# The incidence of multiple sclerosis in New Zealand: A prospective, nationwide population-based study

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## BACKGROUND

Incidence studies are a well validated tool to better elucidate the cause and risk factors of a disease and plan effective preventive and management strategies. New Zealand (NZ) is ideally suited to such an observational study as it has a geographically well-defined population of manageable size (4,242,048) with a latitude extending from $35^0$S to $48^0$S and a uniformly accessible health care system.

Worldwide, the incidence of multiple sclerosis (MS) appears to be increasing. Currently there are no national estimates of the incidence of MS in NZ. Only two studies[1,2] have been undertaken to measure the incidence of MS in NZ, both are regional, and were conducted between two and four decades ago. It is likely that changes in diagnostic criteria, improved case ascertainment and a possible increase in incidence mean that these lack current validity. The 2006 NZ national MS prevalence study[3] reported a high prevalence of MS in NZ (73.1 per 100000 population) as well as a 3 fold increase in prevalence between northern ($35^0$S) and southern regions ($48^0$S). The current study was designed to survey the incidence of MS in NZ, examine its relationship with latitude, ascertain changes in incidence over time and investigate possible environmental risk factors.

**AIM**: To survey the national incidence of MS and examine its relationship with latitude in New Zealand.

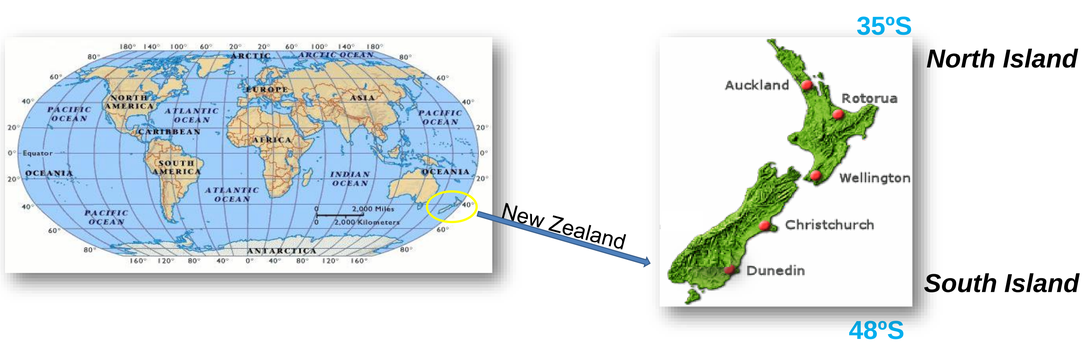


Figure 1. World Map with New Zealand's Latitudinal Extent

## METHODS

The NZ National MS Incidence Study is a prospective, nationwide, population-based observational study that surveyed the incidence of MS in NZ over a period of 2 years between June 1st 2012 and May 31st 2014. All cases diagnosed with MS (revised McDonald criteria (2011))[4] during the study period, and resident in NZ at the time of diagnosis were included. Patients with clinically isolated syndromes, possible MS and neuromyelitis optica were excluded.[5] The incident cases were recruited through multiple sources including hospital and private neurology clinics, MS Societies, specialist neuro-ophthalmology clinics and neuroimaging centres. In regions with no designated neurologist, general physicians notified incident cases. The study was approved by the Multi-region ethics committee and all participants completed a written consent.

All participants were sent a self-administered questionnaire that included demographic and personal information including place of residence, education and employment history, smoking habits and quality of life. Clinical information including the date and nature of first symptoms, MS phenotype, date of diagnosis, relapse history, para-clinical tests (CSF, visual evoked potentials), MRI reports and disability assessments were provided by the notifying neurologist or physician. Disability at the time of diagnosis was assessed by a neurologist/physician using the Expanded Disability Status Scale (EDSS).[6] The population demographics were obtained from the 2013 NZ census and incidence was age standardised to the European standard population.

For analysis of incidence by latitude, the country was divided into six broad latitudinal regions from North to South. For each region, a population weighted centroid (PWC) was calculated and this centroid was taken as the latitudinal reference point for that region. The age standardised incidence (ASI) with 95% confidence intervals (CI) were calculated for each region. The latitude gradient was estimated using a simple linear regression model on the population weighted centroid latitudes south of Auckland ($37^0$S). The current incidence was compared with earlier regional incidence data using incidence rate ratios with Poisson confidence intervals.

