

Multiple sclerosis in Latter Day Saints (Mormons)

Hawkes CH, Ramkumar N, Baker R, Lyon JL. Multiple sclerosis in Latter Day Saints (Mormons).

Acta Neurol Scand 2007; 115: 260–264.

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Background – Compliant members of the Church of Jesus Christ of Latter Day Saints (LDS, Mormons) have a low incidence of heart and lung disease that may relate to their healthy life style. We wished to determine whether multiple sclerosis (MS) was less frequent in this religious body. **Methods** – To ascertain this, diagnostic and treatment coding records were accessed from the Deseret Mutual Benefit Administrators (DMBA) for the 6 year period 1997–2002. DMBA is a medical insurance company that provides medical insurance to all employees of LDS Church in the US. This information was combined with prescribing records for disease modifying treatment, principally beta-interferon and Copaxone which are medications specific to MS. **Results** – Using various search strategies we derived an approximate MS prevalence of 45–64/100,000. **Conclusion** – Comparison with MS rates from Utah and other states of comparable latitude suggest that strict LDS have an MS prevalence that is lower than expected and may reflect their healthy life style.

**C. H. Hawkes¹, N. Ramkumar²,
R. Baker², J. L. Lyon²**

¹Essex Neuroscience Centre, Oldchurch Hospital, Essex, UK; ²Department of Family and Preventive Medicine, Salt Lake City, UT, USA

Key words: multiple sclerosis; Mormons; Latter Day Saints; epidemiology

Christopher H. Hawkes, Essex Centre for Neurology and Neurosurgery; Oldchurch Hospital, Romford, Essex RM7 0BE, UK
Tel.: +44 1708 708 055
Fax: +44 1708 506506
e-mail: chrishawkes@msn.com

Accepted for publication October 11, 2006

Introduction

Preliminary evidence suggests that the prevalence of multiple sclerosis (MS) is low in strict religious societies. In the isolated Moslem community in Thugbah, Saudi Arabia, a door-to-door survey revealed just one instance of MS in 23,227 inhabitants (1). Likewise in rural Kashmir (also Moslem based) there were no cases of MS at all in a house to house survey of 63,645 individuals (2). The significance of these surveys is tempered by the effect of genetic isolation and probable lack of access to modern diagnostic facilities. Latter Day Saints (Mormons, and LDS hereafter) originated in 1830 in New York State but came to settle predominantly in Utah from 1847. Most of the LDS population of Utah originate from Northern Europe and in general have a healthy life style with low consumption of alcohol, tobacco, coffee or tea and there is a strong emphasis on marriage. This is reflected by the low incidence of many illnesses such as heart disease, lung and cervical cancer, and Utah was ranked the third healthiest State overall in 2003 (United Health Group 11th Annual report). About 70% inhabitants of Utah (popula-

tion ~2.25 million) are LDS but not all are compliant. The Deseret Mutual Benefit Administrators (DMBA) is a medical insurance agency which provides medical cover only for employees of this Church and their families in the US (~60,000 people) of whom 70% live in Utah. The LDS Church requires its employees to be compliant with its health code that proscribes use of alcohol, tobacco, coffee and tea for all employees. Those with pre-existing illness are not prevented from joining but all must observe Church health standards. Initial observations on cervical cancer in LDS showed a low prevalence and this ultimately aided the discovery of the human papilloma virus (3) now known to cause this disorder. In view of the low prevalence of illness generally in LDS, we wished to determine whether MS in strict LDS is less frequent than expected, in the hope this might provide clues regarding the aetiology of MS.

Method

Diagnosis or treatment claims for MS were identified from the DMBA file of medical claims for the 6 year period 1997–2002 using the International

