage algorithms worked adequately as indicated by the few record-pairs that required manual linkage.

Because the weights of variable-comparisons are calculated based on a judgement of the frequency with which record-pairs match in this sub-set of the dataset, and because computerized record linkage is simply a computerization of a series of decisions about the similarity of records, the number of records chosen to calculate weights (and the fraction of the dataset which that number represents) is not, ultimately, important. What is important is that the researcher realize that if a larger fraction of a dataset is used to calculate weights, then the record linkage procedure will have a better chance of being efficient. However, the record linkage process may not need to be computerized if this is the case. It could be performed manually for the whole dataset since this is necessary anyway for the sub-set upon which weights are to be calculated. Conversely, attention to manual linkage steps between computerized steps in a record linkage program like ours becomes very important if the data sub-set used to calculate weights is small.

The algorithms developed for this study are probably specific for use on studies of GBS. Certain characteristics about the occurrence of GBS enabled a high degree of certainty about the validity of linked record-pairs. In HMRI data, the health-care number, which is family-specific, functioned essentially as a unique identifier because of the absence of transmission of this condition from person to person. The calculated weight for this variable was actually infinity, but a value of 500 was given in order to make the numbers and calculations involved comprehensible. Also, persons of all ages can be affected by this syndrome, making the variable birthdate a more valuable linkage tool for a group of records selected without an age bias (as was done in this study).

GBS Descriptive Epidemiology

GBS is a rare disease. Because of this, an advantage of this study over previous ones is the size of the population from which cases were taken. Community-based studies of GBS occurrence, involving smaller populations required long periods of time to accumulate sufficient person-years for incidence rate estimation. In some studies, so few cases accumulated that the accuracy of the GBS incidence rate estimate might be questioned if random fluctuations of such small case frequencies are considered.

In terms of the number of GBS cases involved, this study supercedes any previous study concerning the community incidence rate of GBS. The results of record linkage of HMRI and Med-Écho data indicate that as many as 2,381 GBS cases were admitted to institutions in Ontario and Québec from 1983-1989. Even after accounting for the maximum proportion of these cases that might have been false-positive misclassifications of GBS, the total number of true cases would still be 1,662. This number is much larger than the number of cases present in most other studies.^{12,13,16,17,18,20,22-27}

The annual number of GBS incident admissions and the annual incidence rate of GBS in each province (standardized to the 1986 Canadian census population) enable evaluation of the trend in incidence rate as well as comparison of the calculated incidence rate of each province. As expected, the mean annual number of cases is larger in Ontario because of its larger population. When the incidence rate is calculated and standardized to the 1986 Canadian census population two phenomena become apparent. The first concerns the consistently greater annual incidence rate of GBS in Québec. There is a 0.28 cases per 100,000 person-years difference between the mean annual incidence rates (2.02 in Ontario, 2.30 in Québec) when this mean is calculated using the 1986 provincial

census population as the denominator. When calculated using the provincial population estimates and projections of off-census years in the denominator, the mean annual incidence rate in Ontario is 2.07, and in Québec is 2.25. This difference is statistically significant ($P < 0.05$). While it is tempting to attribute this difference to some provincial etiological difference such as a difference in immunization policies - for example the use of OPV in Québec as opposed to the use of IPV in Ontario during the years of interest - the more conservative approach would be to consider the provincial differences in case documentation including the inherent differences between the two databases, or the differences in the approach of this study to each of these databases.

There was no indication that there is a difference between Ontario and Québec physician's diagnosis of GBS from the chart reviews performed. The only indication that there might be a difference in case documentation between the provinces comes from the number of records extracted for each diagnosis of interest. Whereas the number of records extracted having ICD-9 codes 357.0 and 375.0 are proportionately less from Med-Écho data (as would be expected with Québec's smaller population and the smaller number of year's data selected), the number of records with codes 357.8 and 357.9 is greater in Québec, indicating that there is a difference either in GBS definition, or translation of written diagnoses into ICD-9 codes between these provinces.

In addition, the difference in incidence rate between the two provinces may have occurred because the two databases differ in their use of diagnostic codes. HMRI data specifies whether a coded diagnosis was the "main" diagnosis - defined as the diagnosis responsible for the highest percentage of bed-days, the "primary" diagnosis - best defined as the reason for admission, a "secondary" diagnosis - indicating the diagnosis of a

complication, and, a "tertiary" diagnosis - indicating an additional diagnosis not affecting the hospital stay to any significant degree. In contrast, Med-Écho lists four "diagnostic finale" codes indicating in order of priority the reason that the hospital admission occurred.

Finally, the provincial difference in incidence rate might have been affected by the difference in the record linkage procedure used for each dataset. There was no variable with the specificity of a health care number in Med-Écho data, making it more difficult to internally link records in these data. Failure to link records inflates the final number of cases obtained. Absence of data from 1980 and 1981 in the Québec record linkage procedure may have decreased the number of cases that were removed which were actually readmissions of GBS cases beginning before the period of interest.

