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Imperfect Testing: Breast Cancer Case Study

What do the results of an imperfect medical test actually mean?

How does one measure the effectiveness of a particular medical test?

How does one compare various available tests?

How does this information affect public policy or personal decision-making?

The results of a mammogram, like those of many tests, are not always correct. A false positive test result may create unnecessary anxiety, while a false negative test result may result in a false sense of security. In this unit, you examine the case of an adult female that learns her mammography test is positive. You use real data to calculate the probabilities of receiving true (or false) test results and discuss the possible implications of a positive test result, given the properties of the test. These properties, which include sensitivity and specificity, help determine the rates of incorrect test results. The importance of disease prevalence is also investigated.

This same woman then has a genetic test through which she learns she has the BRCA gene mutations associated with breast cancer. You investigate what it means to have this mutation and how scientists are working on medical treatments that can be tailored to a particular genetic profile. Finally, knowing their mother is positive for the BRCA mutation leads to a dilemma for her daughters, who must then decide if they will be tested for this BRCA allele, since results from testing for this allele still do not definitively determine whether or not a woman will develop breast cancer.

Unit Goals and Objectives

Goal: Students will understand what cancer is, how some forms might be detected, and how it might be treated.

Objectives:
- Review a case study and, using prior knowledge, draw conclusions about the given mammogram.
- Explain what a mammogram is and what it is used for.
- Explain what cancer is, how it affects normal tissue, and how it might be treated.
- Define angiogenesis, biopsy, benign tumor, carcinogens, cancer, chemotherapy, mammogram, false negative test result, false positive test result, malignant tumor, metastatic cancer, oncogenes, proto-oncogenes, radiation, telomeres.

Goal: Students will understand how to use data collected in a simulation to calculate conditional probabilities.

Objectives:
- Construct a tree diagram that models the outcomes of supplied data.
- Calculate the probability of an event.
- Use a tree diagram to calculate conditional probabilities.
- Interpret probability in the context of a given situation.
- Define tree diagram, true negative test result, true positive test result.
Goal: Students will understand the meaning of true positive, false positive, true negative, and false negative test results and be able to calculate their probabilities using real-world breast cancer data.

Objectives:
- Use real breast cancer data to create a table, draw a tree, and calculate conditional probabilities.
- Interpret and analyze the calculated probabilities and relate them to the real world.
- Define complement, conditional probability, dependent events, probability, probability tree.

Goal: Students will understand the use of four properties of a test (positive predictive value [PPV], negative predictive value [NPV], specificity, and sensitivity) and the prevalence in the population to evaluate tests.

Objectives:
- Explain the concepts of specificity and sensitivity.
- Describe how changes in sensitivity and specificity affect one another and the PPV and NPV.
- Explain the concepts of positive predictive value and negative predictive value.
- Use Bayes’ Rule to calculate the positive predictive value and the negative predictive value of a test if the sensitivity of the test, the specificity of the test, and the prevalence of the disease in the population are known.
- Evaluate the effect of disease prevalence on the PPV and NPV of a test.
- Define Bayes’ Rule, negative predictive value, positive predictive value, prevalence, sensitivity, specificity.

Goal: Students will understand the process a pharmaceutical company follows to test and market a new drug and practice interpreting trees from the drug developer’s perspective.

Goal: Students will understand how an individual’s genetic makeup can affect his or her response to drug treatments and how prescriptions can be tailored to the individual to create personalized medicine.

Objectives:
- Create and use probability trees to examine the effectiveness of particular drugs versus adverse side effects.
- Compare the perspective of the drug company versus the drug taker (patient).
- Evaluate the potential benefits and possible pitfalls of genetic profiling.
- Define BRCA, haplotypes, pharmacogenetics, personalized medicine, SNP, SNP profile.

Goal: Students will understand the case study and the ethical questions involved.

Objectives:
- Review a case study and explore the options to the dilemma presented.
- Participate in a discussion of the difficult decisions that might be made in this particular situation.
- Reasonably support his/her answers to the questions being asked using terminology learned throughout the unit.
Lesson 1  
**Cancer Facts and Mammograms**

Cancer impacts the lives of millions of Americans every day. In 2007 the American Cancer Society estimated that more than 11.5 million people in the United States were either currently or previously diagnosed with cancer. This number only counts actual cancer patients. The impact of cancer is significantly multiplied when you consider the effect each of these cancer patients’ condition has on family members, friends, employers and health care providers. The 2007 data estimates that about 2.6 million of the U.S. cases were breast cancer patients.

The following outline of frequently asked questions about cancer provides a starting point for this unit’s study.

**Cancer Frequently Asked Questions (FAQ)**

**What is cancer?**
*Cancer* is a condition in which cells in the body grow in an uncontrolled way. These cells typically do not perform their “normal” function (e.g., a cancerous pancreas cell does not secrete its normal hormones). A clump of these cells is called a tumor.

