ONLINE MATERIAL THAT ACCOMPANIES CHAPTER 3

Box 1. Sensitivity and specificity for measure validation: a quantitative example

Suppose that we collect data on participant reports of smoking in the past 24 hours, and the measure of blood level of cotinine among 200 people. Our data are described in Table 1.

Box 1, Table 1. Self-report of smoking versus blood cotinine level among 200 people

	Blood cotinine≥300 ng/mL	Blood cotinine<300 ng/mL	**Total**
Self-report smoking ≥20 cigarettes per day	 20	 2	**22**
Self-report smoking <20 cigarettes per day	 10	 168	**178**
Total	**30**	**170**	**200**

How do we assess the validity of the self-report of smoking? Two measures are of central importance. First, we would want to know, among those who have blood cotinine ≥300 ng/mL, what proportion report that they smoke ≥20 cigarettes per day? This is known as the sensitivity of the self-report measure. That is, among those actually exposed to a pack-a-day (measured via blood cotinine), what proportion of people actually reports their exposure? The sensitivity of our measure is thus 20/(20+10)=0.67 or 67%. That is, 67% of people who actually smoked a pack of cigarettes in the past 24 hours reported that they smoked a pack of cigarettes in the past 24 hours.

Further, among those who have blood cotinine <300 ng/mL, what proportion report that they smoke less than 20 cigarettes per day? This is known as the specificity of the self-report measure. That is, among those actually were not exposed to a pack-a-day, what proportion actually reported that they were not exposed? The specificity of our measure is thus 168/(2+168)=0.99 or 99%. That is, 99% of people who actually did not smoke a pack of cigarettes in the past 24 hours reported that they did not smoke a pack of cigarettes in the past 24 hours.

In sum, we have sensitivity of 67% and a specificity of 99% for our self-report measure of smoking. We can conclude that people who do not heavily smoke are very likely to accurately report that they do not heavily smoke, whereas people who do heavily smoke are less likely to be accurate reporters.

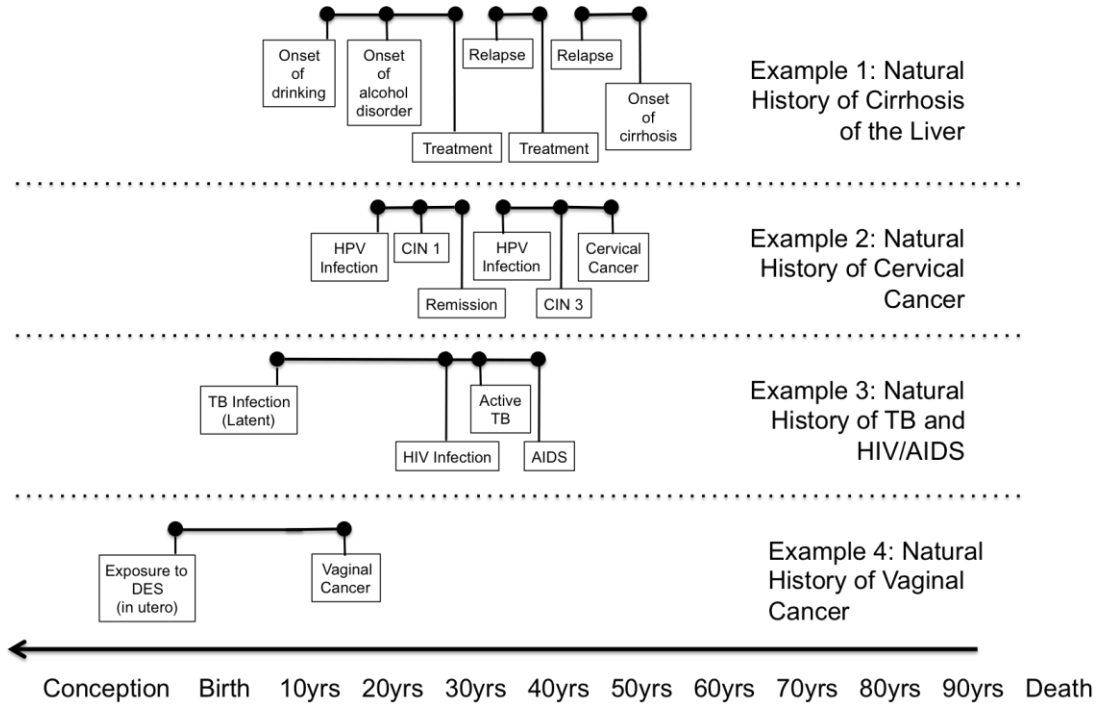
While there is no empiric rule for sensitivity and specificity values that are necessary for a measure to be deemed valid, we would want to be concerned about using a measure that correctly classifies exposed persons only 67% of the time. This means that we are going to

