Prevalence of multiple sclerosis in a residential area bordering an oil refinery

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Abstract—*Background:* Community concerns about a potential excess of multiple sclerosis (MS) prompted this study. *Objective:* To determine the period prevalence of MS in a community bordering a closed oil refinery and a control community. *Methods:* Cases seen by a neurologist during 1998 to 2001 were obtained from area neurologists and hospital discharge data. Population data were obtained from the year 2000 US Census. Patient data were abstracted by a trained abstractor onto a standardized report form. A consulting neurologist reviewed the form and made a final diagnosis using the Poser criteria plus the category of presumed. Age-adjusted prevalence rates and rates of agreement were calculated. *Results:* The direct age-adjusted period prevalence for both sexes and all races for the entire study area was 113 per 100,000 (95% CI = 93 to 136). For white subjects only, the prevalence was 123 per 100,000 (95% CI = 102 to 147). With use of an indirect method of age adjustment, the number of observed cases in the community bordering the refinery was similar to the number of cases expected (standardized morbidity ratio = 130.8, 95% CI = 62.3 to 199.3), based on rates from the comparison area. The agreement between the treating neurologist (for definite plus probable cases) and the consulting neurologist (for definite plus probable plus presumed cases) was good ($\kappa = 0.5733$). *Conclusions:* The prevalence of multiple sclerosis (MS) for this area was generally consistent with prevalence estimates calculated in previous studies in other areas. No significant excess was seen in the exposed area. MS was more prevalent in females than in males. The overall agreement between the consulting and treating neurologist was good.

NEUROLOGY 2004;63:1796–1802

Prevalence estimates of multiple sclerosis (MS) vary widely by gender and race[1,2] as well as by age and latitude. A prevalence of 57.8 per 100,000 population was reported based on a 1976 survey of physicians and hospitals.[3] This was adjusted to reflect changes in the US population and improved diagnostic techniques,[4] resulting in an adjusted prevalence estimate of 95 per 100,000 population. Data from the National Health Interview Survey provided a prevalence estimate of 85 per 100,000 for the period 1989 to 1996.[5] A 50% increase was observed in the number of women reporting MS.[5] Prevalence estimates for specific locales published since 1970 range from 22 to 160 per 100,000. The highest reported prevalence is from a 1985 study using the centralized diagnostic index at the Mayo Clinic.[6] In that study, the age- and sex-adjusted point prevalence per 100,000 persons was 170.8 (95% CI = 143 to 198) for Olmsted County and 177.3 (95% CI = 142 to 212) for Rochester, MN (44° N latitude) on January 1, 1985. In Weld and Larimer Counties, CO (41° N latitude), the point prevalence per 100,000 was 84 (95% CI = 73 to 96) on January 1, 1982.[7]

This study was conducted in response to community concerns about a perceived excess of MS in an area bordering a closed oil refinery. The communities selected for investigation (Sugar Creek and Independence, MO) lie immediately to the east of Kansas City, MO (39° N latitude).[8] Similar studies of MS prevalence are being conducted in Ohio and Texas.

From 1904 through 1982, an oil refinery was operated in Sugar Creek, MO.[8-10] Numerous spills and leaks of crude oil and other chemical products were documented on site. Subsurface soils were contaminated off-site; a groundwater plume had migrated into a neighboring residential area. Pollutants of concern include benzene, xylene, and toluene. Up to 5,000 parts per billion of benzene had been detected off-site.[8,9]

A Medline search was conducted concerning environmental chemical exposures and MS. The search covered the period from January 1, 1985, to January

Additional material related to this article can be found on the *Neurology* Web site. Go to www.neurology.org and scroll down the Table of Contents for the November 23 issue to find the title link for this article.

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Supported by Agency for Toxic Substances and Disease Registry (to the Jackson County, MO, Health Department; cooperative agreement no. U50/ATU789115-02-1). The Jackson County Health Department contracted with the University of Kansas Medical Center investigators for methodologic design, data analysis, and reporting.

Received April 9, 2004. Accepted in final form July 20, 2004.