## RESULTS

A total of 245 incident cases were identified during the study period. The annual ASI of MS in NZ was 3.0 per 100,000 population (CI 2.4 - 3.5). The incidence was 1.4 (CI 1.0 - 2.0) for males and 4.4 (CI 3.5 - 5.3) for females. The female to male sex ratio was 3.3:1.

MS onset was relapsing-remitting in 90% and progressive in 10% of cases. The mean age at the onset of symptoms was 37.6 ± 12.0 years (range: 13.7 - 71.7 years) and the mean age at diagnosis was 42.4 ± 13.0 years. In 25.5%, the first symptoms occurred over the age of 40 years and in 18%, the first symptoms occurred over the age of 50 years. The mean disability at the time of diagnosis was 2.3 ± 1.6 as measured by EDSS.

A latitudinal gradient was seen with ASI increasing 3.8 times from North ($37\ ^0$S) to South ($48^0$S) ($p<0.001$). The earlier regional study conducted in 1981[2] showed a 2.7 times increase in incidence between the northern region of NZ (Waikato, $37.9^0$S) and the southern region (Otago-Southland, $45.8^0$S). The present study shows a significantly higher gradient (4.5 times, $p = 0.03$) in incidence between the corresponding northern and southern regions.

## DISCUSSION

This is the first prospective, nationwide, population-based MS incidence study worldwide. The study confirms that NZ is a high risk country for MS with a striking north to south latitudinal gradient in incidence. Unlike a number of northern hemisphere studies[7,8] which have shown a decrease in latitudinal gradient over time our study shows no attenuation of the latitude gradient, in fact there has been a 1.8 times increase in incidence gradient over the last three decades. The 3.8 times increase in the incidence of MS from the north to the south mimics the latitudinal gradient seen in MS prevalence in NZ.

Whether these increases reflect changes in environmental or genetic factors or a combination of both remains unknown. Similarly why it differs from that seen in the Northern hemisphere remains unclear.

The mean age at onset in our cohort of 37.6 years (SD 12.0) is higher than previously reported. This may in part be due to increased certainty in diagnosis in the older population due to an increased availability of MRI and improved diagnostic criteria. Interestingly, this finding is similar ((37.6 ± 7.9) to that found in an Australian study[9] which examined the role of environmental factors in first demyelinating cases (n = 216). The reasons reported for this apparent increase, which would seem to be confirmed by our cohort, are that - southern latitudes may influence disease differently than the northern latitudes, and the mean age reported may more realistically reflect the true mean age of onset of MS in the overall population.

## CONCLUSIONS

We report the results of the first prospective, population-based MS incidence study to include an entire country. The incidence of MS is high in NZ with a striking latitude gradient which appears to have increased over the three decades. The age at onset of symptoms is higher than that reported in the northern hemisphere.

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### References

1. Hornabrook RW. The prevalence of multiple sclerosis in New Zealand. Acta Neurol Scand 1971;47:426-38
2. Skegg DC, Corwin PA, Craven RS, et al. Occurrence of multiple sclerosis in the north and south of New Zealand. J Neurol Neurosurg Psychiatry 1987;50:134-39.
3. Taylor BV, Pearson J.F., Clarke G, et al. MS prevalence in New Zealand, an ethnically and latitudinally diverse country. Mult Scler 2010;16:1422-31.
4. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria. Ann Neurol, 2011;69:292-302.
5. Wingerchuk DM, Hogancamp WF, O'Brien PC, et al. The clinical course of neuromyelitis optica (Devic's syndrome). Neurology 1999; 53: 1107-14.
6. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). Neurology 1983; 33: 1444-52
7. Ascherio A, Munger KL. Environmental risk factors for multiple sclerosis: part I: the role of infection. Ann Neurol 2007;61:288–99.
8. Herna´n MA, Olek MJ, Ascherio A. Geographic variation of multiple sclerosis incidence in two prospective studies of US women. Neurology 1999;53:1711–18.
9. Taylor BV, Lucas RM, Dear K, et al. Latitudinal variation in incidence and type of first central nervous system demyelinating events. Mult Scler, 2010,16:398-405.