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# The Increasing Prevalence of Multiple Sclerosis in New Zealand

Sridhar Alla[a, b] John Pearson[b] Laëtitia Debernard[a, b] David Miller[a, b, d]
Deborah Mason[a–c]

[a]New Zealand Brain Research Institute, [b]Christchurch School of Medicine and Health Sciences, University of Otago, and [c]Department of Neurology, Christchurch Hospital, Christchurch, New Zealand; [d]Queen Square MS Centre, UCL Institute of Neurology, London, UK

**Key Words**
Multiple sclerosis · Prevalence · New Zealand · Sex ratio · Latitude gradient

**Abstract**
***Background:*** New Zealand (NZ) has a high prevalence of multiple sclerosis (MS). Worldwide, the prevalence of MS appears to be increasing. ***Objectives:*** To review all published prevalence studies undertaken in NZ to determine whether the prevalence of MS in NZ is increasing. ***Methods:*** PubMed, Medline, Scopus, Web of Knowledge, EMBASE, AMED and CINAHL were searched to identify studies reporting the prevalence of MS in NZ. Prevalence rates from the National MS Prevalence study in 2006 were compared with earlier prevalence rates for the same regions using Poisson regression. ***Results:*** Prevalence rates reported in the earlier regional studies ranged from 23.6 to 68.5/100,000 population; in the same regions in 2006, the range was 47.6–134.2/100,000 population. Prevalence rates were significantly increased in all regions studied except for the Bay of Plenty. The increase in prevalence was seen in both sexes. The sex ratio remained constant over time. ***Conclusions:*** In studies spanning almost 40 years (1968–2006), the prevalence of MS within the same regions of NZ has significantly increased whereas the sex ratio and latitudinal gradient have remained stable.



## Introduction

Multiple sclerosis (MS) is a chronic inflammatory demyelinating central nervous system disease resulting in the damage to the myelin sheath surrounding the axons of nerves in the brain, spinal cord and optic nerves [1]. The resultant lesions or plaques are the source of a wide range of clinical symptoms such as visual disturbances, sensory and motor abnormalities, gait and balance problems, and bladder/bowel dysfunction. MS is thought to be an immune-mediated disease with susceptibility arising from multiple genetic and environmental factors [2]. The degree to which environmental and genetic factors contribute is controversial and subject to ongoing debate [3–5].

A number of studies [6–9] on the prevalence and incidence of MS in the northern hemisphere suggest a steady rise in the absolute number of cases identified. In the southern hemisphere, repeated surveys in the previously surveyed regions of Australia [10–13] have also shown a consistent trend of increasing prevalence and incidence of MS over time. The increase in prevalence has been attributed to multiple factors including improved case ascertainment and access to medical services, changes in diagnostic criteria, increased survival, changing population demographics and a true increase in disease incidence. In addition studies in the northern hemisphere

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Sridhar Alla
New Zealand Brain Research Institute
66 Stewart Street
Christchurch 8011 (New Zealand)
E-Mail allsr357@gmail.com

have indicated a substantial increase in female-to-male sex ratio mainly due to an increase in the incidence of MS in women [14–16]. A recent study analyzing the sex ratio trends over time in MS populations from different geographical areas in the world has shown a modest increase in female-to-male sex ratio over time in the relapsing-remitting form of MS [15].

New Zealand (NZ) is a geographically well-defined, southern hemisphere country with latitude extending between 35 and 48°S. The largest ethnic affiliation is European (78%) followed by indigenous Māori (14%), and smaller populations of Asian, Pacific people and others [17]. The recent (2006) NZ National MS Prevalence Study (NZNMSPS) [18] reported a prevalence of 73.1/100,000 population, with a 3 times higher prevalence rate in the south (48°S) than the north (35°S). NZ's indigenous Māori population had a substantially lower prevalence of MS with a rate of 24.2/100,000 population [18]. To our knowledge, no systematic review has been undertaken of all published prevalence studies of MS in NZ and it has not been determined whether MS prevalence and sex ratio are changing over time. This study aims to systematically identify and review all published prevalence studies of MS in NZ and use these results to explore trends in overall prevalence and in the sex ratio and latitudinal gradient of the disease over time.