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26, 2004. No citations were found concerning MS and either benzene or petroleum. A possible association between MS and solvents was mentioned in several publications[11-13] but not in others.[14,15] A possible association between MS and trace metals, including zinc and heavy metal wastes (especially cadmium and chromium), in sewage and river water[16-18] was also mentioned.

Factors that have been shown to be risks for the development of MS include female sex, Caucasian race, genetic susceptibility, and family history of MS. Factors that have been hypothesized to be risks include reduction in solar ultraviolet radiation, multiple viruses (canine distemper, Epstein–Barr, human herpes 6, etc.), sex hormones, dietary fat/fatty acids, reduction in vitamin D, some environmental agent more common in cold climates, and organic solvents.[19-23] With regard to organic solvents in particular, there has not been much specificity as to the particular chemical.[20]

The study was designed to calculate the prevalence of MS in Independence and Sugar Creek, MO, and then calculate the overall prevalence for the two cities combined. We sought to determine whether proximity (and potential exposure) to Sugar Creek were associated with an increased prevalence of MS, which might suggest the influence of organic chemicals on the development of this disease.

Methods. Cases were identified without directly contacting patients. The primary data source for case ascertainment was medical records from the offices of neurologists practicing in the study area or in contiguous areas. Patients were considered for inclusion in the case count if they had an office visit between January 1, 1998, and December 31, 2001. Records with the following International Classification of Disease (9th rev.) codes or corresponding conditions were considered for inclusion in the study: MS (340), other demyelinating diseases (341.8, 341.9), transverse myelitis (323.9), and optic neuritis (377.3).

Residence in the study zip codes (64050 to 64058 inclusive) was required for inclusion in the case count. The zip code was determined by the address indicated on the patient's medical record. The areas chosen for comparison were Sugar Creek, the city with closest proximity to the refinery, and Independence, a city contiguous to Sugar Creek with similar socioeconomic characteristics but farther away from the refinery. The zip code areas chosen for Sugar Creek (64053 plus 64054), although not identical to that city's boundaries, provided a rough approximation to the area of greatest potential exposure to the refinery. The zip code areas chosen for Independence (64050 plus 64052 plus 64055 to 64058), although not identical to that city's boundaries, provided a rough approximation to an area of lesser potential exposure to the refinery. Zip code 64051 was a post office box number and was not utilized.

Zip codes were independently verified by means of entering street addresses into a US Census Bureau database. Supplementary information from the US Post Office or the Kansas City area telephone directory was occasionally utilized to confirm an address. Zip code tabulation areas were obtained from the census bureau and used for the prevalence calculations.

A standard form was used by an abstractor, who was trained and supervised by the principal investigator and the project neurologist. The form was developed in collaboration with investigators at the Agency for Toxic Substances and Disease Registry (ATSDR), Ohio and Texas. Clinical examination and attack histories were collected as well as laboratory and MRI results. The form included history of relapses, neurologic exam findings, evoked potentials, spinal fluid results, and MRI results of the neck and cervical spine. Descriptive variables that were collected, if available, included sex, race/ethnicity, occupation, family history of MS, country/state of birth, treating physician's MS diagnosis, criteria used to determine diagnosis, date of diagnosis, and date of symptom onset. Individual identifiers (i.e., name, address, and social security number) were recorded to ensure accurate counts of cases and avoid duplicate counting from other sources. (See a copy of this form in the supplementary material on the *Neurology* Web site at www.neurology.org.)

Initial contact was made with the Mid-America Chapter of the National Multiple Sclerosis Society. The society provided us with the total number of registered MS patients within each zip code included in the study. The names of treating neurologists were also provided.

A listing of neurologist offices in Clay and Jackson Counties in Missouri and Johnson and Wyandotte Counties in Kansas was created. Each office was asked to run a search of its patient database to identify the number of patients that fell within the parameters of the study. Once completed, arrangements were made for the abstractor to review the identified charts. Hospitals in the same area were contacted with the same request. In both cases, we utilized electronic hospital discharge and/or neurologist records for case ascertainment. Nursing homes in the study area were also contacted.

The State of Missouri's Department of Health and Senior Services' Center for Health Information Management and Evaluation was contacted for death certificate information within the inclusion criteria for address and time period of the study and with MS listed in Part I (immediate cause of death) or in Part II (other major conditions).

