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J Neurol Neurosurg Psychiatry published online November 20, 2010
doi: 10.1136/jnnp.2010.215186

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Trends in the epidemiology of multiple sclerosis in Greater Hobart, Tasmania: 1951 to 2009

Steve Simpson Jr,¹ Fotini Pittas,¹ Ingrid van der Mei,¹ Leigh Blizzard,¹ Anne-Louise Ponsonby,² Bruce Taylor¹

ABSTRACT
Hobart, Tasmania has been the site of two major studies of multiple sclerosis (MS) frequency, in 1951—1961 and 1971—1981. Since then, there have been no studies of MS frequency in Hobart.

Methods Using a prevalent cohort of 226 cases in 2001 and 265 in 2009, the authors undertook a two-stage survey of MS frequency in Hobart. Combined with the published data from the two preceding studies, the authors conducted a time-trend analysis of MS epidemiology over 1951—2009.

Results The age-standardised prevalence in 2001 was 96.8/100 000, and 99.6/100 000 in 2009, a significant increase from the 1961 prevalence of 32.5/100 000 (p<0.001). Female prevalence increased over each time point; male prevalence increased between 1961 and 2001 but was unchanged thereafter. Incidence over 2001—2009 was 3.7/100 000, significantly increased from the 1951—1961 incidence of 2.2/100 000 (p=0.004), though the majority of this was between 1951—1961 and 1971—1981. Mortality fell by half from 2.4/100 000 in 1951—1959 to 1.0/100 000 in 2001—2009—this decreased mortality and an older cohort contribute to the increase in prevalence. Neither prevalence (p=0.48) nor incidence (p=0.18) sex ratios changed significantly between 1951 and 2009.

Conclusions Between 1951 and 2009, the age-standardised prevalence of MS in Hobart increased threefold, and the incidence nearly doubled. Part of the increase in prevalence was due to an increased longevity, decreased mortality and increased incidence. Differences in patterns by birthplace may be explained by the Australian assisted-migration programme of 1945—1981. These data do not demonstrate the strong and significant changes in sex ratio observed elsewhere.

INTRODUCTION
Multiple sclerosis (MS) is a disease of complex aetiology, including genetic and environmental elements.¹ A key part of unravelling MS aetiology comes from studies investigating its occurrence and distribution within communities and globally. Time-trend studies, where serial cross-sectional studies are analysed over time, describe the evolution of MS in populations. These studies allow hypothesis generation about MS aetiology and provide invaluable data for the resource allocation and care for those affected.

Australia has played an important role in MS research, with a number of epidemiological studies undertaken.²⁻⁶ Two landmark studies provided important data concerning the geographic and temporal distribution of MS: the first, by McCall and colleagues² in 1968, and the second, by Hammond and colleagues³ in 1988, investigated the epidemiology of MS in the cities of Newcastle (NSW), Perth (WA) and Hobart (TAS). Both studies demonstrated a significant latitudinal gradient characterised by higher prevalence and incidence rates with increasing latitude: the MS prevalence and incidence in Hobart (42.8°S) were nearly double that of Newcastle (32.9°S) and Perth (51.6°S). Indeed, other work has demonstrated that the MS prevalence in Hobart is over six times that of northern Queensland.⁴ This latitudinal gradient has also been observed in New Zealand,⁷ Japan,⁸ France⁹ and the USA,¹⁰ and has been borne out in meta-analyses of prevalence¹¹ and incidence.¹² Additionally, both prevalence and incidence increased between the McCall² and Hammond³ studies in each of the three study sites. This temporal gradient continued in 1996, when Barnett and colleagues¹⁰ undertook a follow-up study in Newcastle in 1997.

While Newcastle has been the focus of continued follow-up in the three-city studies, there have been no follow-up studies in Hobart. We have thus undertaken a two-stage survey of MS frequency in Hobart in 2001 and 2009, and here present the results of a time-trend analysis of MS epidemiology in Hobart over the 58-year period from 1951 to 2009.

METHODS
Study region and population
The Greater Hobart Statistical Division, hereafter referred to as Hobart, lies astride the lower Derwent River in the island state of Tasmania, at latitude 42.8°S. Since 1961, the statistical division has grown from 272 km² to its present size of 1360 km² (figure 1).

Despite the 400% increase in area, the population increased only 86.9% between 1961 and 2009, from 113 932 to 212 959. The population structure changed appreciably, however, from a ‘youth-bulge’ distribution in 1961 and 1981, to an ‘apple-core’ distribution in 2001 and 2009, reflecting an older age structure (figure 2).

