Temporal Changes in the Age at Multiple Sclerosis Onset: Importance of Controlling for Equal Observation Time

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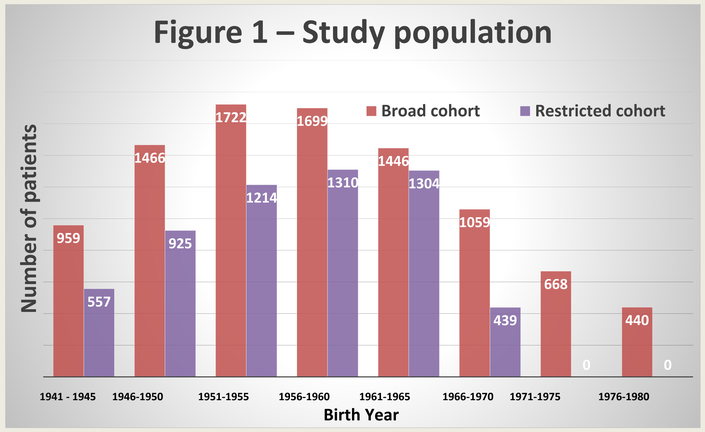
BACKGROUND

- Previous studies have examined whether changes in the age at multiple sclerosis (MS) onset have occurred over time, but findings have been inconsistent.
- If a substantial change has occurred, it could have important implications for health care planning and may indicate shifts in environmental etiological factors.
- It is challenging to assess these trends. For example, when comparing recent birth cohorts to earlier birth cohorts, spurious findings may result if insufficient time is allowed for individuals from the recent birth cohort to develop MS.

OBJECTIVE

- To investigate temporal trends in age at onset in MS patients from three Canadian provinces, and assess the impact of controlling for equal observation time between birth cohorts.

Figure 1 – Study population



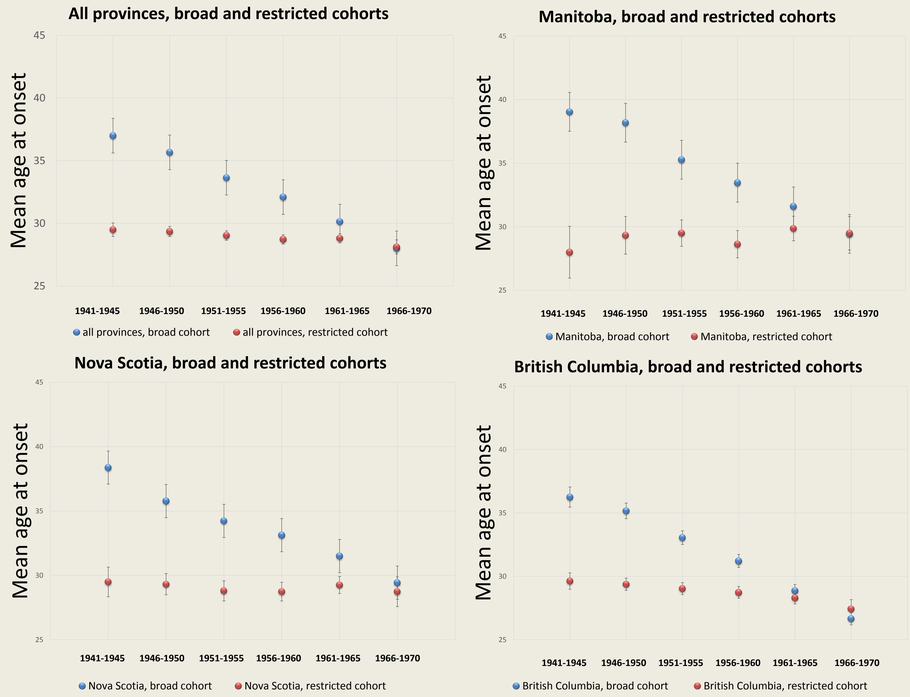
METHODS

- We accessed data from MS clinic databases in British Columbia (BC), Manitoba (MB) and Nova Scotia (NS). The BC and NS databases were established in 1980, while the MB database was established in 1998.
- Patients with definite MS as established by Poser or McDonald criteria were grouped by birth year (1941-1980) into 5 year blocks.
- Initially, the 'broad' cohort including all MS patients was analyzed, both as the entire population and separately by province. A 'restricted' cohort was then created to allow an equal observation time for each birth cohort, in which all patients had reached at least age 40 (80th percentile for onset age) by study end (12/31/2007) and had MS onset by age 40.
- Trends in the age at onset of MS were assessed using linear regression.

RESULTS

- A total of 9459 MS patients were included (BC=5423, MB=1419 and NS=2617). See Figure 1 for the distribution across birth years for the 'broad' and 'restricted' cohorts.
- *Broad cohort:* steep decline in the age at onset: from 37.0 (SD:10.8) years for the earliest birth group (1941-1945) to 28.0 (SD:6.4 years) for the 1966-1970 birth group and 23.3 (SD:4.2) for the most recent birth group (1976-1980). The mean average decrease in age at onset between consecutive birth groups was 1.9 years (Figure 2).
- *Restricted cohort (n=6003):* Decrease in the mean age at onset still evident - 30.0 (SD:6.7) years for the earliest birth group and 28.3 (SD:6.0) years for the 1966-1970 birth group, p<0.001). The mean average decrease in age at onset between birth groups was 0.2 (Figure 2).
- However, the decrease in average age was considerably smaller in the restricted broad cohort, at 0.3 years between each consecutive birth groups.

Figure 2 – Mean age at onset over time*



*the error bars in Figure 2 represent standard errors of the mean

CONCLUSIONS

- After ensuring equal observation times, our time restricted analyses of three large MS clinic databases indicate a small decrease in onset age over four decades of birth cohorts.
- The results demonstrate how estimates of change in the age at MS symptom onset between birth groups over time can be significantly inflated when observation time differs between birth cohorts.
- Comparable observation times should be accounted for when addressing trends in the demographics of MS.

STRENGTHS:

- This study used a large dataset including MS patients from three provinces in eastern, central and western Canada.
- The follow up period was long, incorporating up to 28 years of ascertainment and 4 decades of birth years.

LIMITATIONS:

- These 3 databases captured more than half of, but not all, MS cases in BC, NS and MB combined. It is possible that age at onset trends are different among patients that did not attend these clinics, although the impact of unequal observation times would likely be the same.

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REFERENCES:

1. Alonso-Magdalena L, R.-P. L., Moral E et al. (2010). Anticipation of age at onset in multiple sclerosis: methodologic pitfalls. *Acta Neurologica Scandinavica, 121*(6) **2.** Celius EG, S. C. (2009). Change in sex ratio, disease course and age at diagnosis in Oslo MS patients through seven decades. *Acta Neurologica Scandinavica. Supplementum.*(189), **3.** Tremlett H, Z. Y., Rieckmann P et al. (2010). New perspectives in the natural history of multiple sclerosis. *Neurology, 74*(24), 11. **4.** Poser CM, Paty DW, Scheinberg L, *et al.* (March 1983). New diagnostic criteria for multiple sclerosis: Guidelines for research protocols. *Annals of Neurology* 13 (3): 227–31

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