To avoid selection bias, self-reported cases or those that might have been identified through MS advocacy groups were not included. However, the local chapter of the Multiple Sclerosis Society provided the names of physicians in their patient registry to ensure that we had a listing of that treating neurologist's office.

Duplicate cases were avoided by comparing the patient's name, address, date of birth, gender, and social security number from the different data sources. If the same person appeared in more than one database, duplication was avoided, but any additional relevant clinical information was abstracted.

A reviewing or consulting neurologist verified all potential cases. This neurologist rated each case according to the Poser criteria of 1983 and classified it as definite (clinical or laboratory supported), probable (clinical or laboratory supported), possible, not MS, presumptive MS, or unknown.[24] If necessary, the neurologist directed the abstractor to collect additional data from the medical record that were required to assess the diagnostic criteria for a specific case.

Discussions with the other neurologists in Ohio and Texas led to the common decision to include the addition of the category of "presumptive MS." This was added to the criteria to enumerate individuals for whom there was strong clinical or historical evidence of MS but insufficient supporting diagnostic records available (such as detailed exams, lumbar puncture results, or detailed history) that would allow categorization based on criteria.

Completed abstract forms for the Missouri study were provided to the principal epidemiologic investigator at the University of Kansas Medical Center (KUMC), who arranged for a copy of the forms to be provided to the consulting neurologist. All patient-identifying information was removed prior to submitting the forms to the KUMC epidemiologic investigator. Subsequently, this investigator submitted this information to the consulting neurologist after removing the name of the treating neurologist, the specific diagnostic code, and the zip code of residence of the case. All abstracted data and all consulting neurologist diagnostic data were entered into a computer at KUMC, and all entries were double checked for accuracy. After providing an initial diagnosis, the consulting neurologist rereviewed all records to provide a final diagnosis.

Utilizing data from the consulting or reviewing neurologist, age- and sex-specific prevalence estimates (and 95% CI) were calculated for the study area. Definite, probable (Poser criteria), and presumptive MS cases ascertained from the surveillance activities for the period 1998 to 2001 were used in the numerator, and the year 2000 census counts for the study area zip code tabulation areas were used in the denominator. Although zip codes were utilized for case ascertainment, zip code tabulation areas were ultimately used to calculate prevalence. The prevalence of MS was calculated for all races combined and for white non-Hispanics.

Table 1 *Outcome of consultant neurologist's review of medical records for cases identified by zip code*

Poser 1983 criteria[24]	No. of reviewed records
Definite	91
Probable	29
Possible	18
Presumptive*	22
Not MS	44
Unknown	12
Total records reviewed	216

* Presumptive category is for those records with strong indications of multiple sclerosis (MS) but insufficient medical record history (or other data) available to confirm diagnosis. This category was used in the final case count of the consulting neurologist but is not a category used in the Poser criteria.

Direct age adjustment was used to calculate prevalence estimates for both sexes and all races and for both sexes and white subjects only for the combined Independence and Sugar Creek area. Direct adjustment was made to the year 2000 Missouri population. The age-specific prevalence in the combined total study area was multiplied by the age-specific Missouri population and then summed up and divided by the total population to achieve age adjustment.

Indirect age adjustment was used to compare the observed number of MS cases in Sugar Creek with the expected number. The year 2000 population and the number of cases in Independence were utilized to calculate a prevalence proportion that was then applied to the age-specific population in Sugar Creek. The sum of these calculations resulted in the expected number of cases in Sugar Creek. Calculations were done for both sexes and all races and for both sexes and whites only.

The Poisson approximation was used both to construct the 95% CI of the prevalence proportion and to compare the number of observed cases with the number of expected cases in Sugar Creek.[25] The terms "prevalence," "prevalence estimate," and "prevalence proportion " are utilized interchangeably; the primary reference term is "prevalence proportion."[26]

Comparison was made between the treating neurologist's diagnosis of definite plus probable and the consultant neurologist's diagnosis of definite, probable, or presumed. An additional analysis left out the consultant neurologist's diagnosis of presumed. A percentage of agreement was calculated, as well as a Cohen κ statistic,[27] which compared the findings from the two neurologists. A positive predictive value was calculated, comparing the two categories of neurologists.

