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Medical Testing

<u>Suggested grade levels</u>: 12 and up.

<u>Possible subject areas</u>: Social studies, health.

<u>Math skills</u>: Percentages and probabilities.

<u>Overview</u>: This module explores issues in medical testing. No test is likely to be 100 percent perfect. The best that we can hope for is that it will give a correct answer with a very high probability. As we will see, the probabilities and percentages can lead to some surprising conclusions.

The concepts in this module are fairly subtle and may require some effort for many students to grasp. However, it may help to dispel misconceptions that people have about medical testing, and simply realizing the existence of these issues can be of value to a consumer.

Student activities: Medical Testing

Medical tests, such as genetic tests and blood tests for various diseases or conditions, are far from infallible. A test can produce two kinds of errors: a <u>*false positive*</u> result (meaning that the test indicates presence of the disease when it is, in fact, not there) or a <u>*false negative*</u> result (meaning that the test indicates absence of the disease when it is in fact present). Thus, when you get a test result, there is a probability of one of these errors occurring.

In general, a population of tested individuals may be divided into four groups:

- True Positives: those who test positive for a condition and are positive (i.e., have the condition),
- False Positives: those who test positive, but are negative (i.e., do not have the condition),
- True Negatives: those who test negative and are negative,
- False Negatives: those who test negative, but are positive.

Of course a patient and her doctor want to know primarily two things: (1) If she tests positive, how sure is she that she really has the disease and (2) if she tests negative how sure is she that she really does <u>*not*</u> have the disease? Typically, medical science can only give us a *probability* and not a 100 percent correct answer. In many cases more testing needs to be done after indication of a positive result. For example if a test for a certain kind of cancer is positive, a biopsy may be ordered to verify the result because the test is not 100 percent accurate.

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Example 1. Here is a question that came up in a nationally syndicated column and is available in detail on the Chance web site:

www.dartmouth.edu/~chance/course/Syllabi/mpls/handouts/section3_8.html

1. Suppose we assume that 5% of all people are drug-users. Suppose a certain drug test is 95% accurate, which means that if a person is a user, the result is positive 95% of the time, and if she or he isn't a user, it's negative 95% of the time.

   a) A randomly chosen person tests positive. How likely is the individual to be a drug-user?

   b) A randomly chosen person tests negative. How likely is the individual *not* to be a drug-user?

2. Now suppose we assume that 20% of all people in a certain group are drug-users and apply the same test as in the problem above to this group.

   a) A randomly chosen person tests positive. How likely is the individual to be a drug-user?

   b) A randomly chosen person tests negative. How likely is the individual *not* to be a drug-user?

   c) What does this suggest about how the test should be you used so as to be most effective?

Example 2: A genetic condition is found that affects 5% of a population. In a city with a million people that means 50,000 people will be affected by the bad gene.

Suppose there is a genetic test for the bad gene that has an error rate of 1% (that is, 1% false negatives and 1% false positives). If we test all one million people, there will be 500 false negatives (1% of 50,000). These 500 people have the bad gene, but it will not be detected.

If false positives also occur at the rate of 1%, then about 1% of the 950,000 people who do not have the bad gene (9,500 people) will test positive.

3. What is the probability that a person has the bad gene if she tests positive?

4. What is the probability that a person does not have the bad gene if she tests negative?

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<u>Now, suppose we decide to retest all those who tested positive.</u>

5. How many people tested positive? What percent of this group would we expect to have the bad gene?

6. If we test this group again, what is the probability that a person has the bad gene if she tests positive?

7. What is the probability that a person does not have the bad gene if she tests negative?

<u>Example 3</u>: Test *<u>Sensitivity</u>* is a medical term defined as the ratio of true positive tests to the total number of affected (positive) patients tested expressed as a percentage. It measures a screening test's ability to correctly identify the presence of a disease. A test with high sensitivity has few false negatives. Test sensitivity is independent of disease prevalence in the community.

Test *<u>Specificity</u>* is a medical term defined as the ratio of true negative tests to the total unaffected patients tested expressed as a percentage. It measures a screening test's ability to correctly identify the absence of disease. A test with high specificity has few false positives. Test specificity is independent of disease prevalence in the community.

The following web sites discuss the improved sensitivity and specificity of the PSA prostate cancer test

www.pslgroup.com/dg/215842.htm
www.devicelink.com/ivdt/archive/96/01/005.html

<u>Paraphrasing from the second web site above</u>: In a larger study (243 subjects), Ward and colleagues used a cutoff ratio of 0.15 to demonstrate 78% sensitivity and 69% specificity in diagnosis of prostate cancer. In contrast, tPSA measurements alone yielded equivalent sensitivity but only 33% specificity. These reports are encouraging, but larger clinical studies are required for determination of the optimal fPSA:tPSA cutoff ratio.

8. What does the figure 78% sensitivity in the above article mean?

9. What does the figure 69% specificity in the above article mean?

10. In a new screening test for Crohn's Disease, 45 patients with known Crohn's Disease were tested and 36 of them had a positive test. 255 patients without Crohn's Disease were also tested and 230 of them had a negative test.

    a) What is the *specificity* of the test?
    b) What is the *sensitivity* of the test?.
    c) Do these data allow us to determine the probability that a person chosen at random from the general population has the disease if she tests positive?