## Methods

*Search Strategy*

The electronic databases PubMed, Medline, Scopus, Web of Knowledge, EMBASE, AMED and CINAHL were used to retrieve articles relevant to the prevalence and incidence of MS in NZ. The search was conducted from the earliest available date for each electronic database to March 2013 using the following key words and boolean operators: 'Multiple Sclerosis' AND 'New Zealand' and 'Incidence' OR 'Prevalence' OR 'Epidemiology'.

The same search terms were used in all of the above databases. An additional manual search of the reference lists of the retrieved articles was conducted to identify articles that might have been missed in the electronic database search. The retrieved articles identified by this search were imported into a bibliographic management software program, EndNote X4 (Thompson Reuters, New York, N.Y., USA), and duplicate entries were excluded. Full texts of all the articles were obtained, and the following selection criteria were applied to determine whether they met the study's inclusion criteria.

*Selection Criteria*

In order to capture as many studies as possible, we used a broad range of inclusion criteria encompassing all original studies published on the prevalence and incidence of MS in NZ without any language restrictions. Similarly, no restrictions were placed on the diagnostic criteria used to define MS. Review type articles, conference abstracts and letters to the editors were excluded from the review as well as mortality data.

*Data Extraction and Quality Assessment*

Data was extracted from the studies that met the inclusion criteria and was tabulated.

The quality of the included studies was assessed using a tool designed for assessing quality of prevalence studies based on a scoring system suggested by Poppe et al. [19]. Each study was scored independently by two members of the research team (S.A. and D.F.M.), and the discrepancies in scoring were resolved by consensus with a third author (J.P.). Studies were grouped into three categories, i.e. 'very good', 'good' and 'poor', based on the proper definition of study population characteristics, methods of case ascertainment, reproducibility of case definition, clear statement of prevalence dates and description of statistical analyses used to derive prevalence figures. If all 5 quality assessment parameters were described completely, the study received a 'very good' rating; if the quality parameters were not clearly described, the study received a 'good' rating, and if the parameters were not described at all, they received 'poor' quality ratings; however, no study was excluded from the review based on quality. The overall quality of the study was defined by the most frequent rating for that study.

*Statistical Methods*

Crude prevalence figures are reported separately for the female, male and total samples. The bayesian 95% confidence intervals were calculated for crude prevalence for the studies where confidence intervals were not available. Prevalence rates and sex ratios in 2006 were compared with earlier prevalence rates and sex ratios for the same regions using Poisson regression [20]. All analyses were limited to persons with probable or definite MS based on criteria in current use at the time of the study. All analyses were conducted using R 2.8.1 (Vienna, Austria).

## Results

A total of 218 articles were identified by the electronic database search and none from hand search. The results of the search strategy and the selection process for inclusion in the review are presented in figure 1. Six articles which met the final inclusion criteria are the basis of the study.

*Data Extraction*

The 6 included studies [18, 21–25] were conducted between 1968 and 2006, and all were considered to be of 'very good' quality based on the study's criteria for quality assessment. All 6 studies used population at risk as a denominator based on contemporary census data. All studies used multiple sources of case ascertainment including hospital case records, MS Society registers, re-