The second phenomenon that is apparent in Figure 3 is that the GBS incidence rate in both provinces is highest in 1987 and lowest in 1988. There are not enough years of data to solidly support an etiological hypothesis which might explain these findings, but these data may suggest that there exists some factor which influences the incidence rate of GBS in both provinces simultaneously. Because these data were extracted from a different database for each province that is administrated at a provincial level, these covariations are likely not dependent upon forces acting at the administrative or surveillance aspects of GBS case counts.

The mean annual GBS incidence rates that were calculated in this study using hospital-service data before correction for false-positive misclassification of GBS cases are higher than results obtained in some previous studies. If the results of our chart reviews are

accounted for in the estimation of GBS incidence rate, then the provincial incidence rate rates would become 1.51 and 1.78 GBS cases per 100,000 person-years in Ontario and Québec, respectively. These values are closer, but still higher than those found in most larger previous studies.^{58,59,60,22,26} The external validity of the results of these studies is unknown. Because this is the largest community study of the occurrence of GBS that involves the entire population of the community to which the study pertains, we should compare it to the studies by Larsen²² in Western Norway and Hankey²⁶ in Western Australia which both found 109 GBS cases and had incidence rates of 1.14 and 1.35, respectively. It may be important to note that Larsen's study took cases from the years 1957-1982, and that this long span of years may have been one reason for that study's low incidence. There was much debate about the boundaries of the case definition of GBS during the 1960's and 1970's with more neurologists accepting an increasing number of variant conditions as the growing field of immunology offered etiological theories that stimulated thinking in terms of etiological definitions as opposed to anatomical/clinical definitions.

The studies by Schonberger et al,³⁰ and Breman and Hayner,⁶⁰ obtained incidence rates of GBS occurring in unvaccinated populations in 1976-1977. These studies had 332 and 87 cases of GBS, and found incidence rates of 0.97 and 0.90 cases per 100,000, respectively. It should be realized that Influenza-A vaccination is given primarily to elderly persons in preparation for the influenza season and that eliminating this vaccinated group from a population survey for GBS would subtract out individuals from age-strata known to have higher incidence rates of GBS (as demonstrated by this study). The age bias present in these studies would have the effect of lowering the observed incidence rate of GBS in the study population. Johnson's study⁵⁹ of US Army recruits

obtained an incidence rate of 1.50 and was probably affected by the same type of age bias.

The mean annual number of GBS cases in each 5-year age-group (Figure 4) shows what those in the health services would know from their experience - that there is a peak frequency of cases that occur in the 65-69 year age-group and another smaller peak that occurs in those around 25-34 years-old. When incidence rates are calculated in these age-groups (Figure 5), there are again major peaks in the older age-groups, but these are shifted to slightly older strata - 75-79 in Ontario and 70-74 in Québec. There also remains a slight peak in the 25-29 year age-stratum in Québec, but no discernable minor peak in incidence rate is present in the Ontario data. When further analysis of these data is performed by also stratifying on sex (Figures 6 and 7), it can be appreciated that the age peak in older persons that was present in Figure 5 in both provinces is mainly due to the higher incidence rate observed in males of these age strata. It also can be seen that the minor peak in age-specific incidence rate that is present in Québec 25-29 year-olds is mostly due to a higher female incidence rate. The last feature to point out in these figures is the noticeably higher incidence rate occurring in Québec males aged 90 years and over (14.7/100,000). This illustrates the sensitivity of incidence rate determinations of this rare disease to fluctuations in numbers of cases when age-and-sex-specific incidence rates are calculated for strata having small denominators.

Seasonality

There appears to be no seasonality of GBS incidence rate in either province when the data are analyzed by calendar month. The 95% CI for each cumulative mean monthly incidence rate (Figures 8 and 9) overlap with all other 95% CI of the same province.

The correlation coefficient of 0.093 obtained for the comparison of provincial monthly case frequencies from 1983-1989 (Figure 11) confirms that there is little correlation between the monthly case counts in each province.

That there is no seasonality to these data should reassure those concerned about the effects of seasonal illness and health events in Canada, such as Respiratory Syncytial Virus, influenza, and other viral respiratory infections, as well as Influenza-A vaccination. A large increase in GBS incidence rate in both provinces during the vaccination season or in the winter months is ruled out by this study.

The Validity of Diagnoses

Examination of the number of hospital days per GBS case in each province reveals a wide range of hospital days which can occur because of, and in association with, this illness. These data are shown in Figures 12 and 13 with the number of hospital days expressed in logarithmic form so that the cases having fewer days can better be appreciated. The maximum number of hospital days recorded for GBS cases in this study was 1,196 in Ontario and 1,135 in Québec. Although there were very few cases having stays in this range, the high number of hospital days in these GBS cases raises the question of the need for reclassification of cases to Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP), or Chronic-GBS. It may also have occurred that in this slowly-resolving condition, which sometimes requires rehabilitation, and occasionally does not resolve all contractures and other resultant deformities, there exists a labelling effect whereby a person given a diagnosis of GBS retains it for many years. While this may be germane to consideration of the costs associated with GBS, it does not affect the incidence rate or classification.