The protocol for this study was approved by the investigational review boards of the Centers for Disease Control and Prevention, KUMC, Kansas City Veteran's Administration Medical Center, and Truman Medical Center.

Results. A total of 12 neurologists' offices and eight hospitals were contacted and participated. There were 61 neurologists associated with these practices.

Of the 216 abstracted records, 120 were classified by the reviewing neurologist as definite or probable according to the Poser 1983 criteria. Including presumptive, there were 142 cases in the relevant zip codes. In contrast, the treating neurologist listed 159 cases as definite or probable. Thus, there was a difference of 39 cases between the original neurologist and the consulting or reviewing neurologist regarding the diagnosis of definite or probable (table 1). A total of 44 cases were diagnosed as "not MS" by the reviewing neurologist. These included peripheral neuropathy, chronic headaches with nonspecific MRI changes, and fibromyalgia syndrome.

Table 2 *Sources for cases identified by zip code*

Source	MS records*	Cases†
Neurologist's office	157	107
General practitioner or other physician	0	0
MS patient advocacy group	0	0
Death certificate	4‡	4‡
Hospital discharge data	57	34
Self-identified	0	0
Other	2	1
Total	220	142

* Records = originally identified by International Classification of Diseases–9th rev. codes as MS or related conditions.
† Cases = MS confirmed by the consulting neurologist as definite or probable using the Poser 1983 criteria or presumed.
‡ For cases identified through both the neurologist's office and the death certificate, the case is also counted under the neurologist office category. Thus, the total number of originally identified "cases" is 216.

MS = multiple sclerosis.

The sources of the 142 cases identified by zip code are indicated in table 2. Four death certificates met the study criteria. Of the four, all had been previously reviewed through a neurologist's office or a hospital. Nine nursing homes were contacted, and eight cases, all residents of the studied communities, were identified. Of those eight, only two had not been seen through a physician's office or hospital. Although demographic information was available, the nursing home records provided little information concerning past history or initial diagnostic information.

With use of zip code tabulation areas, the distribution of cases by sex, age, race/ethnicity, and residence (consulting neurologist; definite, probable, or presumptive) is presented in table 3. A total of 139 cases were found, with 14 in Sugar Creek (population 9,915) and 125 in Independence (population 110,884). Three cases that resided in legitimate zip codes in eastern Independence dropped out of the legitimate zip code tabulation areas, resulting in a reduction of the number of cases from 142 to 139. The largest ethnic group by far was non-Hispanic white. In terms of cases, the great majority were female and resided in Independence. The overall prevalence was 115 per 100,000 (95% CI = 94 to 139).

MS was more prevalent in females (177 per 100,000; 95% CI = 151 to 206) than males (48 per 100,000; 95% CI = 35 to 64). The prevalence in Sugar Creek (141 per 100,000; 95% CI = 77 to 237) was similar to that in Independence (113 per 100,000; 95% CI = 93 to 136).

Table 4 includes only definite plus probable MS cases and excludes presumed cases. The results show patterns similar to that found in table 3, which includes presumed cases. Prevalence of MS is higher in females than in males, and the prevalence estimate is similar in Sugar Creek and Independence.

Because the prevalence estimates in the two towns were similar, the data were also analyzed combined. With use of the direct method of age adjustment and zip code tabulation areas, the MS 4-year period prevalence rate for the entire study area was 113 per 100,000 (95% CI = 93 to

Table 3 *Descriptive characteristics of cases and respective stratum-specific prevalence based on zip code tabulation areas: definite, probable, and presumed cases*

	MS cases*	Population†	Stratum-specific prevalence (95% CI)
Total	139	120,799	115 (94–139)
Sex			
Female	111	62,870	177 (151–206)
Male	28	57,929	48 (35–64)
Age,‡ y			
<30	11	47,683	23 (12–41)
30–39	19	17,244	110 (66–172)
40–49	42	18,172	231 (202–263)
50–59	47	14,078	334 (245–444)
60–69	13	10,247	127 (68–217)
≥70	7	13,375	52 (21–108)
Race/ethnicity			
Hispanic	0	2,450	—
Non-Hispanic white	136	108,957	125 (104–149)
Non-Hispanic black	1	2,984	—
Other/unknown	2	6,408	—
Residence§			
Independence	125	110,884	113 (93–136)
Sugar Creek	14	9,915	141 (77–237)

* Cases include those with either a definite or a probable diagnosis according to the Poser 1983 criteria. In addition, the category of presumptive was included.
† Data from year 2000 US Census.
‡ Age at diagnosis calculated as of January 1, 2000.
§ Residence at time of the most recent physician visit.