Classification of Disease 9th Revision (ICD-9) code for MS (340). This provides a 6-year 'prevalence window' for disease ascertainment. Duplicate names were removed and patients assigned to 10-year age groups for each sex spanning the ages 1–64 years. Data for those over 64 years were unreliable and excluded because employees then obtain medical coverage from the Federal-funded health insurance program. Age- and sex-specific prevalence rates were calculated for each year using these cases and compared to all active employees of the Church. Some patients were recorded as MS on the basis of a single claim, but we did not regard this as a definite instance of disease unless there was a further claim in this category. In the less strict analysis we incorporated single claims whilst in the more strict analysis a potential case of MS was accepted only if there was a second claim within the 5 year period of study. We captured further potential MS cases from DMBA prescribing records. Patients in receipt of disease modifying treatment (DMT) such as beta-interferon (Avonex (Biogen Idec, Cambridge, MA, USA), Betaferon (Betlex Laboratories, Montville, NJ, USA), Rebif (Merck Serono, Rockland, MA, USA) or Glatiramer (Copaxone (Teva Neuroscience, Kansas City, MO, USA)) were considered to be a definite case as these products are only licensed for MS. Thus a single claim for one of these drugs was accepted as a definite instance of MS. Several patients identified by this approach were not always identified by the initial disease code approach as detailed above. DMT cases were combined with those identified by diagnostic coding and duplicate names were removed. This produced two data sets: (i) those receiving DMT plus additional patients making a single claim as in the less strict approach and (ii) those receiving DMT plus additional patients making two or more claims as in the more strict approach. Patients in the entire 6 year period were grouped by age and sex for the two data collection methods to provide an approximate prevalence estimate of MS from 1997 to 2002.

Comparison with Olmsted County data

Data from Olmsted County were used up to age 64 years (4) to compare with the LDS figures. Grouped data logistic regression was implemented to model the log odds of being an MS case in the two population groups, with subject status indicator (LDS vs Olmsted), age (six age groups) and gender covariates. This allowed age- and gender-adjusted comparison of the proportions of the population at risk with MS (prevalence) in the LDS vs Olmsted. The analysis was repeated

for the strict and less strict MS case identification. Analysis was implemented in Stata 9.2 (Stata Corporation, College Station, TX, USA).

Results

The average annual DMBA population in the age group 1–64 years over the 6 year study period was 60,871 and during this time there were 81 individual claims for DMT. There were 206 claims listed under ICD-9 diagnostic code of 340 using the less strict approach and 162 claims using the more strict method. Combining DMT information and diag-

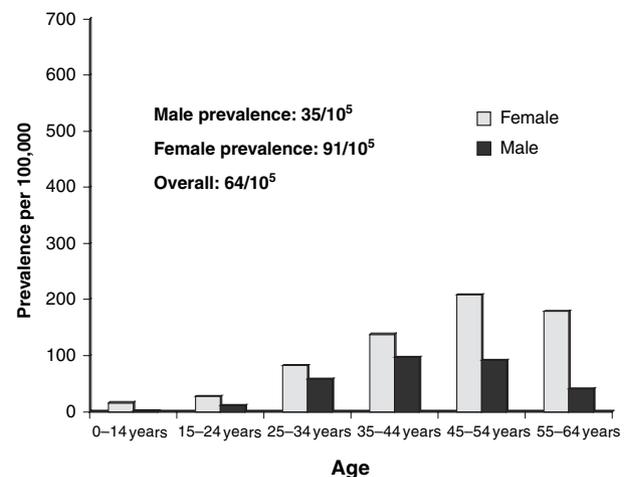


Figure 1. Prevalence of multiple sclerosis in Mormons subscribing to Deseret Mutual Benefit Administrators, pooled 1997–2002. Latitude of Salt Lake City (UT) is 41°N. The less strict case selection analysis is shown which this gives an upper limit to estimated prevalence rate. Mean annual population at risk: 60,871. Vertical axis is scaled from 0 to 700/10⁵ to allow comparison with Olmsted County – see below.

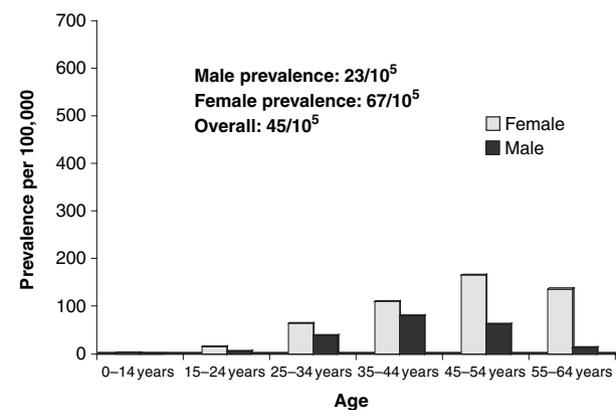


Figure 2. Prevalence of multiple sclerosis in Mormons subscribing to Deseret Mutual Benefit Administrators, pooled 1997–2002. Latitude of Salt Lake City (UT) is 41°N. The more strict case selection analysis is shown which this gives a lower limit to estimated prevalence rate. Mean annual population at risk: 60,871. Vertical axis is scaled from 0 to 700/10⁵ to allow comparison with Olmsted County – see below.



