

Lab: Descriptive Epidemiology of Multiple Sclerosis

Background: Multiple sclerosis (MS) is an episodic and progressive neurologic disease. Patients generally have acute episodes of neurologic dysfunction and then return to near normal, but generally not completely normal function. Over a long period of time, there is progressively worsening function. Because “episodic” is part of the definition, a diagnosis can generally not be made after the first episode. Often years may elapse between the onset of disease and its official diagnosis. Until recently (with the introduction of Betaseron and other drugs) there were few treatment options available that showed any evidence of slowing the progression of neurological dysfunction.

Instructions

1. Review section 2.4 in the text. (*Optional:* Complete the Review Questions for section 2.4.)
2. Read this article: 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. [[Link to full text article](#)]
3. Answer the following questions.

Questions

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

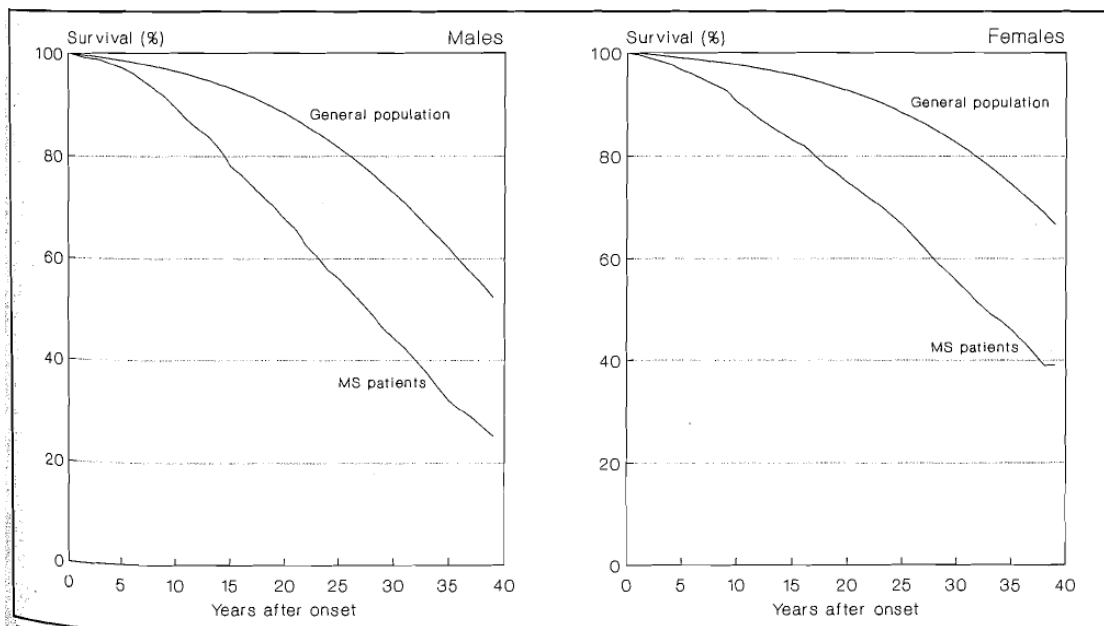


Figure 1. Actuarial survival probability of Danish MS patients and of the general population.

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 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 the table):

- The first column reports the **No. of observed deaths**. This is a type of *incidence count*.
- The second column reports the **No. of expected deaths** and the third column lists **person-years** in the study population. Each year each live person contributed 1 person-year to the group. Thus, the 3,741 person-years reported in this table is equivalent of 3741 persons living for one year. Note that:

$$(\text{Expected no. of deaths}) = (\text{Rate in reference population}) \times (\text{Person-years in study population})$$

Therefore,

$$(\text{Rate in reference population}) = (\text{Expected no. deaths}) / (\text{Person-years in study population})$$

Thus, we can infer that the rate in this reference population = $(6.6) / (3,741) = .0018 = 1.8$ per 1000 person-years.

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

$$\text{SMR} = (\text{No. of observed deaths}) \div (\text{No. of expected deaths})$$

In this case, $\text{SMR} = 47 \div 6.6 \approx 7.1$, indicating that the group had a mortality rate about 7 times that of the reference population. (The table lists the SMR 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**.

- The next column is the **95% confidence interval for the SMR**. In this case, the confidence interval suggests that the “true” SMR is between 5.20 and 9.41.

e) The next column lists the **Excess death rate**:

Excess death rate = (Observed death rate) – (Expected death rate)

Recall that the general formula for a “rate”¹ is:

$$\text{Rate} = \frac{\text{no. of cases}}{\text{person - years}} \times \text{multiplier}$$

The observed death rate (per 1000 person-years) in this group =

$$\frac{\text{No. of observed deaths}}{\text{Person - years}} \times 1000 = \frac{47}{3,741} \times 1000 = 12.6.$$

Recall that the expected death rate inferred in part “b)” of this list was determined to be 1.8 (per 1000). 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 also called the **risk 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!

¹ This is a non-technical definition of “rate.” Chapter 6 introduces more formally definitions of “rate”.