Context and case ascertainment
The 2001 prevalence study was done as part of the MS Longitudinal Study, with prevalence day on 7 August 2001. The 2009 prevalence study was done as part of the MS Prevalence and Genetics Study, with prevalence day on 1 January 2009. Both studies were approved by the Southern Tasmania Health and Medical Research Ethics Committee.

Cases for both prevalence studies were identified by direct neurological referral or vicariously via the local MS Society or participation in other MS studies conducted by the Menzies Research Institute, University of Tasmania, Hobart, Australia. Accepted 21 July 2010 Morse Children’s Research Institute, University of Melbourne, Melbourne, Australia. Correspondence to Bruce Taylor, Menzies Research Institute, University of Tasmania, Private Bag 23, Hobart TAS 7001 Australia; bruce.taylor@utas.edu.au

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Institute. All cases were diagnosed by a neurologist prior to inclusion in either prevalence study.


Only cases satisfying the requirements for definite MS by the 2001 McDonald13 criteria in 2001 and the 2005 McDonald14 criteria in 2009 were included. In the McCall study, the Allison and Millar criteria15 were used, including probable, early-probable and possible cases. In the Hammond study, the

Figure 1  (A) Location of Tasmania within Australia and Greater Hobart within Tasmania. (B) Growth of the Greater Hobart Statistical Division (SD) over 1961–2009. Light shaded areas show the boundaries in 1961; darker shaded areas show the boundaries in 1981; thick lines demarcate current boundaries. Alternate names for statistical localised areas in 1961 or 1981 versus present are denoted by the appropriate year.

Figure 2  Change in age/sex distribution and population of Greater Hobart, 1961–2009.
Rose criteria were used, including definite, probable and possible cases.

**Epidemiological measures**

**Divisions of epidemiological measures**

There are two major divisions of prevalence, incidence and mortality used in this analysis: by sex and by birthplace. Sex is divided into male and female, with the value for all persons referred to as the total. Birthplace is divided into Australian-born, which includes those persons born in any of the states of Australia, and overseas-born, which includes those persons born outside the territorial borders of Australia; the value for all persons, regardless of birthplace, is referred to as the aggregate.

**Calculation of epidemiological measures**

Crude point prevalence was calculated by dividing the number of cases in the study region on prevalence day by the population on prevalence day, expressed as a proportion per 100 000.

Crude mean annual incidence rate (incidence) was calculated by dividing the number of new cases with symptom-onset and living in the study region during the observation period by an estimate of the person-years of observation on the population at risk. For comparability across studies, total person-years were calculated as the midpoint population multiplied by the length in years of the observation period. Incidence was expressed as a rate per 100 000 person-years. The crude mean annual mortality was calculated in an analogous manner.

To calculate prevalence by birthplace for 2001 and incidence by birthplace for the period 2001–2009, populations by birthplace from the 2001 and 2006 censuses were used, respectively. To calculate the 2009 prevalence by birthplace, we assumed that the proportions of overseas-born and Australian-born in each 5-year age group in 2009 were identical to those in the 2006 Census.

**Calculation of distributions by birthplace**

For the McCall and Hammond studies, prevalence and incidence were not reported with stratification by birthplace and by sex. Using the distribution by sex and by birthplace provided in each publication, we were able to calculate the distribution by birthplace and by sex of prevalence for each study and incidence for the Hammond study.

**Age standardisation**

All age standardisation was done using the direct method. No single population could be used for age standardisation in this analysis, given the variability in the presentation of age-specific rates in the McCall and Hammond publications. Total prevalence and prevalence by birthplace were age-standardised to the 1961 Hobart population. This was necessary because neither the McCall nor the Hammond studies provided age-specific prevalence by birthplace. To allow comparisons with 1961, we standardised prevalence in 2001 and 2009 to the 1961 population. The prevalence data reported for the Hammond study are standardised to the 1981 Australian population and are not strictly comparable—to assess possible confounding bias, we performed a sensitivity analysis between 1971–1981 and 2001–2009, standardising the latter to the 1976 Hobart population, the population used to calculate mortality during 1971–1981.

Incidence by birthplace was age-standardised to the 1981 Australian population. This population was used to standardise incidence by birthplace in the Hammond study. The McCall study did not report incidence by birthplace.

Sex-specific prevalence and incidence by birthplace for 1971–1981 are not age-standardised, as these values were not provided as age-specific rates. Sex-specific prevalence by birthplace for 2001 and 2009, and sex-specific incidence by birthplace for 2001–2009 were age-standardised to the 1981 Hobart population to allow comparability with the crude sex-specific values from the Hammond study.