MS = multiple sclerosis; (—) = data not presented or calculated for fewer than five cases.

Table 4 *Descriptive characteristics of cases and respective stratum-specific prevalence based on zip code tabulation areas: definite plus probable cases only*

	MS cases*	Population†	Stratum-specific prevalence (95% CI)
Total	117	120,799	97 (79–117)
Sex			
Female	94	62,870	150 (127–175)
Male	23	57,929	40 (29–53)
Age,‡ y			
<30	9	47,683	19 (11–28)
30–39	15	17,244	87 (70–106)
40–49	40	18,172	220 (193–251)
50–59	37	14,078	263 (232–296)
60–69	12	10,247	117 (98–140)
≥70	4	13,375	30 (20–42)
Race/ethnicity			
Hispanic	0	2,450	—
Non-Hispanic white	114	108,957	105 (86–126)
Non-Hispanic black	1	2,984	—
Other/unknown	2	6,408	—
Residence§			
Independence	105	110,884	95 (77–115)
Sugar Creek	12	9,915	121 (101–145)

* Cases include those with either a definite or a probable diagnosis according to the Poser 1983 criteria. Presumed cases were excluded.
† Data from year 2000 US Census.
‡ Age at diagnosis calculated as of January 1, 2000.
§ Residence at time of the most recent physician visit.

MS = multiple sclerosis; (—) = data not presented or calculated for fewer than five cases.

136) for both sexes and all races. For whites only, the age-adjusted rate was 123 per 100,000 (95% CI = 102 to 147) (results not shown). If the data are restricted to definite plus probable cases only (Poser), the 4-year period prevalence for all cases decreases from the above 113 per 100,000 to 96.9 per 100,000 (95% CI = 78.7 to 117.2).

If the data are further restricted to definite plus probable cases only (Poser) for a 3-year period (1998 to 2000), to eventually compare with the results from Ohio and Texas, the 3-year period prevalence is 87.7 (95% CI = 70.6 to 107.3).

With use of the indirect method of age adjustment and zip code tabulation areas, the number of observed MS cases did not exceed the number of expected cases (standardized morbidity ratio [SMR] = 130.8, 95% CI = 62.3 to 199.3, including presumed cases; SMR = 133.3, 95% CI = 57.9 to 208.8, excluding presumed cases) (table 5). When data from the treating neurologist were used or when the data were restricted to whites only, the results were also similar (results not shown).

With use of zip code tabulation areas, there were 156 cases identified as definite or probable MS by the treating neurologist, but only 117 cases identified as definite or probable MS by the consulting neurologist (table 6). Of the 156 cases identified as definite or probable by the treating neurologist, 128 of them were identified as definite, probable, or presumed by the consulting neurologist. Thus, the overall agreement was 0.82 (128 ÷ 156; Cohen κ = 0.5733). Conversely, of the 139 cases identified as definite, probable, or presumed by the consulting neurologist, 128 were identified as definite or probable by the treating neurologist (agreement = 0.92). The positive predictive value for the treating neurologist's diagnosis of definite MS compared with the consulting neurologist's diagnosis of definite MS was 58.9% (76 ÷ 129 × 100). (If the presumed cases are removed from the analysis, κ = 0.439.) For the 42 cases identified as possible by the treating neurologist, only 6 were diagnosed as possible by the consulting neurologist. Major reasons for the discrepancies included an inadequate attack history and no evidence of abnormality on physical exam.