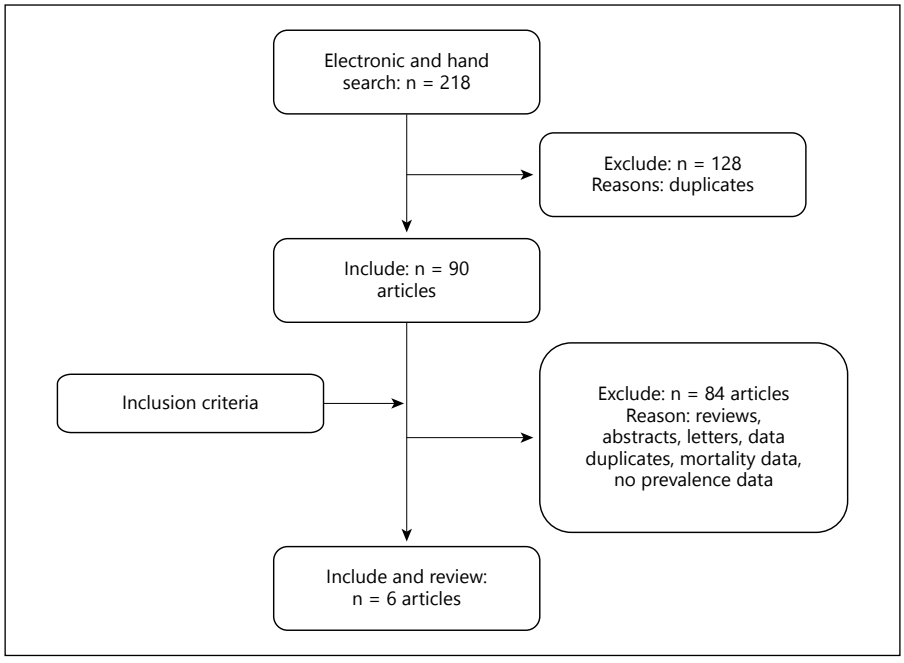


**Fig. 1.** Flow diagram of the search strategy and selection criteria.

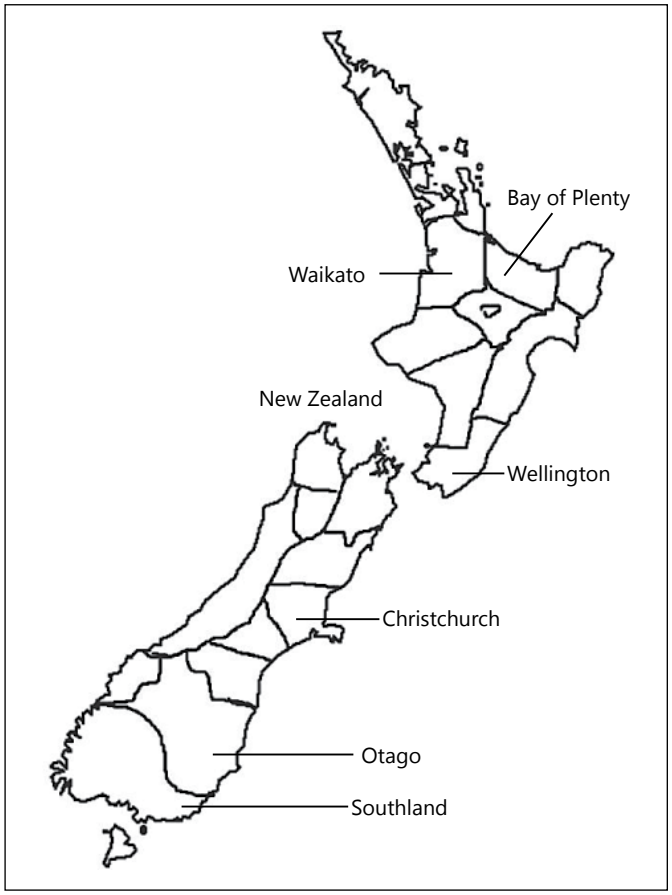


**Fig. 2.** The 5 study regions.

cords of neurologists and general practitioners to capture the cases.

One prevalence study was undertaken on a national level (NZNMSPS) in 2006 [18] whereas the other 5 were regional studies conducted in 5 regions (fig. 2) at distinct latitudes from north to south: Waikato (1981) [24], Bay of Plenty (2001) [21], Wellington (1968 and 1983) [23, 25], Christchurch (1971) [22] and Otago-Southland (1981) [24]. In all the studies, the diagnosis was confirmed by study neurologists. The criteria for MS diagnosis were not uniform amongst the studies [26–28], and only 2 more recent studies [18, 21] used magnetic resonance imaging findings in support of MS diagnosis.

The age- and sex-standardized prevalence reported in NZNMSPS [18] was 73.1/100,000 population. The crude prevalence for the 5 earlier regional studies [21–25] ranged from 23.6 to 68.5/100,000 population (table 1); in the same regions in 2006 [18], it ranged from 47.6 to 134.2/100,000 population.