**How does cancer kill people?**
Cancer is the number 2 cause of death in the U.S., and one of the leading causes of death worldwide. Basically, cancer kills because the cancer cells grow uncontrolled and crush the normal healthy cells until the normal cells die. If this occurs in a critical area like the brain or liver or pancreas, the body cannot survive and the organism dies.

**What causes the cells to become cancerous?**
A variety of things may cause a cell to become cancerous. We call these things *carcinogens*. Carcinogens include radiation, chemicals, some viruses, and even repetitive trauma. In the end, the thing they all have in common is that they mutate the cell’s DNA to cause the cell to misbehave.

**What mutations are needed for cancer?**
Cancer requires several mutations to occur. Some of these are:

1. Proto-oncogenes mutate to become oncogenes.
2. Tumor suppression genes are disabled.
3. Angiogenesis factors are released.
4. Telomerase genes are reactivated.

**Whoa, one at a time — What are proto-oncogenes and oncogenes?**
*Proto-oncogenes* are normal genes that help regulate cell division. They basically tell the cell to undergo mitosis. When they are mutated into *oncogenes*, the cells will divide excessively.
So now we have made cancer?
Not exactly. The tumor suppression genes should stop the oncogenes’ mutation and excessive cell division. Tumor suppression genes perform several functions. One of these is to watch the DNA for mutations and either fix those mutations or signal apoptosis, or cell death. Basically, the cell will fall apart and the immune system will eat it. Commonly studied tumor suppression genes are p53 and BRCA. Another group of tumor suppressors regulate cell division. When normal cells divide, for example to heal a wound in your skin after it has been cut, they know to stop dividing when they bump up against other cells. This is known as contact inhibition and ensures that the healing process doesn’t overgrow the wound. Tumor suppression genes help regulate this process by stopping cell division at the correct time. In order for cells to become cancerous, mutations must occur that disable the tumor suppression genes.

Okay, so now we have cells dividing rapidly without a way to shut them off. Now we have cancer, right?
Not necessarily. These two mutations still would not ensure a cancer cell’s survival. Cancer cells require a significant amount of energy to support their growth and division. Therefore, a third mutation is that cancer cells secrete a chemical that promotes angiogenesis, or the growth of new blood vessels to feed the cancer. Interestingly, some tumors not only secrete angiogenesis chemicals locally for their own growth, but also secrete angiogenesis inhibitors into the bloodstream to prevent potential competing tumors from growing elsewhere in the body and stealing nutrients. Scientists have isolated these angiogenesis inhibitors and are trying to use them as treatments against cancer.

![Figure 1.1: Angiogenesis](image)

So now the cancer has genes to tell it to divide (oncogenes), has shut off the genes that will stop it from dividing (tumor suppression genes), and has a good blood supply to get its nutrients. Surely we must have cancer cells now!
There is still one more obstacle to overcome if a cancer cell wants to thrive. There are a limited number of times cells can divide during their lifetime due to the sections of DNA called telomeres. Therefore, cancer cell division should be limited and no cancer should be able to get very large.
But earlier you said that cancer kills because the cells grow uncontrolled. How can that be if they are limited in the number of times the cells can divide?

Exactly, and this is the reason we need one more mutation. But first, let’s examine the telomeres a bit further. The telomeres are non-coding, repeating nucleotide sequences at the ends of the DNA strands. In humans and most mammals the sequence is TTAGGG. These telomeres act like aglets. Aglets are the plastic sheaths at the end of your shoelaces that protect the ends of the shoelaces and prevent fraying. Telomeres do the same thing for DNA strands so the ends do not become damaged during mitosis. However, each time the cell divides, the telomeres shorten. When the telomeres reach a certain “shortness,” the cell will no longer divide because it would be risking damage to important coding regions of the DNA. The cell will become senescent: it will simply grow old until it dies. In fact, this process is one of the reasons we age and our body loses the ability to heal as well as it could when we were younger.

What does this have to do with cancer?

Hold on, we are getting there. Our cells also have the ability to produce an enzyme called telomerase. This enzyme can restore the telomeres to their normal length and thus allow the cell to divide indefinitely. Telomerase is actively produced when you are an embryo since one cell must turn into trillions of cells to make you. However, the genes that produce telomerase are then turned off and we begin our aging process. Cancer cells reactivate the gene that produces telomerase so they can divide without limitation.

Hey, wait a minute. If my cells would still produce telomerase, does that mean I wouldn’t age?

Perhaps. Researchers are working on experiments now to see if we can turn on the telomerase genes and prevent or slow aging. Maybe you could study this in the future and help extend the human life span to hundreds of years. But that is a topic for another day.