Cases of GBS having few hospital days are of greater concern to this study because of their numbers. Those cases having 3 or less hospital days, for example, might be suspected to be misclassified as GBS, if one expects longer hospitalizations to occur in this illness. This type of false-positive misclassification could occur if, for example, a person with weakness in the extremities is given a diagnosis of GBS in an institution not having the specialized tests needed to secure the diagnosis, or if an analysis of CSF is normal (as it often is in the early stages of the illness), or if a lumbar puncture is not performed. Such a "case" may be transferred after only 1-3 days in this first admission to a tertiary-care center where the diagnosis of GBS is ruled out. It can be seen that although this "case" was finally classified correctly as not a case of GBS, the diagnosis of GBS from the first admission still exists and this is entered into the HMRI and Med-Écho database as another "case" of GBS.

Reassurance concerning amount of contamination in our data by these short GBS "cases" comes from two sources. Firstly, Figures 14 and 15 depict the number of hospital-days in incident admissions of GBS in each province. A logarithmic scale on the X-axis of these figures is necessary to reveal the short first-admissions in these Poisson distributions. Continuing the consideration of cases of 1-3 days as potentially creating a problem in these results, those incident admissions of 1-3 days can be examined specifically, knowing that any short case must have a short incident admission. There are 220 short incident admissions in Ontario, and 125 in Québec. Figures 12 and 13 show that there are 86 and 62 short cases in Ontario and Québec, respectively. Subtracting the number of short cases from the number of short incident admissions in each province reveals that 134 (61%) short incident admissions in Ontario, and 63 (50%)

short incident admissions in Québec are readmitted to hospital at some time with a diagnosis of GBS.

Secondly, 12% (2 cases) of those Québec charts categorized as false-positives (category 1 or 2), and 17% of those Ontario charts categorized as false-positives have less than 4 days in the incident admission of the case. These percentages are only slightly different, and are actually lower, than the values for all incident admissions of a province: 15% for Québec, and 20% for Ontario, respectively. As well, the mean numbers of days per incident admission in the false-positives found on chart review were 43.6 for Québec and 17.2 for Ontario, which compare with values of 29.8 and 24.7, respectively, for all incident admissions for each province. One would expect a higher percentage of short incident admissions in the false-positive group, as well as a smaller mean number of days compared to all incident admissions if these short GBS cases actually contain an increased fraction of false positive cases.

When reviewed charts of GBS cases from each database were examined to determine the proportion of false-positives, the odds ratio describing the likelihood that a false-positive incident admission would be from a stratum-B institution is 2.3 or 1.25 for Ontario, and 2.8 or 2.4 for Québec, depending on whether the indeterminate category was, or was not, included with the true-positive cases. This suggests that cases admitted at least once to a tertiary care institution are more likely to be true-positives. Chart review of an admission at a tertiary care institution would therefore be more likely to confirm the diagnosis of GBS. The choice to review only incident admissions, whether or not these came from primary care institutions, may have inflated the number of false positive diagnoses. A more complete review of charts for this type of study seems necessary in

order to eliminate the bias introduced by review of only incident admissions, which may act against cases admitted initially to peripheral hospitals.

Figures 16 and 17 show the number of hospital admissions per case in Ontario and Québec, respectively. In Ontario the range of admissions per case is from 1-33, with single cases of 11, 12, 21, 24 and 33 admissions occurring only once; while in Québec, the range is from 1-12 admissions with one case having 12 admissions. A high number of admissions for a case of GBS is unlikely, as might be indicated by the mean number of admissions per case in each province (1.8 in Ontario and 1.4 in Québec), but the few high numbers of admissions per case can be accepted for this study if the treatment of plasmapheresis is considered as a factor causing this high number of admissions. Although there is no specific treatment code for plasmapheresis in the CCP,⁶¹ this treatment would likely be recorded under another specific code (code 13.04 - Note: this coding system was devised circa 1978 when plasmapheresis was not in wide use, and therefore this treatment does not have a code of its own - it is subsumed under the code for transfusion of packed red blood cells). It was found in this study that cases having a large number of admissions generally had single-day admissions towards the end of the case. In these single-day admissions, it was characteristic that the procedural code 13.04 was found, perhaps explaining the high number of admissions as being part of an administrative phenomenon in institutions electing to record a single day's treatment as an admission.

Regional Incidence rates

There appears to be no strong geographic influence when the crude GBS incidence rate is determined by CD and displayed on a map. The Ontario map (Figure 18) displays

four conveniently chosen levels of incidence rate within census districts. Most census districts have a mean crude annual incidence rate per 100,000 person-years of either 1.0 to <2.0 or 2.0 to <3.0 which is close to the provincial mean. The five CDs in Ontario having incidence rates less than 1.0 or greater than 3.0 all have populations less than 75,000, indicating that these extreme values of incidence rate may be influenced by the instability inherent in rates when dealing with small populations. The two CDs having incidence rates less than 1.0 are both border regions. If out-migration would decrease the GBS incidence rate in any regions, it would likely affect those regions lying on provincial or national borders. The high incidence rate in Sudbury Regional Municipality might be explained by misclassification of the place-of-residence of afflicted persons from Sudbury district who, in some degree, would come to this regional municipality for their health-care. The high incidence rate of GBS in Grey and Bruce counties remains unexplained.