Of the 216 records reviewed of potential cases having seen a neurologist in the 1998 to 2001 period, 30 were seen by a neurologist only in 2001. Of these, 13 were diagnosed in 2001 and would not have been found if the year 2001 had been excluded from the study. An additional patient probably would not have been found if the year 2001 had

Table 5 *Standardized morbidity ratio for Sugar Creek, MO, based on zip code tabulation areas, including or excluding presumed cases*

	Expected cases*	Observed cases	SMR	95% CI
Included†				
Female	8.5	10	117.6	(44.7–190.5)
Male	2.2	4	181.8	(3.6–360.0)
Total	10.7	14	130.8	(62.3–199.3)
Excluded				
Female	7.2	9	125.1	(43.4–206.9)
Male	1.8	3	163.8	(0.0–349.2)
Total	9.0	12	133.3	(57.9–208.8)

* Expected cases based on observed prevalence in Independence using zip code tabulation areas.
† Presumed cases were either included or excluded in this analysis.

SMR = standardized morbidity ratio.

been excluded because of an unknown diagnosis date and a 2001 symptom date. Three more patients might not have been found if the time period had excluded 2001 because of either an unknown diagnosis or an unknown symptom date. The remaining 13 patients had been seen by a neurologist prior to 1998.

Discussion. The overall period prevalence proportion of 113 per 100,000 (95% CI = 93 to 136) is not significantly different from the prevalence found in other studies in nearby states (e.g., Colorado). It is significantly lower than the prevalence in Minnesota, thus showing the north–south latitude gradient that has been previously described. Study methods differ between the three areas, however, including the use of point prevalence in Colorado and Minnesota vs period prevalence in this study. However, the period prevalence findings from this study will eventually be comparable with the results from the Ohio and Texas studies, thus allowing for the issue of an inverse association of MS prevalence with latitude to be more carefully assessed.

We found a higher prevalence of MS in females than in males and a higher prevalence in age groups 40 to 49 and 50 to 59. This is similar to the findings of the National Health Interview Study.[5] The MS prevalence proportion in Sugar Creek was similar to that found in Independence. Virtually all of the cases were from the neurologists' offices, which is not surprising, given the relatively extensive network of specialty practice in Kansas City.

The possibility of incorrect zip codes being used, thus possibly leading to incorrect zip code prevalence calculations, should not be ignored. However, when we verified zip codes for definite, probable (Poser criteria), and presumptive cases (n = 142), we found that although some individual zip codes changed, all zip code areas (64053 plus 64054 for Sugar Creek and 64050 plus 64052 plus 64055 through 64058 for Independence) were confirmed.

The overall agreement between the treating neurologist and the consulting neurologist was good for comparing definite plus probable with definite plus probable plus presumed.[28] However, the agreement between the neurologists for the diagnosis of possible was very low; thus further illustrating the problematic use of this category in epidemiologic studies of MS.

This project has several strengths. First, there are limited data available for regional MS prevalence estimates, particularly for specific age strata and race/ethnicity groups. This study has helped to fill that epidemiologic gap. Second, the referral patterns for this disease typically involve a neurologist for clinical diagnosis. There are a limited number of neurologists serving this study area, allowing for a cost- and time-effective approach to data gathering. This case ascertainment approach, supplemented with additional data-gathering sources, has enabled us to evaluate the completeness of the neurologists' data. By comparing our total cases with those of the Multiple Sclerosis Society, we were able to ascertain that at least we had case counts that approximated the records of that society (n = 159 vs 162; see below). We had complete cooperation from all neurologists' practices and hospitals. We were also able to obtain death certificates for this population. Data from these certificates did not add anyone that we had not previously identified as a patient. Third, this study area, in conjunction with two other study areas currently doing similar research, representing different latitudes, may allow for an evaluation of the purported latitude gradient for MS previously observed in the United States and elsewhere.

Table 6 *Comparison of treating neurologist's diagnosis with consultant neurologist's diagnosis based on zip code tabulation areas*

Treating neurologist's diagnosis	Consultant neurologist's diagnosis							
	Definite (1)	Probable (2)	Presumed (3)	1 + 2 + 3	Possible	Not MS	Unknown	Total
Definite	76	15	18	109	9	7	4	129
Probable	10	7	2	19	3	1	4	27
Possible	2	5	0	7	6	26	3	42
Other	0	2	2	4	0	10	1	15
Total	88	29	22	139	18	44	12	213

MS = multiple sclerosis.