**Population data**

All population data were obtained from the relevant quinquennial Census or annual population estimates published by Australian Bureau of Statistics (ABS). All immigration data were obtained from the ABS or the Australian Bureau of Immigration and Multicultural affairs.

**Statistical analysis**

Poisson regression was used to assess the significance of changes over time in all epidemiological measures—binary (0/1) terms were included as covariates for each 10-year age-group and for sex, while study year was included as a continuous covariate, with population entered as an offset. In assessing the change over time, the coefficient of the year term was used; in assessing the change in the sex ratio, the coefficient of a (sex×year) product term was assessed.

To assess the significance of differences in characteristics of the 2001 and 2009 case samples, a two-sample t test and $\chi^2$ test were used.

All statistical analyses were carried out using STATA/SE for Windows software (Version 10.1; StataCorp LP).

**RESULTS**

**2001 and 2009 studies**

In 2001, 526 people were identified as potential MS cases. Of these, 63 were excluded for not having a clinically definite diagnosis on prevalence day, and 47 were not living in the study region, leaving 229 eligible cases. The majority (80.8%) of these were recruited from other MS studies conducted by the Menzies Research Institute, with the remainder recruited by neurologist referral (19.2%).

In 2009, 371 people were identified as potential MS cases. Of these, 45 were excluded for not having a clinically definite diagnosis on prevalence day, and 41 were not living in the study region, leaving 265 eligible cases. The majority of these were prevalent cases in the 2001 study (63.4%), with the remainder recruited by referral from a neurologist (10.2%), the local MS Society (25.0%) or other studies (5.4%).

Table 1 shows the characteristics of the 2001 and 2009 cases. Only the mean age changed significantly between 2001 and 2009 (p=0.01).

**Prevalence: 1961 to 2009**

Table 2 shows the age- and sex-specific prevalence for each of the four studies. Figure 3 depicts the age-standardised prevalence values by sex over the four studies. There was a significant increase in the total (p<0.001), male (p=0.001) and female
(p<0.001) prevalence between 1961 and 2009. The majority of this change occurred between 1961 and 2001, while the change between 2001 and 2009 was not significant (p=0.87).

Prevalence by birthplace: 1961 to 2009
Table 3 shows the prevalence by sex and birthplace for each of the four studies; figure 4 shows the total prevalence over time by birthplace. The total prevalence among Australian-born has been rising consistently since 1961 (p<0.001). Overseas-born prevalence also increased between 1961 and 2009 (p=0.05), but this occurred via a significant increase between 1961 and 1981 (p<0.001), before falling between 1981 and 2001 (p=0.31) and between 2001 and 2009 (p=0.16). Standardising to the 1991 population, rather than the 1961 population, did not alter these findings.

Figure 5 shows the change in prevalence for males and females by birthplace and for the aggregate. The patterns of change for males and females are similar. The changes in the aggregate reflect those of the Australian-born, due to the much larger numbers of cases contributed by this source. Of note is the difference in trend by sex among the Australian-born between 2001 and 2009, with males deceasing while females continue to increase, though neither of these changes reach statistical significance.

The total aggregate incidence increased significantly between 1951–1961 and 2001–2009 (p=0.04), from 2.2 in 1951–1961, to 3.6 in 1971–1981 and 3.7 in 2001–2009. However this change was confined to the first two periods (p=0.04), with no significant change thereafter (p=0.91).

Figure 6 shows the change in incidence by sex and birthplace between 1971–1981 and 2001–2009. While total and aggregate incidence remained unchanged between 1971–1981 and 2001–2009, the incidence for overseas-born groups decreased significantly (p<0.001 for males and total; p=0.006 for females). Among Australian-born, only female incidence increased significantly (p=0.017), while males and the total were statistically unchanged.

Prevalence and incidence sex ratios: 1951 to 2009
As shown in figure 7, there was no change in the aggregate prevalence sex ratio (PSR) between 1961 and 2009 (p=0.58), or in the Australian-born PSR (p=0.50) or overseas-born PSR (p=0.66) (figure 7).