The Québec maps (Figure 19 and 20) also show that most census districts in this province have crude GBS incidence rates between 1.0 and 3.0. There is a greater proportion of census districts within Québec that have incidence rates lying outside of these values compared to Ontario, probably because of the smaller populations that reside within most Québec CDs (Appendix I). Like Ontario, all CDs with incidence rates less than 1.0 or greater than 3.0 also have populations less than 75,000. It is probable that out-migration of GBS cases to institutions in Ottawa, Ontario, explains the low incidence rate in the Québec CDs of Gatineau (0.50), Pontiac (0.72) and Papineau (0.71). Examination of the residence code of those HMRI records of Québec residents that were unable to be linked to Med-Écho GBS cases verifies this.

Conclusions

A methodology suitable for surveillance of GBS in Ontario and Québec, using HMRI and Med-Écho data was devised.

It is possible to internally link records in the HMRI and Med-Écho databases into personal histories (cases) of a condition. Two sets of algorithms were devised, one set each for use on HMRI and Med-Écho data. These algorithms linked records to the same case of GBS on a probabilistic basis.

The crude, and age and sex standardized GBS incidence rate was described for Ontario and Québec for the period 1983-1989. Age and sex specific incidence rates, as well as geographical patterns within each province were described. The GBS incidence rate, age and sex standardized to the 1986 Canadian census population, obtained through record linkage of hospital service data, is 2.02/100,000 person-years in Ontario and 2.30/100,000 person-years in Québec. The difference between these values may be a true difference, or an artifact of either database management or the record linkage procedure used.

The high percentage of false positive diagnostic misclassifications discovered on examination of incident admissions indicates concern for the validity of HMRI and Med-Écho data for epidemiological purposes. Verification of diagnoses through more extensive chart reviews than used in this study may be necessary for study of some conditions using these data.

Despite these drawbacks, data from these sources can be used to follow trends in GBS incidence rate. Surveillance for GBS using the methods described in this study to detect a possible increase in GBS incidence rate is feasible.

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Appendix A

Other Designations for Guillain-Barré Syndrome

(Arnason BGW. Acute Demyelinating Polyradiculoneuropathies. In: Dyck PJ, Thomas PK, Lambert ES, eds. *Peripheral Neuropathy*, 2nd ed. Philadelphia: Saunders, 1984:2050-100.)

- idiopathic polyneuritis
- acute febrile polyneuritis
- infective polyneuritis
- postinfectious polyneuritis
- acute toxic polyneuritis
- acute polyneuritis with facial diplegia
- acute infectious neuronitis
- polyneuronitis
- mononeuronitis
- radiculoneuronitis
- polyradiculoneuronitis
- myeloradiculoneuronitis
- myeloradiculitis
- acute inflammatory demyelinating polyradiculoneuropathy
- Guillain-Barré-Strohl syndrome
- Landry-Guillain-Barré syndrome
- acute immune-mediated polyneuritis
- acute inflammatory polyneuropathy

Appendix B

Diagnostic Criteria for Guillain-Barré Syndrome

(according to the U.S. National Institute for neurological and communicative disorders and stroke)

I. Features Required for Diagnosis.

- A. Progressive motor weakness of more than one limb. The degree ranges from minimal weakness of the legs, with or without mild ataxia, to total paralysis of the muscles of all four extremities and trunk, bulbar and facial paralysis, and external ophthalmoplegia.
- B. Areflexia (loss of tendon jerks). Universal areflexia is the rule, although distal areflexia with definite hyporeflexia of the biceps and knee jerks will suffice if other features are consistent.

II. Features Strongly Supportive of Diagnosis.

- A. Clinical features (ranked in order of importance).
 - 1. Progression. Symptoms and signs of motor weakness progress rapidly but cease to progress by four weeks into the illness. Approximately 50% of patients will reach the nadir by two weeks, 80% by three weeks, and more than 90% by four weeks.
 - 2. Relative symmetry. Symmetry is seldom absolute, but usually if one limb is affected, the opposite is affected as well.
 - 3. Mild sensory symptoms or signs.
 - 4. Cranial nerve involvement. Facial weakness occurs in approximately 50% of patients and is frequently bilateral. Other cranial nerves may be involved, particularly those innervating the tongue and muscles of deglutition, and occasionally the extraocular motor nerves. On occasion (less than 5%), the neuropathy may begin in the nerves to the extraocular muscles or other cranial nerves.
 - 5. Recovery. Usually begins two to four weeks after progression stops but may be delayed for months. Most patients recover functionally.
 - 6. Autonomic dysfunction. Tachycardia and other arrhythmias, postural

hypotension, hypertension, and vasomotor symptoms (when present) support the diagnosis. These findings may fluctuate, however, and care must be exercised to exclude other bases, such as pulmonary embolism, for these symptoms.

