Lab: Descriptive Studies
Part A: Multiple Sclerosis

Instructions

1. Read pages 49 – 55 in Chapter 2. PPT slides for Chapter 2 are available.
2. Complete the Review Questions for section 2.4.
3. Read this background and abstract:

Background: Multiple sclerosis (MS) is both an episodic and progressive form of neurologic degeneration. Patients generally have acute episodes of neurologic dysfunction and then return to near normal, but generally not completely normal function. Thus, 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.

Abstract from the article: We estimated survival probability and excess death rates for patients with MS on the basis of data from the Danish Multiple Sclerosis Registry, which includes virtually all patients diagnosed with MS in Denmark (population, five million) since 1948. We reviewed and reclassified all case records according to standardized diagnostic criteria. By linkage to the Danish Central Population Registry, we lost to follow-up only 25 patients who had emigrated. The median survival time from onset of the disease was 28 years in men (compared with 40 years in the matched general male population) and 33 years in women (versus 46 years). The median survival time from diagnosis was 22 years in men (versus 37 years) and 28 years in women (versus 42 years). The excess death rate between onset and follow-up (observed deaths per 1,000 person-years minus the expected number of deaths in a matched general population) was 14.3 in men, which was significantly higher than in women (12.0). Excess mortality increased with age at onset of MS in people of each sex. The 10-year excess death rate has decreased significantly in recent decades. Excess mortality was highest in cases with cerebellar symptoms at onset.

4. Look over the lab questions (below).
5. 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. [Link to the full article.] Comment: You do not need to understand every element of the article to get a lot out of this lab.
6. Discuss the lab questions online.
7. Answer the question.

Questions

1. Here are the survival curves from the article. Survival curves plot the percent of a cohort surviving over time. What do these survival curves tell you about the natural history of multiple sclerosis?

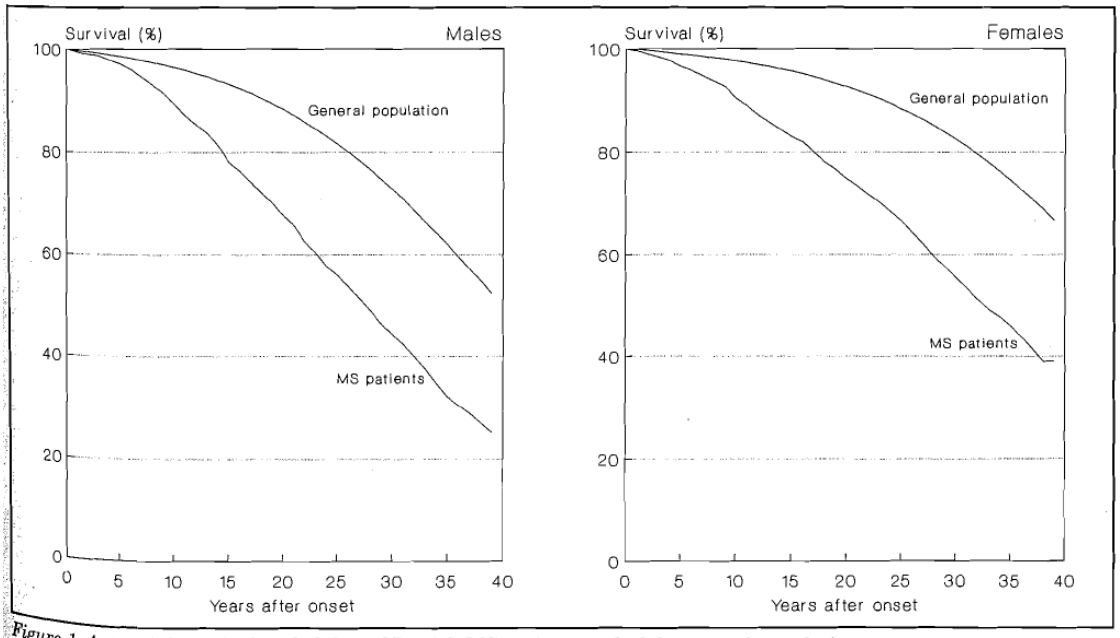

Figure 1. Actuarial survival probability of Danish MS patients and of the general population.

2. Use a reliable medical source (such as the Merck Manual Home Edition or Merck Manual for Health Care Professionals) to list additional features in the natural history of multiple sclerosis. Also use this source to list known risk factors for the disease.

3. Here is a screenshot of Table 1 from the article. You are going to learn about several **epidemiologic statistics** by following the logic of this table.

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.

- The first column reports the **observed number of deaths** (47 in this group). This is a type of incidence count. Incidence counts are merely the number of new occurrences over time.
- The second column reports the **expected number of deaths**. This was calculated from published sources. Although the calculations are not shown, the table states that we expected

6.6 deaths in this group. [For future reference: Expected number = (expected rate) × (person-years in the study group).]

- The next column lists the **person-years** of observation. Every year, a live person accumulates 1 person-year. The 3,741 person-years is the equivalent of 374 individuals living on average 10 years each. It is also the equivalent of 7482 people living on average 5 years each. (Get it?)
- The next column is the **standardized mortality ratio (SMR).** This is the (observed number of cases) ÷ (expected number of cases). An SMR of 1 means 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. The SMR is a type of **relative risk.** You will frequently encounter various relative risk measures in the public health literature. In this case, $47 \div 6.6 \approx 7$, indicating that the groups had a mortality rate that was 7 times [higher] than expected.
- The **confidence interval for the SMR** is a statistic that quantifies the precision of the SMR estimate. This statistic takes into account the random variability associated with the number of occurrences in any group.
- Note that the basic formula for a "rate" is:

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

For example, the observed death rate per 1000 individuals in men under 20 is equal to $\frac{\text{No. of observed deaths}}{\text{Person - years}} \times 1000 = \frac{47}{3{,}741} \times 1000 = 12.6$. The expected death rate is $\frac{\text{No. of expected deaths}}{\text{Person - years}} \times 1000 = \frac{6.6}{3{,}741} \times 1000 = 1.8$.

Comment: This is a non-technical definition of a rate. In Chapter 6, we will distinguish between true rates and other types of "rates."

- The **excess rate** = (Observed rate) – (Expected Rate). Notice that an excess rate of 0 would tell you that the observed death rate is equal to the expected death rate. The excess rate quantifies the increase in risk in absolute terms. For men under 20 in this study, the excess rate = 12.6 – 1.8 = 10.8.

Now let us consider some of these statistics for women with onset at age < 20.

3a. Calculate the observed death rate in this group.

3b. Calculate the expected death rate.

3c. Calculate the SMR. Interpret what this means.

3d. Calculate the excess rate in this group. Find this result in Table 1. Interpret what this means.

Part B. The War on Cancer (Optional)

Read Bailer JC III, Gornik HL. Cancer undefeated. *NEJM* 1997 (May 29); 336:1569-1574; correspondence *NEJM* 1997 (Sept 25); 337:935-938. Here's the link to the pdf file.

Read: Kramer BS, Klausner RD. Grapping with cancer – defeatism versus the reality of progress. *NEJM* 1997 (Sept 25); 337:931-934. Here's the link to the pdf file.

1. What are the respective advantages and disadvantages of mortality data and incidence data for comparing the burden of cancer in a population over time?

2. Do you think that the "war" metaphor is appropriate for public health initiatives? What are some of its advantages and disadvantages?

3. Has the War on Cancer been lost? Should resources be shifted from research on cures (treatments) to research on prevention? Why?