Prevalence: 1968–2006

Compared with the earlier regional surveys that took place between 1968 and 2001, the 2006 national survey identified a significantly higher number of cases in each of the 5 regions studied. There were statistically significant 1.5- to 3-fold increases in the total, female and male prevalence rates in 2006 when compared with the earlier studies (1968–1983) conducted in Waikato, Wellington,

**Table 1.** Prevalence of MS in NZ and comparison between the regional and 2006 NZ National Prevalence Study

| Study | Location | Point prevalence day | Regional prevalence | | NZNMSPS 2006 | | Prevalence ratio | p value for the differences in prevalence between earlier study to 2006 NZNMSPS |
|---|---|---|---|---|---|---|---|---|
| | | | cases | prevalence | cases | prevalence | | |
| Hornabrook [23] | Wellington | 1 August 1968 | | | | | | |
| Total | | | 112 | 37.8 (31.5–45.5) | 387 | 86.3 (78.2–95.4) | 2.28 (1.85–2.81) | <0.001 |
| Female | | | 82 | 55.5 (44.7–68.9) | 284 | 123.1 (109.6–138.2) | 2.21 (1.73–2.83) | <0.001 |
| Male | | | 30 | 20.2 (14.2–28.9) | 103 | 47.4 (39.1–57.4) | 2.34 (1.56–3.51) | 0.001 |
| Cuningham [22] | Christchurch | 23 March 1971 | | | | | | |
| Total | | | 103 | 37.4 (30.9–45.4) | 558 | 107.2 (98.6–116.4) | 2.86 (2.32–3.53) | <0.001 |
| Female | | | 69 | 49.5 (39.1–62.6) | 410 | 153.9 (139.8–169.6) | 3.11 (2.41–4.01) | <0.001 |
| Male | | | 34 | 25.1 (17.9–35.0) | 148 | 58.2 (49.5–68.3) | 2.32 (1.60–3.37) | <0.001 |
| Skegg et al. [24] | Waikato | 24 March 1981 | | | | | | |
| Total | | | 65 | 23.6 (18.5–30.0) | 182 | 47.6 (41.2–55.0) | 2.02 (1.52–2.68) | <0.001 |
| Female | | | 47 | 34.4 (25.8–45.7) | 133 | 68.3 (57.7–81.0) | 1.99 (1.43–2.77) | <0.001 |
| Male | | | 18 | 13.0 (8.2–20.5) | 49 | 26.1 (19.7–34.5) | 2.01 (1.17–3.46) | 0.011 |
| Skegg et al. [24] | Otago-Southland | 24 March 1981 | | | | | | |
| Total | | | 195 | 68.6 (59.6–78.9) | 382 | 134.5 (121.7–148.7) | 1.96 (1.65–2.33) | <0.001 |
| Female | | | 147 | 103.5 (88.1–121.7) | 286 | 198.3 (176.7–222.7) | 1.91 (1.57–2.33) | <0.001 |
| Male | | | 48 | 33.7 (25.5–44.7) | 96 | 68.7 (56.3–83.9) | 2.03 (1.44–2.88) | <0.001 |
| Miller et al. [25] | Wellington | 30 June 1983 | | | | | | |
| Total | | | 209 | 61.3 (53.5–70.2) | 387 | 86.3 (78.2–95.4) | 1.41 (1.19–1.67) | <0.001 |
| Female | | | 149 | 87.1 (74.2–102.2) | 284 | 123.1 (109.6–138.2) | 1.41 (1.16–1.72) | <0.001 |
| Male | | | 60 | 35.3 (27.4–45.4) | 103 | 47.4 (39.1–57.4) | 1.34 (0.98–1.84) | 0.07 |
| Chancellor et al. [21] | Bay of Plenty | 15 January 2001 | | | | | | |
| Total | | | 86 | 50.0 (40.0–62.0) | 132 | 51.3 (43.3–60.9) | 1.02 (0.78–1.34) | 0.882 |
| Female | | | 70 | 79.5 (63.0–100.5) | 97 | 73.3 (60.1–89.4) | 0.92 (0.68–1.25) | 0.601 |
| Male | | | 16 | 19.3 (11.9–31.3) | 35 | 28.1 (20.2–39.0) | 1.45 (0.81–2.63) | 0.214 |

Figures in parentheses are 95% confidence intervals, derived by the bayesian method; p value differences are for Poisson regression.