7. Afebrile at onset of neuritic symptoms.

8. Variants (not ranked by importance).

- a) Fever at onset of neuritic symptoms.
- b) Severe sensory loss with pain.
- c) Progression beyond four weeks. Occasionally a patient will continue to progress for many weeks beyond four or will have a minor relapse.
- d) Cessation of progression without recovery or with major permanent residual deficit.
- e) Sphincter function. Usually the sphincters are not affected, but transient bladder paralysis may occur during symptom evolution.
- f) Central nervous system involvement. Ordinarily, Guillain-Barré syndrome is considered a disease of the peripheral nervous system, but evidence of CNS involvement is controversial. In occasional patients, such findings as severe ataxia interpretable as cerebellar in origin, dysarthria, extensor plantar responses, and ill-defined sensory levels are demonstrable and need not exclude the diagnosis if other features are typical.

B. Cerebrospinal fluid features.

1. Cerebrospinal fluid protein. Elevation of CSF protein after the first week of symptoms or demonstration of rise on serial lumbar punctures.

2. Cerebrospinal fluid cells. A CSF cell count showing ten or fewer mononuclear leukocytes per cubic millimeter.

3. Variants.

- a) No CSF protein rise one to ten weeks after symptom onset (rare).
- b) The CSF counts of 11 to 50 mononuclear leukocytes per cubic millimeter.

C. Electrodiagnostic features.

1. Approximately 80% of patients will have evidence of nerve conduction slowing or block at some point during the illness. Conduction velocity is usually less than 60% of normal, but the process is patchy, and not all nerves are affected. Distal latencies may be increased to as much as three times normal.

Use of F wave responses often provides good indication of slowing over proximal portions of nerve trunks and roots. Conduction studies may not become abnormal until several weeks into the illness. As many as 20% of patients will have normal conduction studies.

II. Features Casting Doubt on the Diagnosis.

- A. Notable persistent asymmetry of weakness.
- B. Persistent bladder or bowel dysfunction.
- C. Bladder or bowel dysfunction at onset.
- D. More than 50 mononuclear leukocytes per cubic millimeter in CSF.
- E. Presence of polymorphonuclear leukocytes in CSF.
- F. Sharp sensory level.

III. Features Ruling Out the Diagnosis

- A. A current history of abuse of volatile solvents such as n-hexane and methyl n-butyl ketone. This includes inhaling paint-lacquer vapors or addictive glue sniffing.
- B. Abnormal porphyrin metabolism, indicating a diagnosis of acute intermittent porphyria. This would manifest as increased excretion of porphobilinogen and δ -aminolevulinic acid in the urine.
- C. A history or finding of recent diphtheritic infection, either faucial or wound, with or without myocarditis.
- D. Features clinically consistent with lead neuropathy (upper limb weakness with prominent wrist drop; may be asymmetrical) and evidence of lead intoxication.
- E. The occurrence of a purely sensory syndrome.
- F. A definite diagnosis of other conditions, such as poliomyelitis, botulism, paralysis, and toxic neuropathies, eg, from nitrofurantoin, dapsone, organophosphorus compounds, which occasionally may be confused with Guillain-Barré syndrome.

Appendix C

Relevant HMRI Variables

- Province in which hospital is located
- Institution (scrambled)
- Fiscal Year
- Institution type
- Chart number
- Health-care number
- Postal code
- Residence code
- Date of birth
- Age
- Sex
- Admit date
- Admit hour
- Admit category (elective; urgent)
- Readmission
- Discharge date
- Institution to type
- Ready for discharge date
- Exit alive
- Coroner
- Autopsy
- Death code
- Supplemental death code
- Main patient service
- Weight
- Manual length of stay
- CMG number
- Diagnoses (for each of 16 possible diagnoses - ICD-9 code)
- Diagnostic type (main, primary, secondary, complication, etc)
- Doctors
- Procedures (3 or 4 CCP codes)

Appendix D**Relevant Med-Écho Variables**

- Période
- No de lot
- Date de saisie
- No d'admission
- No de dossier medical
- Code de l'établissement
- Type de l'établissement
- Etat civil
- Date de naissance
- Sexe
- Code postal du bénéficiaire
- Code municipal du bénéficiaire
- RSS-DSC-CLSC du bénéficiaire
- Lieu de naissance
- Admission antérieure
- Code d'occupation
- Date d'accident
- Code de provenance
- Type de provenance
- Date d'admission
- Diagnostic d'admission
- État à l'admission
- Service 1-4
- No de jours 1-4
- Diagnostic final 1-4
- Diagnostic 1-15 (supplémentaire)
- Décès
- Date du congé
- Date de sortie
- Séjour total
- Code de destination
- Type de destination
- Région du bénéficiaire
- DSC du bénéficiaire
- CLSC du bénéficiaire
- MRC du bénéficiaire

Appendix E**ICD-9: Category 357 - Inflammatory and toxic neuropathy**

357.0 Acute infective polyneuritis
Guillain-Barré syndrome

357.1 Polyneuropathy in collagen vascular disease

Polyneuropathy in:

disseminated lupus erythematosus (710.0)
polyarteritis nodosa (446.0)
rheumatoid arthritis (714.0)

357.2 Polyneuropathy in diabetes (250.5)

357.3 Polyneuropathy in malignant disease (140-208)

357.4 Polyneuropathy in other diseases classified elsewhere

Polyneuropathy in:

amyloidosis (277.3)
beriberi (265.0)
deficiency of B vitamins (266.-)
diphtheria (032.-)
herpes zoster (053.1)
hypoglycaemia (251.2)
mumps (072.7)
pellagra (265.2)
porphyria (277.1)
sarcoidosis (135)
uraemia (585)

