

BIOS 600: Principles of Statistical Inference

Case Study: Breast Cancer Screening

Fall 2012

Reading

- ▶ Pagano and Gauvreau, Chapter 6, Section 6.3-6.4

What Does a Positive Mammogram Mean?

Suppose that 1% of women at age forty who participate in routine screening have breast cancer. 85% of women with breast cancer will have positive mammographies. 10% of women without breast cancer will also get positive mammographies. A woman in this age group had a positive mammography in a routine screening.

What is the probability that she actually has breast cancer?

Write your best guess here:

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Most doctors get the same wrong answer on this problem - usually, only around 15% of doctors get it right (Casscells, Schoenberger, and Grayboys 1978; Eddy 1982; Gigerenzer and Hoffrage 1995; and many other studies). Most doctors estimate this probability to be in the range of 70-85%.

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The correct answer is 7.9%, obtained as follows.

- ▶ Out of 10,000 women, 1% or 100 have breast cancer; we expect 85 of those 100 (85%) to have positive mammograms.
- ▶ From the same 10,000 women, 99% or 9900 will not have breast cancer, and of those 9900 women, 990 (10%) will also get positive mammograms.
- ▶ Total number of women with positive mammograms:
 $990 + 85 = 1075$
- ▶ Of the 1075 women with positive mammograms, only 85 have cancer, so expressed as a proportion, this is $\frac{85}{1075} = 0.079$ or 7.9%. This is the *conditional probability* of breast cancer given a positive mammogram.
- ▶ Thus the 40 year-old woman with a positive mammogram is still much more likely to learn that she is cancer-free than that she has cancer during follow-up.

Statistical Terminology

Let A be the event that someone has disease and let B be the event that a screening test is positive

- ▶ *Prevalence*: proportion of subjects who have a disease at a given point in time (1% for breast cancer at 40), $\Pr(A)$
- ▶ *Sensitivity*: probability of a positive test result given that the individual really has the disease, $\Pr(B \mid A)$
- ▶ *False positive rate*: probability of a positive test result given that the individual is disease-free, $\Pr(B \mid \bar{A})$
- ▶ *Specificity*: probability of a negative test result given that the individual is disease-free (1-false positive rate), $\Pr(\bar{B} \mid \bar{A})$
- ▶ At the time of screening, we do not know A but only know B , so we are interested in the *positive predictive value*: probability of disease given a positive test result, $\Pr(A \mid B)$

Risk applet online

Breast Cancer Screening Animation

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How do we formalize our thought process mathematically?

- ▶ To start, we know that a 40 year old woman has a 1% chance of having breast cancer (*prior probability*).
- ▶ Once we saw her positive mammogram, we updated that chance to 7.9% (*posterior probability*).
- ▶ This reasoning is formalized in *Bayes's Theorem*, which describes how we update our *prior* probabilities (the 1%) once we obtain additional data (the mammogram result), and is given by

$$\Pr(A \mid B) = \frac{\Pr(B \mid A)\Pr(A)}{\Pr(B)} = \frac{\Pr(A \cap B)}{\Pr(A)}.$$

Bayes's Theorem

$$\Pr(A \mid B) = \frac{\Pr(B \mid A)\Pr(A)}{\Pr(B)}$$

- ▶ A=breast cancer, B=positive mammogram
- ▶ Out of 10,000 women, 1% (prevalence) or 100 have breast cancer $\rightarrow \Pr(A) = 0.01$ and $\Pr(\bar{A}) = 0.99$
- ▶ We expect 85% of women with cancer to have positive mammograms $\rightarrow \Pr(B \mid A) = 0.85$; this is called the *sensitivity* of the mammogram
- ▶ We expect 10% of the women without cancer to have positive mammograms $\rightarrow \Pr(B \mid \bar{A}) = 0.10$; the fraction of women without cancer who have negative mammograms (0.90) is called the *specificity* of the mammogram
- ▶ How do we get $\Pr(B)$?

Bayes's Theorem

$$\Pr(A \mid B) = \frac{\Pr(B \mid A)\Pr(A)}{\Pr(B)}$$

- ▶ How do we get $\Pr(B)$?
 - ▶ B is the event of a positive mammogram
 - ▶ The event B occurs both in the group with breast cancer and in the cancer-free group
 - ▶ So we can write $B = (B \cap A) \cup (B \cap \bar{A})$, which means everyone with a positive mammogram either has breast cancer and a positive mammogram (true positive) or no breast cancer and a positive mammogram (false positive)
 - ▶ Because A (cancer) and \bar{A} (no cancer) are mutually exclusive, then we can use the additive rule to get $\Pr(B) = \Pr(B \cap A) + \Pr(B \cap \bar{A})$