Christchurch and Otago-Southland, but the prevalence was essentially unchanged compared with the prior study (2001) in the Bay of Plenty.

Sex Ratio over Time

A difference in prevalence rates between sexes was consistently reported in all studies, which showed that females have a higher prevalence of between 2.5 and 3 times than males. There were no significant changes in sex ratios ($p > 0.05$) over time (1968–2001) between earlier studied regions and NZNMSPS (2006) for the same regions (fig. 3).

Latitude Gradient

The study of Skegg et al. [24] conducted in 1981 showed a 2.9 times higher prevalence of MS in the southern regions (Otago-Southland) of NZ than the northern regions (Waikato). The NZNMSPS (2006) showed a similar gradient (2.8 times) in prevalence between the same southern and northern regions, indicating a constant gradient in the prevalence of MS in NZ over the period of 25 years between the studies (table 1).

## Discussion

The review identified 1 national and 5 regional prevalence studies reporting the prevalence of MS in NZ. Some variation in the prevalence rates among the regions and between the two islands is evident. The major finding of this review is that between 1968 and 2006, the prevalence of MS appears to have significantly increased throughout NZ; the only exception was in the Bay of Plenty, and the unchanged prevalence there is probably explained by the

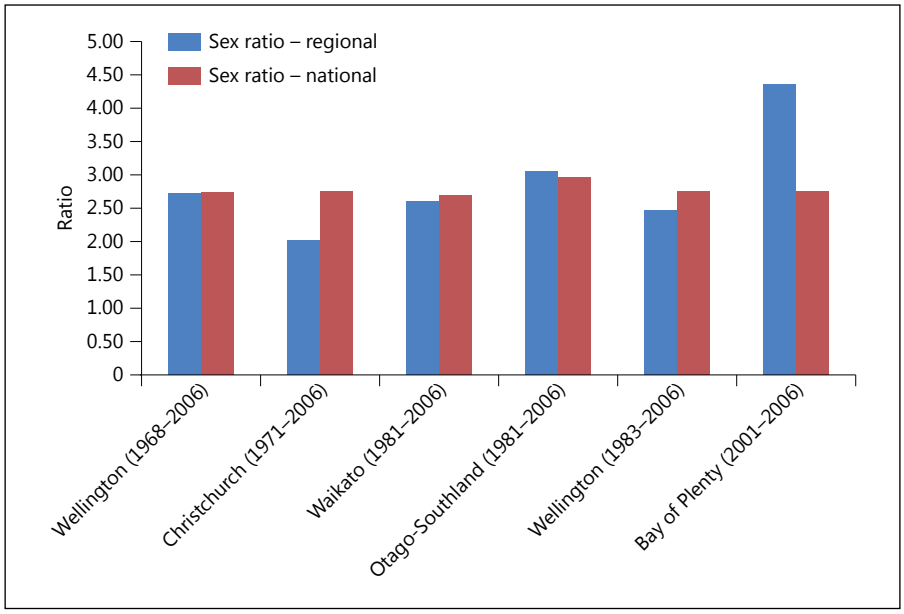


**Fig. 3.** Comparison between previous regional sex ratios (1968–2001) and the 2006 national sex ratios by region.

previous survey in that region having taken place only 5 years earlier (2001). The other major findings are that in spite of an increase in overall prevalence over a period of several decades, the female-to-male sex ratio and latitudinal gradient in the prevalence of MS were essentially constant over this period.