357.5 Alcoholic polyneuropathy

357.6 Polyneuropathy due to drugs
Use additional E code, if desired, to identify drug

357.7 Polyneuropathy due to other toxic agents
Use additional E code, if desired, to identify toxic agent

357.8 Other

357.9 Unspecified

Appendix F

Algorithm 1: HMRI

```
*****
```

This algorithm was programmed in SAS for use on HMRI data.

```
*****
```

```
PROC SORT DATA=GBS.REALCASE;
BY BDATE ADATE DDATE;
RUN;
```

```
DATA TEMP1;
RETAIN Y M D I H DD;
RETAIN PC1 PC2 CHAR1 CHAR2 ' ' R1 R2 RES1 RES2 ' ' S ' ' C '
';
```

```
YEAR=Y;
MONTH=M;
DAY=D;
HLTHCNO=H;
PC1=CHAR1;
PC2=CHAR2;
R1=RES1;
R2=RES2;
DISCDATE=DD;
```

```
SET GBS.REALCASE;
DROP Y M D YEAR MONTH DAY PC1 PC2 CHAR1 CHAR2 I R1 R2 RES1 RES2
S C H BDATDIFF DAYDIFF CHARDIF1 CHARDIF2 DD
SEXDIFF INSTDIFF HLTHDIFF RESDIF1 RESDIF2 CHRTRDIFF DATEDIFF;
```

```
Y=YEAR(BDATE);
M=MONTH(BDATE);
D=DAY(BDATE);
CHAR1=SUBSTR(PCODE,1,3);
CHAR2=SUBSTR(PCODE,4,3);
RES1=SUBSTR(RESCODE,2,2);
RES2=SUBSTR(RESCODE,4,2);
```

```
DISCDATE=INPUT(DDATE,YYMMDD6.);
HLTHCNO=HCNO+0;
```

```
*IF YEAR EQ Y THEN YEARDIFF=25;
IF MONTH EQ M AND DAY EQ D THEN BDATDIFF=45;
```

Algorithm 1: HMRI (continued)

IF DAY NE D THEN DAYDIFF=-55;

IF CHAR1 EQ PC1 THEN CHARDIF1=50;

IF CHAR1=' ' OR PC1=' ' THEN CHARDIF1=0;

IF (CHAR1 NE PC1) AND (CHAR2 EQ PC2) THEN CHARDIF2=40;

IF (CHAR1 EQ PC1) AND (CHAR2 EQ PC2) THEN CHARDIF2=250;

IF CHAR2=' ' OR PC2=' ' THEN CHARDIF2=0;

IF SEX EQ S THEN SEXDIFF=10;

IF SEX NE S THEN SEXDIFF=-60;

IF INSTIT EQ I THEN INSTDIFF=40;

IF INSTIT NE I THEN INSTDIFF=-5;

IF HLTHCNO EQ H THEN HLTHDIFF=500;

IF HLTHCNO NE H THEN HLTHDIFF=-200;

IF HLTHCNO < 1000 OR H < 1000 THEN HLTHDIFF=0;

IF RES1 EQ R1 THEN RESDIF1=40;

IF RES1 NE R1 THEN RESDIF1=-50;

IF RES1=' ' OR R1=' ' THEN RESDIF1=0;

IF RES1='00' OR R1='00' THEN RESDIF1=0;

IF RES2 EQ R2 THEN RESDIF2=30;

IF RES2 NE R2 THEN RESDIF2=-35;

IF RES2='00' OR R2='00' THEN RESDIF2=10;

IF RES2=' ' OR R2=' ' THEN RESDIF2=0;

IF RES1 EQ R1 AND RES2 EQ R2 THEN RESDIF2=50;

IF CHARTNUM EQ C THEN CHRTRDIFF=500;

IF CHARTNUM NE C THEN CHRTRDIFF=-8;

IF (ADATE-DD) > 0 AND (ADATE-DD) > 90 THEN DATEDIFF=-10;

IF (ADATE-DD) > 0 AND (ADATE-DD) <= 90 THEN DATEDIFF=20;

IF (ADATE-DD) > 0 AND (ADATE-DD) <= 20 THEN DATEDIFF=50;

IF (ADATE-DD) > 0 AND (ADATE-DD) <= 5 THEN DATEDIFF=100;

IF (ADATE-DD)=0 THEN DATEDIFF=300;

IF (ADATE-DD)=1 THEN DATEDIFF=200;

IF (ADATE-DD) >=-10 AND (ADATE-DD) <=-1 THEN DATEDIFF=-10;

IF (ADATE-DD) < -10 THEN DATEDIFF=-50;

TOTLDIFF=SUM(BDATDIFF, DAYDIFF, SEXDIFF, INSTDIFF, HLTHDIFF,
RESDIF1, RESDIF2, CHRTRDIFF, CHARDIF1, CHARDIF2, DATEDIFF);