incorrectly label people who are actually exposed 33% of the time. This will have implications for our interpretation of results and the validity of our study findings, which we introduce in greater detail in Chapter 9.

Box 2. Duration, critical windows, and latency across the life course

Below we describe four examples of how exposures may vary in duration and occurrence across the life course, and how they may influence health indicators of interest.

Box 2, Figure 1. Critical windows and duration of exposures: examples from four health indicators



Example 1. For an individual who develops cirrhosis of the liver, the history of alcohol consumption may begin in adolescence, with the onset of an alcohol use disorder about five to seven years after drinking onset. Throughout adulthood, the individual may have periods of time in which she abstains from drinking, or drinks heavily, as well as periods of treatment, remission and relapse, before the onset of cirrhosis in late life. For cirrhosis, the duration and amount of exposure to alcohol most likely have the strongest effect on the onset of cirrhosis.

Example 2. All cervical cancer begins with an infection with human papillomavirus, which is most often transmitted through sexual activity. The natural history of cervical cancer then involves a progression of stages though cervical intraepithelial neoplasms with graded severity. An individual woman may acquire HPV in her late teens and progress to CIN 1, then remission may spontaneously occur. A second infection with HPV could lead rapidly through CIN stages to CIN 3, and then the onset of cervical cancer. Thus, this illustrates the concept of duration and timing of exposure. In our example, one infection with HPV led to no health problems, whereas a

second infection led to cervical cancer.

Example 3. The relation between tuberculosis and HIV illustrates the concept of long latency periods for many exposures of interest. An individual may acquire TB early in life but remain asymptomatic throughout much of the lifespan. The individual in our example acquires TB early in life and then acquires HIV during adulthood. At the time the individual acquires HIV, the TB then becomes active, which promotes a faster transition from HIV to AIDS. This illustrates latency of exposure and the potential influence on health. The individual in this example had a latent infection of TB that was activated with a co-occurring infection.

Example 4. The importance of life course epidemiology is perhaps no more readily apparent than in the example of DES and vaginal cancer. DES is a synthetic version of the hormone estrogen that was commonly given to women early in pregnancy as it was believed to reduce the risk of miscarriage. Daughters of women who used DES in pregnancy demonstrated demonstrably higher incidence of vaginal cancer, usually manifesting in their teenage years (Herbst, Ulfelder et al. 1971). Thus, an exposure (mother's use of DES) that occurred while these young women were *in utero* influenced their health more than a decade later with an increase in the risk of vaginal cancer. Longer-term follow-up studies of the children of women who used DES in pregnancy have found a higher incidence of reproductive problems and other cancers as well (Hoover, Hyer et al. 2011); emerging evidence indicates that health effects of DES exposure *in utero* may extend to the children of women exposed as well (Palmer, Wise et al. 2005, Titus-Ernstoff, Troisi et al. 2008, Titus-Ernstoff, Troisi et al. 2010). This illustrates the concept of critical windows as well as latency. Exposure to DES *in utero*, during a period of rapid development, was influential in the development of vaginal cancer, but only decades after the exposure occurred.

Citations

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