Our data showing an increasing prevalence over a period of decades is consistent with several studies conducted in the northern hemisphere [6–9] and in another southern hemispheric country, Australia [10–13]. Repeated surveys in several Australian cities including Perth, Newcastle and Hobart, Tasmania, have shown increases in MS prevalence between 1951 and 2009 [10–13]. There are multiple potential factors that could contribute to the increase in prevalence [6, 7, 9]. First, it is possible that this represents a true increase in disease frequency, which, if correct, is due to as yet undetermined factors. Secondly, improvements in diagnosis and the advent of magnetic resonance imaging and new diagnostic criteria may lead to earlier diagnosis and greater detection of clinically milder cases [29]. Thirdly, general improvement in health care services and awareness of the condition may be increasing case ascertainment. Finally, increasing long-term survival may be due to improved general medical care and the possible beneficial effect of disease-modifying treatments [30]. That the latitudinal gradient in the prevalence of MS has remained constant over time suggests that factors other those accounting for the gradient per se may be responsible for the overall increase in prevalence.

A number of explanations have been put forward for differences in prevalence rates between the two islands. Proposed mechanisms for the higher disease prevalence at more southerly latitudes include: (i) a greater genetic susceptibility in the southern population, a large proportion of whom originated from Scotland and the British Isles which also exhibits a high prevalence of MS [23, 31]; (ii) a smaller population of Māori, who may have a reduced genetic susceptibility to MS [25]; (iii) a lower ambient winter ultraviolet radiation exposure with consequently decreased vitamin D levels [18, 32, 33], and (iv) an increased susceptibility to Epstein-Barr viral infection at higher latitudes [18, 32, 33]. Further studies would be needed to specifically investigate the potential contribution from these or other risk factors.

A recent meta-analysis [15] with data from 13 countries from throughout the world found a modest increase in sex ratio from 2.35 to 2.73 over time among MS patients, particularly in females with the relapsing-remitting MS phenotype. Individual studies from several countries including the USA [16], Canada [14], Japan [34] and Iran [35] have also reported an increase in female-to-male sex ratio over time. However, we did not observe a significant change in sex ratio over time between the studies. Although not significant, there appears to be an unusually high female-to-male sex ratio in the Bay of Plenty region in 2001 [21]. The most likely explanations other than chance for a high sex ratio difference are an undercount of males with MS in 2001 due

to a lack of complete ascertainment, migration of males with MS into the region between 2001 and 2006 or an increase in incidence between 2001 and 2006. The small number of cases in the region and lack of evidence against migration or increased incidence makes it difficult to differentiate any cause of the relatively high sex ratio in 2001 from stochastic variation.

The lack of evidence for a change in sex ratio is also true of studies from Sweden [36] and Australia [13]. Suggested explanations [14, 15] for a change in sex ratio – where it has been seen – include altered environmental factors such as solar ultraviolet radiation exposure resulting in altered vitamin D biological activity, latitude-sensitive gene-environment interactions, and changes in lifestyle factors such as changing roles of women in workforce, outdoor activity, dietary habits, alteration in menarche, and timing and number of childbirths. Our findings suggest that such changes – if they have occurred in NZ – have not led to a change in disease susceptibility according to sex.

Although not included in the review, we acknowledge a number of studies that are either review type articles or have reported MS hospital admission/discharge data and mortality data in NZ [31, 37–39]. The review has used crude prevalence rates in comparing studies due to nonreporting of sex- and age-standardized prevalence in 4 of the 5 regional studies, to avoid bias in our results. However, the increase in prevalence remained statistically significant when the available age- and sex-standardized prevalence rates were used to compare between the earlier [24] and the national study [18] for Waikato and Otago-Southland regions. All 5 regional studies used census-defined geographical regions and included patients resident in the study area for the estimation of prevalence. The best available local resources were utilized to capture as many cases as possible at the time of the study, none used capture-recapture methodology; thus, the completeness of the case ascertainment cannot be fully confirmed.

## Conclusions

In studies spanning almost 40 years (1968–2006), the prevalence of MS within the same regions of NZ has significantly increased (by 1.5–3 times) whereas the latitudinal gradient of prevalence has stayed the same. The stable prevalence in the Bay of Plenty with 2 studies undertaken only 5 years apart is a striking contrast with the large increases seen with longer intervals of 23–38 years in the other 4 regions. The increase in prevalence may reflect improved case ascertainment and access to medical services, changes in diagnostic criteria, increased survival, and a true increase in disease incidence. A formal incidence study could help elucidate whether there is a true change in the frequency of the disease, and such a study is now under way.

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## Disclosure Statement

Conflict of interest: none.

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