Algorithm 1: HMRI (continued)

```
S=SEX;  
I=INSTIT;  
C=CHARTNUM;  
H=HLTHCNO;  
DD=DISCDATE;  
RUN;
```

```
PROC FREQ;  
TABLES TOTLDIFF;  
RUN;
```

```
DATA GBS.GBARCASE;  
RETAIN G 0;  
GROUP=G;  
SET TEMP1;  
DROP G;  
IF TOTLDIFF > 100 THEN GROUP=G;  
IF TOTLDIFF <= 100 THEN GROUP=G+1;  
G=GROUP;  
RUN;
```

Appendix G

Algorithm 1: Med-Écho

```
*****
```

This algorithm was programmed in SAS for use on Med-Écho data.

```
*****
```

```
PROC SORT DATA=ECHO.GBSR;
BY BDATE ADATE DDATE;
RUN;
```

```
DATA TEMP1;
RETAIN Y M D I DD DEST;
RETAIN PC ' ' R ' ' S ' ' C ' ' ;
```

```
YEAR=Y;
MONTH=M;
DAY=D;
DD=DDATE;
```

```
SET ECHO.GBSR;
```

```
Y=YEAR(BDATE);
M=MONTH(BDATE);
D=DAY(BDATE);
```

```
IF MONTH=M THEN MNTHDIFF=10;
IF MONTH^=M THEN MNTHDIFF=-500;
IF DAY=D THEN DAYDIFF=75;
IF DAY ^=D THEN DAYDIFF=-70;
```

```
IF PCODE EQ PC THEN PCDIFF=200;
IF PCODE NE PC THEN PCDIFF=-25;
IF PCODE=' ' OR PC=' ' THEN PCDIFF=0;
```

```
IF SEX EQ S THEN SEXDIFF=10;
IF SEX NE S THEN SEXDIFF=-500;
```

```
IF INSTIT EQ I THEN INSTDIFF=40;
IF INSTIT NE I THEN INSTDIFF=-5;
```

Algorithm 1: Med-Écho (continued)

```
IF RESCODE EQ R THEN RESDIFF=50;
IF RESCODE NE R THEN RESDIFF=-30;
IF RESCODE=0 OR R=0 THEN RESDIFF=0;

IF CHARTNUM EQ C THEN CHRTRDIFF=500;
IF CHARTNUM NE C THEN CHRTRDIFF=-5;

IF (ADATE-DD)>0 AND (ADATE-DD)>90 THEN DATEDIFF=-10;
IF (ADATE-DD)>0 AND (ADATE-DD)<=90 THEN DATEDIFF=20;
IF (ADATE-DD)>0 AND (ADATE-DD)<=20 THEN DATEDIFF=50;
IF (ADATE-DD)>0 AND (ADATE-DD)<=5 THEN DATEDIFF=100;
IF (ADATE-DD)=0 THEN DATEDIFF=300;
IF (ADATE-DD)=1 THEN DATEDIFF=200;
IF (ADATE-DD)>=-10 AND (ADATE-DD)<=-1 THEN DATEDIFF=-10;
IF (ADATE-DD)<-10 THEN DATEDIFF=-50;

IF DEST=INSTIT THEN DESTDIFF=100;
IF DEST^=INSTIT THEN DESTDIFF=-15;
IF DEST=0 THEN DESTDIFF=0;

SCORE=SUM(MNTHDIFF, DAYDIFF, SEXDIFF, INSTDIFF, DESTDIFF,
          RESDIFF, CHRTRDIFF, PCDIFF, DATEDIFF);

S=SEX;
I=INSTIT;
C=CHARTNUM;
PC=PCODE;
R=RESCODE;
DD=DDATE;
DEST=DESTCODE;
RUN;

PROC FREQ;
TABLES SCORE;
RUN;
```

Algorithm 1: Med-Écho (continued)

```
DATA ECHO.Grouped;  
RETAIN G 0;  
GROUP=G;  
SET TEMP1;  
DROP G;  
IF SCORE > 200 THEN GROUP=G;  
IF SCORE <= 200 THEN GROUP=G+1;  
G=GROUP;  
RUN;
```

Appendix H

Ontario Regional Incidences by Census District

Census District	Population	Cases	Incidence
Durham Regional	326180	38	1.664287
Haliburton	11965	2	2.387917
Metro Toronto	2192720	301	1.961035
Northumberland	67705	12	2.531993
Peel Regional	592165	62	1.495722
Peterborough	105055	20	2.719664
Simcoe	238410	31	1.857544
Victoria	52595	6	1.629704
York Regional	350600	40	1.629859
Brant	106265	14	1.882087
Dufferin	32635	5	2.188711
Haldimand-Norfolk	90120	15	2.377782
Halton	271390	42	2.210840
Hamilton-Wentworth	423395	69	2.328120
Niagara Regional	370130	64	2.470175
Waterloo Regional	329405	52	2.255148
Wellington	139440	21	2.151463
Frontenac	115220	13	1.611823
Hastings	109350	17	2.220916
Lanark	49645	7	2.014302
Leeds & Grenville	84580	10	1.689018
Lennox & Addington	34355	4	1.663305
Ottawa-Carleton	606640	82	1.931011
Prescott & Russell	57620	4	0.991719
Prince Edward	22425	3	1.911132
Renfrew	88965	7	1.124038
Stormont, D. & G	102980	17	2.358294
Algoma	132195	15	1.620982
Cochrane	95040	16	2.405002
Manitoulin	10330	1	1.382935
Muskoka	40305	8	2.835522
Nipissing	79140	13	2.346655
Parry Sound	33830	7	2.955956
Sudbury District	25770	6	3.326127
Sudbury Region	152475	13	1.217998
Timiskaming	40310	6	2.126378
Bruce	59420	16	3.846709
Elgin	70335	11	2.234206