Figure 3. USA State map showing relative use of disease modifying treatment (DMT) for 2003 according to population census in same year expressed per 100,000. Numbers for each State represent all annual DMT prescriptions for 2003 adjusted for population of each State. Information kindly provided by IMS Health. Mean for whole of USA is 20.4/100,000.

nostic coding entries by the less strict analysis yielded 232 cases of MS and by the more strict approach there were 165 cases. This information was used to calculate age and sex prevalence rates (Figs 1 and 2) to give an overall prevalence using the less strict approach of $64/10^5$ and a more strict method of $45/10^5$. These estimates need to be compared with rates expected for people living at comparable latitude who are not strict LDS. We were permitted to use data supplied by Intercontinental Medical Statistics Health (IMS) relating to prescription of DMT in 2003 on a state-wide basis for the whole of USA. The IMS Health data provided relate to the retail channel (this includes chain stores, food stores and independent pharmacies) but did not include the long-term care channel or mail order service which comprise 35–45% of the overall market. Nonetheless it permits a relative estimate of MS prevalence in USA and this is displayed in Fig. 3.

As mentioned above the LDS prevalence rate was compared with that from Olmsted County (4). Using the analysis with less strict case selection, the age- and gender-adjusted reduction in odds of being an MS case in the LDS vs Olmsted group was 58% (95% CI: 41–71%; $P < 0.0001$). This is close to a 58% reduction in prevalence. Using stricter case selection criteria the age- and gender-adjusted reduction in odds of being an MS case in

the LDS vs Olmsted group was 70% (95% CI: 55–80%; $P < 0.0001$). This is close to a 70% reduction in prevalence.

Discussion

The MS prevalence rate we have derived for LDS is an approximation at $45\text{--}64/10^5$ and this places

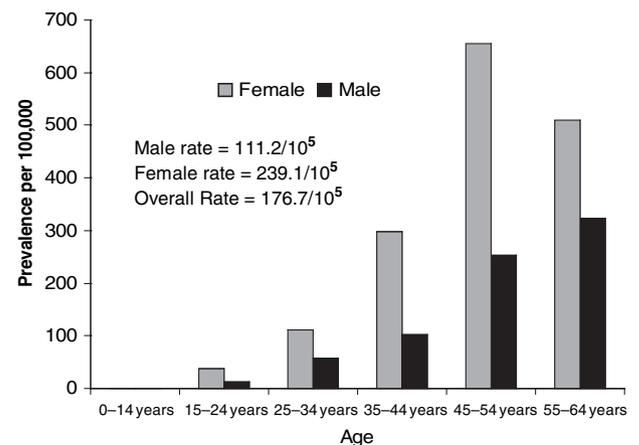


Figure 4. Crude prevalence rate of multiple sclerosis for Olmsted County, Minnesota, December 2000. Population at risk restricted to those aged 1–64 years is $110,037/10^5$. Latitude 44°N , approximately 200 miles due north of Salt Lake City. Modified with permission from Mayr et al. (4).

strict LDS in the 'medium' prevalence bracket, comparable to France or Italy. Prevalence estimates using medical insurance claims have been applied in several diseases such as diabetes (5), melanoma (6), AIDS (7), stroke (8) and rheumatoid arthritis (9). Sensitivity estimates using claims records alone vary between 54% and 96% depending on the disease in question. Where two or more methods are used for case ascertainment (as we did), sensitivity and specificity improve considerably usually to 90% or more (5, 7) but diagnostic errors still occur. We are not aware of any comparable study for MS but our dual method (claims and DMT) should possess both high sensitivity and specificity.