The incidence sex ratio (ISR) increased between the 1971–1981 and 2001–2009 study periods, from 1.1 (95% CI 0.8 to 1.6) to 2.1 (95% CI 1.4 to 3.0), but this was not significant (p=0.18). The ISR among the Australian-born increased almost significantly (p=0.06) from 1.2 (95% CI 0.9 to 1.6) to 1.9 (95% CI 1.5 to 2.5). Among the overseas-born, the ISR was 1.1 (95% CI 0.6 to 2.1) in 1971–1981; the 2001–2009 ISR was undeterminable as the male overseas-born incidence in 2001–2009 was zero.

Mortality and longevity
The mortality decreased from 2.4/100 000 in 1951–1959 to 1.1/100 000 in 1971–1981 (p=0.02), and remained statistically unchanged thereafter (1.0/100 000 in 2001–2009, p=0.81). The mean age of the prevalent cohort increased significantly between 1961 to 2009, from 41.0 to 46.4 years (p=0.02). This increase was stronger among males, increasing from 40.1 to 47.8 years (p=0.01); for females, the mean age increased from 41.4 to 45.9 years (p=0.26).

DISCUSSION
We have undertaken a two-stage study of MS frequency in Hobart between 2001 and 2009 and, in combination with previously published studies, have conducted a time-trend analysis of MS epidemiology in Greater Hobart over the 58-year period from 1951 to 2009. This is the longest such study of MS frequency in the Southern hemisphere and comparable in length with the longest study durations in the Northern hemisphere.20 21 We found high rates of MS, with crude prevalences of 116.1/100 000 in 2001 and 125.2/100 000 in 2009, a marked increase from the 1961 prevalence of 32.5/100 000. This persists after age standardisation, now a threefold increase to 2009 prevalence 99.6/100 000, increasing by 14/100 000 every 10 years. The signifcant effect of age-standardisation reflects the ageing of the Hobart population over this interval and accounts for a portion of the increase in prevalence.

Over 2001–2009, we observed a crude incidence of 3.7/100 000, nearly double the 1951–1961 incidence of 2.2/100 000; this increase persists on age standardisation. Importantly, we observed significant differences by birthplace in the trends in both prevalence and incidence. Australian-born prevalence and incidence showed a steady increase over time, while overseas-born prevalence and incidence increased markedly up to 1981, whereupon prevalence and incidence fell precipitously. The 2001–2009 age-standardised mortality was 1.0/100 000, less than half that of the 1951–1961 period (2.4/100 000). This reduced mortality, along with a significant increase in the mean age of the prevalent cohort, from 41.0 to 46.4 years, manifest in increased case longevity.
<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>1961*</th>
<th>1981</th>
<th>2001</th>
<th>2009</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Prevalence/100000</td>
<td>Cases</td>
<td>Prevalence/100000</td>
</tr>
<tr>
<td>0-9</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<td>10-19</td>
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<td>0</td>
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<tr>
<td>20-29</td>
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<td>11</td>
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<td>61</td>
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<td>60+</td>
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<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Total</td>
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<td>12.4</td>
<td>31</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Prevalence is per 100000 with 95% CI. Figures in parentheses are prevalence age-sex standardised to the 1961 Greater Hobart population.

*For the 1961 study, the age-specific counts and prevalence rate were provided only for the 10-29 age group, rather than 10-39 and 20-29 as in the subsequent studies.
has been a considerable change in the Hobart population migration between cases and non-cases, but we also have no information regarding differential ascertainment. In our study area, between 1951 and 2009, the age-standardised incidence increased from 2.2/100 000 to 8.7/100 000, contributing to increased prevalence. Globally, Hobart incidence for the 2001 period (3.7/100 000) was 1.5 times higher than the 1986–1996 Newcastle incidence (2.4/100 000); this persisted on age standardisation. Globally, Hobart’s 2009 age-standardised prevalence (99.6/100 000) is comparable with those found in contemporaneous studies at similar latitudes: the West Coast/Canterbury (42.5°S) region of New Zealand in 2006 (86.6/100 000), the Otago/Southland (46.2°S) region of New Zealand in 2006 (109.4/100 000) and Ferrara province (44.8°N) in Italy in 2004 (95.0/100 000).

Epidemiology by place
Hobart (42.8°S) had the highest reported prevalence and incidence of MS in Australia at all time points. In the current study, the 2001 Hobart prevalence (116.1/100 000) was nearly double that of Newcastle (32.9°S) in 1996 (59.1/100 000). The incidence for the 2001–2009 period (3.7/100 000) was 1.5 times higher than the 1986–1996 Newcastle incidence (2.4/100 000), this persisted on age standardisation. Globally, Hobart’s 2009 age-standardised prevalence (99.6/100 000) is comparable with those found in contemporaneous studies at similar latitudes: the West Coast/Canterbury (42.5°S) region of New Zealand in 2006 (86.6/100 000), the Otago/Southland (46.2°S) region of New Zealand in 2006 (109.4/100 000) and Ferrara province (44.8°N) in Italy in 2004 (95.0/100 000).

