Lab: Descriptive Epidemiology of Multiple Sclerosis

Background: Multiple sclerosis (MS) is an episodic and progressive neurologic disease. Patients have acute episodes of neurologic dysfunction and then return to near normal function with progressively worsening function over time. Because "episodic" is part of the definition of multiple sclerosis, a diagnosis cannot often be made after the first episode—year may elapse between the onset of disease and its definitive diagnosis. Until recently there were few treatment options available that showed any evidence of slowing the progression of neurological dysfunction.

Read: Bronnum-Hansen H, Koch-Henricksen N, Hyllested K. (1994). Survival of patients with multiple sclerosis in Denmark: a nationwide, long-term epidemiologic survey. Neurology, 44, 1901 - 1907.

Questions

1. What do *these survival curves* tell you about the natural history of multiple sclerosis?

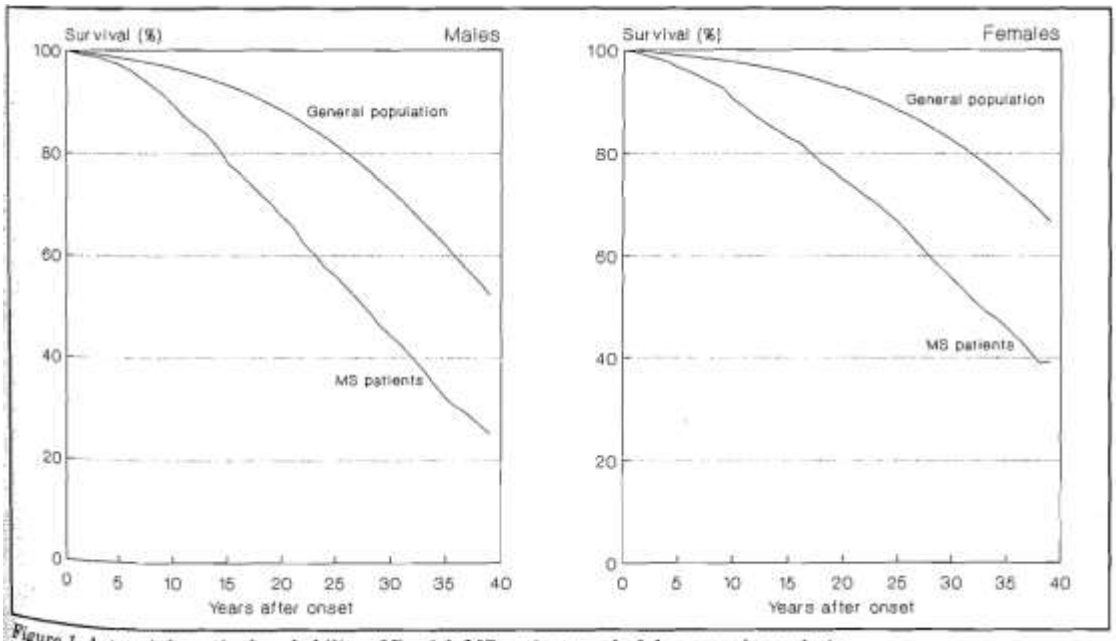

Figure 1. Actuarial survival probability of Danish MS patients and of the general population.

2. Natural history, risk factors, suspected pathogenic mechanism.

(a) Use the Merck Manual for Health Care Professionals (link is active) to list salient features in the natural history of multiple sclerosis. In addition, list known risk factors.

(b) Describe the pathogenic mechanisms that are thought to cause MS.

3. Here are the first couple of lines from Table 1 from the article:

Table 1. Standardized mortality ratios and excess death rates from onset and from time of diagnosis of MS

Age at onset (yr)	Sex	No. of observed deaths	No. of expected deaths	Person-years	Standardized mortality ratio	95% Confidence interval	Excess death rate	95% Confidence interval
<20	Men	47	6.6	3,741	7.07	5.20-9.41	10.8	7.5-14.9
	Women	54	7.1	6,370	7.59	5.70-9.91	7.4	5.3-9.9
	All	101	13.7	10,111	7.34	6.00-8.96	8.6	6.8-10.8

Let us focus on the data for men with disease onset at less than 20 years of age (first row of table):

a) The first column reports the number of deaths ("No. of observed deaths").

b) The second column reports the number of deaths that would be expected in a sub-cohort of this size and age if the mortality was that of the general population ("No. of expected deaths"). The third column lists the person time in the sub-cohort ("person-years"). Because the expected rate R = A / T, where A is the expected number of deaths and T is the sum of person-time, we can infer that the expected rate = (6.6) / (3,741) = .0018 = 1.8 per 1000 person-years.

c) The next column is the standardized mortality ratio (SMR), defined as

SMR = (No. of observed deaths) ÷ (No. of expected deaths)

In this case, SMR = 47 ÷ 6.6 ≈ 7.1, indicating that the MS men in this age range had a mortality rate that was 7 times that of the reference population. (The table lists the SMR in this group as 7.07.)

Note that an SMR of 1 indicates that the observed number of cases equals the expected number of cases. An SMR of more than 1 means that the observed rate is greater than expected, and an SMR of less than 1 indicates that the observed rate is less than expected. Thus, the SMR is a type of **relative risk**.

d) The next column is the 95% confidence interval for the SMR. In this case, the confidence interval suggests that, after accounting for the imprecision of the estimate, the SMR is somewhere between 5.20 and 9.41.

e) The next column lists the Excess death rate, defined as (Observed death rate) – (Expected death rate). The Observed death rate in this group per 1000 person-years = 47 / 3,741 person-years = 12.6. The expected death rate (from part *b*) is 1.8 per 1000 PYs. Therefore, the excess death rate = 12.6 – 1.8 = 10.8 (per 1000), indicating 10.8 additional death per 1000 person-years in this group. This statistic is often referred to as the rate difference or "risk" difference. The last column is the 95% CI for the rate difference.

3. Calculate these basic epidemiologic measures for the cohort of women with onset at age < 20. In each instance, find the comparable result in Table 1. In addition, interpret each of these statistics.

3a. The observed death rate

3b. The expected death rate

3c. The SMR

3d. The excess rate

4. In descriptive epidemiology we express disease occurrence according to person, place, and time variables.

4a. What **person variables** are analyzed in this study?

4b. How was **place** analyzed?

4c. Besides time of survival, what other **time variable** is analyzed?

5. List the **data sources** used in this study. Describe the information provided by each data source.

6. List U.S. data sources comparable to the Danish sources. Group discussion encouraged!