Fourth, the methods and case abstract forms developed for this project may serve as prototypes for other region-specific surveillance efforts for MS and other related diseases. Fifth, by using 4 years of case finding (instead of fewer years), we have increased our sample size and thereby obtained more stable prevalence estimates. If the year 2001 data had been excluded from our database, a number of cases would have been excluded that had been diagnosed and treated for this disease. The narrower the time window used for prevalence estimation, the greater the likelihood of missing the less severe cases. Thus, an adequate time window is of critical importance and needs to be considered when comparing prevalence proportions from different geographic areas. Sixth, the agreement rate between the treating neurologist and the consulting neurologist was good, particularly when the use of probable and presumed cases was added to definite cases.

This project also has several limitations. The primary limitation is the possibility for underascertainment of cases, through either population mobility or other reasons. In recent years, a number of individuals have left the Sugar Creek area after having their property purchased by the oil company during the 1999 to 2001 period. Sixty-six houses and nine lots with demolished houses have been purchased. It is not known if all the previous owners (n = 112) continue to reside within the study boundary area. Some of these families probably also had children. Thus, the total number of individuals involved in the buyouts is unknown. If these individuals left the Sugar Creek area and have MS, then this would have the effect of reducing the true prevalence in Sugar Creek. This large out-migration, in conjunction with movement internal to the study area, also makes it difficult to provide a reasonable estimate of point prevalence. Without contacting patients to verify residential status, we were unable to estimate prevalence at a specific point in time. In addition, when the refinery was shut down 21 years ago, a number of employees were transferred to other locations. Many of them could have resided in Sugar Creek. Second, besides being unable to account for the degree of out-migration of patients, we also may be unable to account for in-migration. We would not have captured cases that recently migrated to the study area if they had not yet visited a neurologist or if their records were incomplete. Third, we are also concerned about possibly missing MS cases who sought medical care outside the health care network of our targeted areas or who may not have access to the medical care system. Fourth, we also may have missed cases either with remitting forms of MS or with more severe forms of MS if they did not have regular contact with a physician. However, the local MS society had 162 cases in their database, which was fairly close to our final list of 159 (definite plus probable according to the treating neurologist) living in the same zip codes. Our inclusion of presumed cases when comparing the two cities also reduced our chances of missing cases and increased our sample size. Fifth, data from nursing homes were limited and lacked sufficient specific health data for our purposes. Sixth, there was a relatively small minority population within the study area. Seventh, zip code tabulation area boundaries do not exactly overlap with zip code boundaries. This has resulted in not only losing some MS cases from the study area to outlying areas but also possibly losing some legitimate cases who live in the correct zip code tabulation areas but not in the zip code areas requested from the neurologist's office.

Although this study provides additional MS prevalence information for the United States and will eventually allow for a more recent evaluation of a north–south latitude gradient of disease, it does not, and cannot, measure MS prevalence among those exposed to the refinery either during its operational period or for a decade or more thereafter. A cohort study of individuals exposed (and unexposed) to the Sugar Creek refinery when it was operating would be needed to determine the incidence and relative risk of developing MS (and other diseases, including brain cancer and leukemia). A case-control study of MS in the Sugar Creek/Independence area is being planned by the ATSDR. Such a study is needed to determine the risk factors for this disease in this population, including the possible relationship of refinery exposure to MS risk.

Acknowledgment

The authors thank the participating neurologists, without whose help the study would not have been possible. The Mid-America Chapter of the National Multiple Sclerosis Society provided both the total number of cases and the names of neurologists in their registry. Margaret Tyler of the Missouri Department of Health and Senior Services provided death certificate information. Melissa Marvel, a graduate student in public health at the University of Kansas School of Medicine, provided data entry assistance. The Agency for Toxic Substances and Disease Registry (ATSDR) provided coordination, guidance and peer review for this study. Dr. Curtis Noonan of ATSDR directed the overall three-state (Missouri, Ohio, and Texas) study, with assistance from Dhelia Williamson.

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