Epidemiology over time
We observed a threefold increase in the age-standardised prevalence from 1961 to 2009. Such increases in prevalence over time are common in serial prevalence studies. Poskanzer suggests that an increase in prevalence in a serially measured population may reflect increased incidence, differential emigration between cases and non-cases, changes in population structure, increased duration of disease and/or changes in case ascertainment. In our study area, between 1951–1961 and 2001–2009, the age-standardised incidence increased from 2.2/100 000 to 3.7/100 000, contributing to increased prevalence (figure 6). We have no information regarding differential migration between cases and non-cases, but we also have no reason to assume such a difference. Figure 2 demonstrates there has been a considerable change in the Hobart population structure, but this has been addressed by age standardisation. Along with an ageing of the population, however, there has been an increase in the mean age of the prevalent MS cohort which, acting in concert with the decreased mortality, manifests in a significantly increased duration of disease in Hobart, accounting for a further component of the prevalence increase.

Specialist neurological care has been provided for MS cases in Hobart throughout the study period, and it is unlikely that changes in prevalence and incidence can be traced to differences in this part of case ascertainment. However, changes in the diagnostic criteria used, from the Allison and Millar criteria used by McCall and colleagues and the Rose criteria used by Hammond and colleagues, to the 2001 and 2005 McDonald criteria used in our prevalence studies, do impact prevalence estimates. In one aspect, the increase in prevalence may be partially due to the increased sensitivity of diagnostic criteria over time, allowing for the detection of less ‘typical’ cases, particularly progressive courses which were not explicitly allowed for under the Allison & Millar criteria. Use by modern criteria of paraclinical evidence such as MRI allows for the inclusion of such cases. At the same time, however, the lower specificity of the earlier criteria, reliant solely on clinical evidence and history, allowed the inclusion of similar but non-MS neurological conditions as ‘possible’ MS, a group which was included in the McCall and Hammond calculations of prevalence and incidence. Studies comparing prevalence using these criteria with the 1994 Poser criteria showed a higher prevalence with the Allison and Millar criteria (3.7% to 18.4%), and the Rose criteria (1.6% to 11.9%). Of note, studies comparing the Poser and 2001 McDonald criteria (the criteria used in our 2001 study), found little (0.7%) or no difference in their diagnostic allocation; a study comparing the 2001 and 2005 McDonald criteria (the criteria used in our 2001 and 2009 studies) found no difference in their specificities. Therefore, the McCall and Hammond studies likely overestimated prevalence, resulting in an estimate of the increase in prevalence and incidence to 2009, which is actually lower than that actually occurring.

Effects of migration
There were significant differences in the changes in prevalence and incidence over time by birthplace. Among Australian-born, there was a steady increase in prevalence and incidence over all study points; among the overseas-born, there were significant increases in the prevalence and incidence up to 1981, whereupon there were significant declines, prevalence falling precipitously after 1981 and incidence being reduced to near zero by 2001–2009. These findings may be explained by the Australian assisted-migration scheme of 1945–1981. Australia was founded and largely populated by immigrants from the UK. Following the Second World War, Australia sought to drastically increase

![Figure 3](https://example.com/figure3.png)

**Figure 3** Prevalence by sex and for total for Greater Hobart: 1961—2009, age-standardised to the 1961 Greater Hobart population. Significance of change from previous study assessed by Poisson regression. *p<0.05; **p<0.01.

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Prevalence/100000</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961</td>
<td>10</td>
<td>20.2</td>
<td>14.3</td>
<td>1</td>
</tr>
<tr>
<td>1981</td>
<td>32</td>
<td>44.8</td>
<td>32.6</td>
<td>1</td>
</tr>
<tr>
<td>2001</td>
<td>62</td>
<td>72.0</td>
<td>56.3</td>
<td>1</td>
</tr>
<tr>
<td>2009</td>
<td>94</td>
<td>108.6</td>
<td>83.1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 3** Prevalence by sex and by birthplace for Greater Hobart, 1961—2009, prevalence values age-standardised to the 1961 Greater Hobart population