Strengths of our study

The age and sex distribution of our sample is in keeping with expectation for MS (see Figs 1, 2 and 4 and ref. 4) suggesting that sampling errors are probably not systematic. We compared the age and sex distribution of our DMBA sample with that for Utah State as a whole using the 2003 census figures and found it to be similar for age/sex apart from a slight deficit of both sexes aged 25–34 years. The LDS church does not endorse faith-based treatment and encourages its members to seek orthodox medical care, although there are no scientific studies of this. The ICD-9 coding-based estimate will have non-systematic magnifying or diminishing effects on the true rate but bias should not be present for cases verified through DMT usage. It is estimated that in 2003, 185,000 MS patients in USA were receiving DMT (IMS Health, personal communication) and assuming this represents 45% of the total MS population this extrapolates to 411,111 people with the disease in USA. Taking the 2003 census population estimate for Utah (2,351,467) this equates to an approximate MS prevalence for Utah of $141.4/10^5$. This is a slight overestimate (about 7% based on ref. 4) as it will include a small number in the over 65 year bracket whereas our LDS sample excludes this group. On the basis of DMT use alone (for DMBA) we derived a 'prevalence' estimate of $28.2/10^5$. If this figure represents 45% of the true DMBA MS rate this equates to a prevalence of $62.7/10^5$ – a figure similar to our estimate based on more liberal case inclusion. All this suggests that our estimate for strict LDS is reasonably accurate and equates to just under half the background rate for Utah.

The MS background rate can be obtained by comparison with data from other states of similar latitude. Northern California which is of similar latitude to Salt Lake City (41°N) has an MS

prevalence of about $140/10^5$ (UCSF MS Resource Centre) while the study from Olmsted County (44°N) about 200 miles (320 km) further north than Salt Lake City, has an overall rate of $164.5/10^5$ for those aged 1–64 years which is significantly raised as shown in Fig. 4. The 2002 estimate from the National MS Society for Utah is given at $130/10^5$. Once more these figures will be a slight overestimate for comparison purposes as our LDS group has no patients over 65 years. The Hospital MS discharge rate for Utah is $80/10^5$ (Utah Department of Health), but such figures are well recognized to underestimate the true population prevalence.

Utah Latter Day Saints emigrated from Northern Europe, during 1840–1890 and would be expected to have a high MS rate on genetic grounds and because of the alleged frequency of intermarriage. Indeed the large state-wide study of military records (10) showed regional variance that was explained in part on the basis of Scandinavian lineage. This trend would add to the significance of our observations but one study that compared intermarriage in LDS compared with other regions found no difference (11).

Weaknesses of our study

The information from prescribing records combined with a 6-year window (1997–2002) based on claims history is an approximation. It may be an underestimate because claims for mild MS might not have been submitted during the 6 year period and those over 64 years were not included. All patient source data were highly confidential and anonymous so we were unable to verify the authenticity of diagnosis or provide any subdivision based on disease type or severity. Combination of DMT usage and claims history as in the more strict approach will offset this drawback partially. Moreover, as mentioned above, where two methods of capture have been used as in other studies, sensitivity and specificity is improved (5, 7). Comparison with the Olmsted County population (Fig. 4) suggests that the pattern of age and sex distribution is similar to ours but at a higher rate. Although the Olmsted County data are one of few robust sources of comparative data, patients often migrate to the Mayo Clinic area because of its superior medical care. Their morbidity statistics are probably accurate and more thoroughly ascertained. Both issues will tend to elevate the Olmsted County MS rate and lessen the validity of our comparison.

Further error might arise because of under-reporting amongst an insured population and

chronic MS sufferers belonging to DMBA might be discouraged from claiming. There is no statistical information on this, but we would expect a relatively high claim rate from insured clients because of easy access to medical care, particularly in Salt Lake City where there is a large medical school and a high concentration of the Utah population reside in its vicinity.

It might be argued that our insured population consisted of Church employees and was therefore unrepresentative. In fact over half the members of DMBA are family members of an employee. Nonetheless there will be some socio-economic group bias which will be difficult to assess. The occupation of those covered by DMBA is not available from their files, but a range of income is. It is known that many are employed in janitorial or custodial work, but a substantial number are employed as teachers, most with advanced degrees. The average income for the contract holder during the period of the study was about \$41,000 with a range from less than \$10,000 to \$100,000 and above.

Our study is the first of its kind for MS and should be viewed as an initial assessment to determine whether those adopting a healthy lifestyle benefit by a lower than expected prevalence of MS. The limitations of this analysis are acknowledged but the most reasonable conclusion is that strictly compliant LDS have a lower than expected prevalence rate for MS and that this may be a reflection of their way of life. A more direct prevalence or incidence study in LDS would be of considerable interest.

Acknowledgements

The authors wish to thank Deseret Mutual Benefit Administrators for allowing access to their anonymized data. We also

thank IMS Health for supply of DMT figures on a state-wide basis.

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