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Instructor's Sheet

Summary of the definitions:

- True Positives: those who test positive for a condition and are positive (i.e., have the condition),
- False Positives: those who test positive but are negative,
- True Negatives: those who test negative and are negative,
- False Negatives: those who test negative, but are positive.

$\frac{TruePositives}{TruePositives + FalsePositives} =$ probability of being positive given you tested positive.

$\frac{TrueNegatives}{TrueNegatives + FalseNegatives} =$ probability of being negative given you tested negative.

$$\frac{TrueNegatives}{TrueNegatives + FalsePositives} = \frac{TrueNegatives}{AllUnaffected} = \text{Specificity}$$

$$\frac{TruePositives}{TruePositives + FalseNegatives} = \frac{TrueNegatives}{AllAffected} = \text{Sensitivity}$$

1. Suppose we assume that 5% of all people are drug-users

(a) A randomly chosen person who tests positive has only a 50% probability of being a drug-user. *Explanation*: 95% of the population is clean, but 5% of that 95% (4.75%) will test positive. Also 5% of the population uses drugs and 95% (4.75%) of them will test positive. Thus, of those who test positive half are users and half are not.

(b) A randomly chosen person who tests negative has a 99.7% probability of *not* being a drug-user. *Explanation*: 95% of the population is clean and 95% of that 95% (90.25%) will test negative. Also 5% of the population uses drugs and 5% of them (0.25%) will test negative. Thus, the ratio of those who test negative and are clean to all those who test negative is 95*.95 /(.95*.95. + 0.05*.05) = 99.7%

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2. Suppose we assume that 20% of all people are drug-users.

   a. A randomly chosen person who tests positive has an 82.6% probability of being a drug-user. *Explanation*: 20% of the population uses drugs and 95% of them (19%) will test positive. Also 80% of the population is clean, but 5% of that 80% (4%) will test positive. Thus, the ratio of those who test positive and are users to all those who test positive is
   0.20*0.95 /(0.20*0.95 + 0.05*.80) = 82.6%

   b. A randomly chosen person who tests negative has a 98.7% probability of *not* being a drug-user. *Explanation*: 80% of the population is clean and 95% of that 80% (76%) will test negative. Also 20% of the population uses drugs and 5% of them (1%) will test negative. Thus, the ratio of those who test negative and are clean to all those who test negative is
   0.80*0.95 /(0.80*0.95. + 0.05*0.20) = 98.7%

   c. As the results of problems 1(a) and 2(a) indicate, the effectiveness of the test in detecting drug users is greater when used in populations known to have a higher percentage of users.

<u>Discussion</u>: Even a test with a seemingly impressive rate of success (95%) can be of little value in detecting a condition if only a small fraction of the population has the condition being tested for (like drug use or a disease). In the case where 5% of the population was using drugs, a positive test only gave a 50-50 chance of detecting drug use. In the case where 20% of the population used drugs, the test was far more effective in detecting drug users, resulting in an 83% probability of detection. Thus the effectiveness of the test in detecting drug users is greater when employed in populations known to have a higher percentage of users.

It is interesting that the test is very effective in detecting *non-users* because in both cases the percentage of non-users is so high.

3. What is the probability that a person has the bad gene if she tests positive? 49500/(49500+9500) = 83.9%

4. What is the probability that a person does not have the bad gene if she tests negative? 940500/(940500+500) = 99.9%

Now, suppose we decide to retest all those who tested positive. Let’s see where that leads:

5. How many people tested positive? (49,500 + 9,500 = 59,000) What percent of this group would we expect to have the bad gene? (49,500/59,000 = 83.9%)

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6. If we test this group again, what is the probability that a person has the bad gene if she tests positive? (99.8%)

7. What is the probability that a person does not have the bad gene if she tests negative? (95%)

8. What does the figure 78% sensitivity in the above article mean? It means that of the subjects tested who were known to have the disease, 78% tested positive.

9. What does the figure 69% specificity in the above article mean? It means that of the subjects tested who were known to not have the disease, 69% tested negative.

10. In a new screening test for Crohn's Disease, 45 patients with known Crohn's Disease were tested and 36 of them had a positive test. 255 patients without Crohn's Disease were also tested and 230 of them had a negative test.

    a) The specificity is 230/255 or 90.2%.

    b) The sensitivity is 36/45 or 80%.

    c) No it does not. We do not know the percentage of the general population that has Crohn’s. In this study, 15% of the 300 subjects had the disease, but it is actually fairly rare.

According to *www.fascrs.org/brochures/crohns-disease.html* *Crohn’s* disease and a similar condition called ulcerative colitis are often grouped together as “inflammatory bowel disease.” The two diseases afflict an estimated two million individuals in the U.S. The population of the United States is approximately 280 million. If 2 million have Crohn's disease, then approximately 7/10 of 1 percent of the population is afflicted. (If it were the case that 15 percent of the population had Crohn’s disease then the probability would be 59 percent.)

References:

- *Lawrence Berkeley National Laboratory has a very nice educational site with information about genetic screening:* www.lbl.gov/Education/ELSI/screening-main.html

- **Chance**: www.dartmouth.edu/~chance/course/Syllabi/mpls/handouts/section3_8.html

- The following two web sites discuss the improved sensitivity and specificity of the PSA prostate cancer test
  www.pslgroup.com/dg/215842.htm
  www.devicelink.com/ivdt/archive/96/01/005.html