<table>
<thead>
<tr>
<th>Year</th>
<th>Cases</th>
<th>Prevalence/100000</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961</td>
<td>1</td>
<td>12.7</td>
<td>8.3</td>
<td>1</td>
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<tr>
<td>1981</td>
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<td>96.8</td>
<td>63.9</td>
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<td>2009</td>
<td>10</td>
<td>26.7</td>
<td>19.1</td>
<td>1</td>
</tr>
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</table>

*Prevalence values for 1981 are not age-standardised to the 1961 population like the other years but are presented as crude, as age-specific prevalence data were not available for age standardisation.
the population, and the Australian government began providing assisted migration, from 1945 until 1981.32 Over this period, 3.8 million migrants came to Australia, the largest fraction (38.8%) coming from the UK,18 32 and the majority (52.8%) of them male.18 32 After the termination of assisted-migration in 1981, the demographics of immigrants shifted, changing from mostly coming from high-prevalence11 12 and higher-latitude (average: 42.9°) nations in Europe and North America (82.2%) to mostly from low-prevalence11 12 and low-latitude (average: 28.4°) nations (57.6%), particularly in Asia/Oceania (32.8%).32

The effects of assisted-migration are now fading, as evidenced by the decreasing prevalence among the overseas-born in 2001 and 2009 (figures 4, 5) and the sharply decreased overseas-born incidence in 2001–2009 (figure 6). However, this mass influx of genetically susceptible immigrants up to 1981, and its abrupt cessation thereafter, had significant effects on MS epidemiology in Hobart over 1951–2009. Therefore, MS epidemiology in Hobart over 1951–2009 is actually a tale of two populations. Only upon extricating these two populations from one another can sense be made of the whole and assumptions about future trends made—such predictions of future trend are important in planning hospital and health services.

Sex ratios over time
We found no significant change in the age-standardised PSR over 1961–2009, in line with other studies.2 6 7 23 33 Only in one location has a significant change in the age-standardised PSR been found, in Ferrara province, Italy between 197837 and 2004,32 increasing from 1.1 to 2.4 (p<0.05).

Among the Australian-born, we observed a near-significant (p=0.06) increase in the ISR between 1971–1981 and 2001–2009, increasing from 1.2 to 1.9. In the aggregate, we found a trend to increased ISR, nearly doubling from 1.1 to 2.1. While this trend did not reach significance, this likely reflects the small number of incident cases in both periods, with insufficient power resulting in a lack of statistical significance. Certainly elsewhere, significant changes in the ISR have been observed: in Canada,39 the ISR increased significantly over 50 years (1.014 per year over 1931–1980). In Oslo,20 the ISR increased significantly, from 1.48 to 2.30 over 1910–1980. While these data do show a smaller increase in the ISR than that observed by others,6 20 33 the trend to increased ISR is in keeping with the literature.38 It may be that this smaller magnitude of the change in ISR is a reflection of a differential effect of latitude on MS risk by sex. Such a result is borne out in our recent work,40 where the ISR of first demyelinating events varied inversely with latitude within Australia, with a 2.7-fold higher sex ratio in Brisbane (27.3°S) than Hobart (42.8°S).

Strengths and limitations
A key strength of this study is the long time-span that was studied. The medical infrastructure and specialist neurological
Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

Acknowledgements

We would like to express our thanks to those persons who assisted with this project, including the neurological evaluations done by the neurologists at the Royal Hobart Hospital: H Castley, M Dreyer and D Jones; database construction by our IT specialist T Albion; administrative assistance and support by C Hurst; and of course, all our study participants, without whom none of our research would be possible.

Funding

The Multiple Sclerosis Longitudinal Study was funded by a grant from the National Health and Medical Research Council of Australia (Project 333105). The Multiple Sclerosis Prevalence and Genetics study was funded by a principle research fellowship from the Menzies Research Institute.

Competing interests

None.

Ethics approval

Ethics approval was provided by the Tasmanian Health and Medical Research Ethics Committee (H6508, H9782).

Contributors

IV, IvdM, FP and A-LP were involved in the conception, planning and acquisition of funding for the 2001 prevalence study; BT, IvdM and FP were involved in the conception, planning and acquisition of funding for the 2009 prevalence study; BT and FP were involved in the acquisition of data for the 2001 prevalence study; BT and SSJ were involved in the acquisition of data for the 2009 prevalence study; SSJ, FP and LB were involved in the conception and implementation of the analyses used in this publication; SSJ, BT, LB and IvdM were involved in the drafting of the manuscript. All authors were involved in the critical revision of the manuscript.

Figure 7 Prevalence sex ratio (female/male) for prevalence by birthplace and for the aggregate. Significance assessed by Poisson regression.