Bayes's Theorem

$$\Pr(A \mid B) = \frac{\Pr(B \mid A)\Pr(A)}{\Pr(B)}$$

- ▶ How do we get $\Pr(B)$?
 - ▶ $\Pr(B) = \Pr(B \cap A) + \Pr(B \cap \bar{A})$
 - ▶ Recall the multiplicative rule of probability states that $\Pr(A \cap B) = \Pr(B \cap A) = \Pr(A)\Pr(B \mid A) = \Pr(B)\Pr(A \mid B)$
 - ▶ So $\Pr(B \cap A) = \Pr(A)\Pr(B \mid A) = 0.01(0.85) = 0.0085$
 - ▶ and $\Pr(B \cap \bar{A}) = \Pr(\bar{A})\Pr(B \mid \bar{A}) = 0.99(0.10) = 0.099$
 - ▶ So $\Pr(B) = \Pr(B \cap A) + \Pr(B \cap \bar{A}) = 0.0085 + 0.099 = 0.1075$
(positive mammograms are fairly common occurrences)

Bayes's Theorem

So figuring out the probability of cancer when the mammogram is positive, we have

$$\begin{aligned}\Pr(A \mid B) &= \frac{\Pr(B \mid A)\Pr(A)}{\Pr(B)} \\ &= \frac{0.85(0.01)}{0.1075} = 0.079\end{aligned}$$

or 7.9%

Example 1: Positive Predictive Value

- ▶ Of 10,000 people in the US, we expect 1 to have HIV and 9999 to be HIV-free
- ▶ Of 10,000 people with HIV, we expect 9980 to test positive when given a diagnostic test for HIV and 20 to test negative
- ▶ Of 10,000 people without HIV, we expect 1 to test positive and 9999 to test negative

What is the positive predictive value of this HIV test?

Example 2: Positive Predictive Value

- ▶ We expect 1.5% of US IV drug users to have HIV
- ▶ Of 10,000 people with HIV, we expect 9980 to test positive when given a diagnostic test for HIV and 20 to test negative
- ▶ Of 10,000 people without HIV, we expect 1 to test positive and 9999 to test negative

What is the positive predictive value of this HIV test in the population of IV drug users?

Example 3: Positive Predictive Value

- ▶ We expect 24.8% of adults aged 15-49 in Botswana to have HIV
- ▶ Of 10,000 people with HIV, we expect 9980 to test positive when given a diagnostic test for HIV and 20 to test negative
- ▶ Of 10,000 people without HIV, we expect 1 to test positive and 9999 to test negative

What is the positive predictive value of this HIV test in this population in Botswana?

Example 4: Positive Predictive Value

Investigators in China conducted a study of an HPV self-test for high-grade lesions in a high risk population.

- ▶ The prevalence of high-grade lesions in this population was 4.3%
- ▶ The sensitivity of the test is 83%
- ▶ Specificity is 86%

What is the probability that someone who has a positive result on the HPV self-test in this population actually has high-grade lesions?

Example 5: Kill the Wabbit

A certain brand of home pregnancy test claims 90.6% sensitivity and 99.9% specificity on the first day of missed menses.

Assuming roughly 10% of test users are actually pregnant, what is the positive predictive value of this pregnancy test?

[Link to the Operatic Allusion](#)

How might you design a better test?

A perfect test has sensitivity=specificity=1. Numerous factors need to be considered when deciding how to design a better test for cancer, including

- ▶ Human costs
 - ▶ HIV test for purposes of screening blood supply must have high sensitivity
 - ▶ HIV test for diagnosing infection in humans should have high sensitivity and high specificity
- ▶ Costs of follow-up if test is positive
- ▶ Whether follow-up is detrimental for false positives
- ▶ Bear in mind that there is a trade-off in general between sensitivity and specificity (can improve one at the cost of the other)

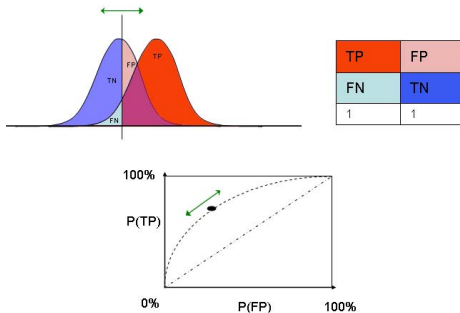
Sensitivity-specificity tradeoff

- ▶ True positive: has both positive test result and disease
- ▶ False positive: has positive test result and no disease
- ▶ True negative: has negative test result and no disease
- ▶ False negative: has negative test result but has disease

Click to explore the [sensitivity-specificity tradeoff](#)

Receiver operating characteristic (ROC) curves

The receiver operating characteristic (ROC) curve is a plot of the sensitivity (true positive rate) against the false positive rate (1 minus the specificity). The area under the ROC curve is often used to describe the quality of a test.



ROC curves

Click to explore [ROC curves for varying distributional separation](#)

Reading for Next Time

- ▶ Pagano and Gauvreau, Chapter 7, Sections 7.1-7.2