Ontario Regional Incidences by Census District (continued)

Census District	Population	Cases	Incidence
Essex	316360	49	2.212669
Grey	74760	18	3.439578
Huron	55995	10	2.551248
Kent	106735	17	2.275328
Lambton	125350	15	1.709499
Middlesex	333420	55	2.356530
Oxford	85360	14	2.343018
Perth	66610	9	1.930212
Kenora	59105	9	2.175305
Rainy River	23030	0	0.000000
Thunder Bay	155670	20	1.835384

Appendix I

Québec Regional Incidences by Census District

CD#	Census District	Population	Cases	Incidence
2	GASPE-EST	40862	3	1.048826
3	GASPE-OUEST	14201	3	3.017896
4	BONAVENTURE	39576	4	1.443877
5	MATAPEDIA	23476	4	2.434097
6	MATANE	29258	9	4.394403
7	RIMOUSKI	69945	17	3.472116
8	RIVIERE-DU-LOUP	40646	5	1.757333
9	TEMISCOUATA	19271	3	2.223919
10	KAMOURASKA	28483	4	2.006209
11	CHARLEVOIX-EST	17573	3	2.438806
12	CHARLEVOIX-OUEST	14201	1	1.005965
13	L'ISLET	21189	2	1.348409
14	MONTMAGNY	24794	4	2.304705
15	BELLECHASSE	23237	3	1.844349
16	MONTMORENCY NO.2	6769	2	4.220923
17	MONTMORENCY NO.1	22951	2	1.244888
20	QUEBEC	466483	84	2.572441
21	LEVIS	103318	14	1.935771
22	DORCHESTER	33798	1	0.422679
23	BEAUCE	75982	11	2.068159
24	FRONTENAC	26390	4	2.165322
25	COMPTON	20110	6	4.262272
26	WOLFE	15223	3	2.815289
27	MEGANTIC	55028	5	1.29804
28	LOTBINIERE	29809	3	1.437725
29	PORTNEUF	60610	6	1.414194
32	CHAMPLAIN	119563	11	1.31431
33	NICOLET	34162	5	2.090878
34	ARTHABASKA	60597	8	1.885996
35	RICHMOND	38653	4	1.478355
36	SHERBROOKE	120551	19	2.251566
37	STANSTEAD	38746	7	2.580912
38	BROME	18047	6	4.749503
39	SHEFFORD	73883	16	3.093694
40	BAGOT	28166	8	4.057577
41	DRUMMOND	72051	3	0.594817

Québec Regional Incidences by Census District (continued)

CD#	Name	Population	Cases	Incidence -
42	YAMASKA	14722	2	1.94073
43	SAINT-MAURICE	109033	12	1.572263
47	MASKINONGE	20877	2	1.36856
49	BERTHIER	32044	2	0.891631
50	RICHELIEU	51837	6	1.653535
51	STE HYACINTHE	57027	14	3.507111
52	ROUVILLE	43859	7	2.280034
53	IBERVILLE	23931	4	2.387817
54	MISSISQUOI	35028	4	1.631348
55	ST JEAN	57617	5	1.239713
56	CHAMBLY	316337	60	2.709588
57	VERCHERES	67610	9	1.901663
58	JOLIETTE	63343	3	0.676588
61	MONTCALM	29252	8	3.906937
62	L'ASSOMPTION	122509	22	2.565409
63	TERREBONNE	206657	28	1.935574
64	ILE-JESUS	284164	28	1.407638
65	ILE-DE-MONTREAL	1752582	337	2.746967
66	LAPRAIRIE	110617	21	2.712061
68	HUNTINGDON	15627	3	2.742506
69	CHATEAUGUAY	61608	8	1.855047
70	BEAUHARNOIS	53106	5	1.345019
72	VAUDREUIL	53421	12	3.209011
73	DEUX-MONTAGNES	75880	12	2.259206
74	ARGENTEUIL	32533	3	1.317344
75	PAPINEAU	40258	2	0.709708
76	LABELLE	34579	5	2.065663
78	GATINEAU	57213	2	0.499387
79	HULL	139966	13	1.326853
80	PONTIAC	19809	1	0.721173
83	TEMISCAMINGUE	53238	12	3.220042
84	ABITIBI	94410	10	1.513157
90	LAC-ST-JEAN-OUEST	62977	5	1.134201
93	LAC-ST-JEAN-EST	47497	5	1.503854
94	CHICOUTIMI	174625	32	2.617855
97	SAGUENAY	104131	14	1.920658
98	NOUVEAU QUEBEC	37183	4	1.536801