Figure 1.2: Telomeres (white) at the end of chromosomes
Okay, back to cancer. Now we know how to make cancer cells and how they cause their damage. Are all tumors equally dangerous?

Tumors (a group of these cells) fall into two basic categories: benign and malignant. A benign tumor is a group of cells that is very slow growing and typically well defined. In other words, it is like a little ball of cells that is not really doing anything or invading the tissue around it. Benign tumors are not very dangerous and can usually be left alone or removed surgically.

Malignant tumors, on the other hand, are invading the surrounding tissue. In other words, they are spreading through the organ they started in. Their borders, or edges, are hard to define and so it is difficult to remove them surgically because it is difficult to tell if you got all of the cancer cells. Because of this, surgeons often remove excess tissue from the area to increase the likelihood that they removed all the cancer cells.

I understand why a malignant tumor in your brain or liver is dangerous, but what if it is in a nonessential body part like the prostate or breast or in the skin on your arm?

The problem with malignant tumors is that they are working their way through the organ they started in. While they are doing that, they may bump into a blood or lymph vessel and cancer cells can enter the bloodstream or lymphatic system. Once they are in these vessels, they can spread to any other part of the body. When this happens, the cancer has metastasized, or, in other words, become metastatic. This is the worst situation – a malignant cancer that has metastasized and is spreading to other parts of the body.

So a cancer that starts off in the breast can end up in the brain?

Yes, that is exactly the problem. If the cancer metastasizes it can end up anywhere. The cancer will always be named for where it originated. So if a tumor is in someone’s brain but came from the breast, it will still fit under the category of breast cancer. It is a primary breast tumor and a secondary brain tumor.
How do we detect these cancers?
Cancers can initially be detected by self-examination, when a person feels an abnormal mass, or through an imaging technique, such as an x-ray, CT scan, MRI, mammogram, etc. Once an abnormal mass is detected, a biopsy is performed, in which a surgeon removes part of the mass with a needle or scalpel. Then the cells are examined under a microscope to determine whether they are cancerous or a benign growth.

If the growth is cancerous, how is it treated?
Cancer treatments are constantly evolving as we learn more about how cells work and more about DNA. Currently, the main options are radiation therapy, chemotherapy, and surgery. These, as well as two other treatments under development, are described in Table 1.1.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>How It Works</th>
<th>Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation</td>
<td>Concentrated high dose radiation targeted at the tumor mutates and kills the cancer cells.</td>
<td>May mutate or damage good cells during the process.</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>Drugs enter the bloodstream and target rapidly dividing cells, which stops the cancer cells from dividing. This takes advantage of the fact that cancer cells require a good blood supply so they also take in large amounts of the drug.</td>
<td>Other cells also divide rapidly and have a good blood supply. This is why a person’s hair may fall out during chemotherapy. Chemotherapy drugs also make some people very sick.</td>
</tr>
<tr>
<td>Surgery</td>
<td>Surgeons cut out the cancer.</td>
<td>If the cancer is malignant, it can be difficult to be certain you have gotten all of it. Therefore, the surgeon may take significantly more tissue than necessary. In a radical mastectomy, not only is the breast removed, but also the chest muscles and lymph nodes in the chest and armpit.</td>
</tr>
<tr>
<td>Genetic manipulation</td>
<td>Scientists are trying to design viruses that would attack the cancer cells and reprogram their DNA to fix the mutations, for example, to reactivate the tumor suppression genes.</td>
<td>This is still a young field and creating the viruses to target specific cells that behave specific ways is a difficult task.</td>
</tr>
<tr>
<td>Angiogenesis inhibitors</td>
<td>Drugs that inhibit the growth of new blood vessels to try and “starve” the cancer.</td>
<td>These drugs affect other parts of the body besides just cancer cells and thus can affect bleeding, blood clotting, the immune system, and fetal development in a pregnant female.</td>
</tr>
</tbody>
</table>

Table 1.1: Cancer Treatment Options

Breast cancer is the most prevalent cancer among U.S. women. The primary medical test used to detect breast cancer is the mammogram. The following outline of frequently asked questions about mammograms provides information for our investigation into cancer testing results.
**Mammogram Frequently Asked Questions (FAQ)**

**What is a mammogram?**
A mammogram is an x-ray of a patient’s breast.

**Why would someone have a mammogram?**
If a woman feels a lump in her breast, she may have a diagnostic mammogram performed to try and diagnose the lump. Other women get screening mammograms. Screening mammograms are done when there are no obvious signs of cancer to try to detect it early in high-risk individuals. It is recommended that all women have a yearly mammogram starting at age 40. Older women, or women with a family history of breast cancer, may get mammograms more often.

**How is it performed?**
The breast is pressed between two plates (breast compression) to prevent motion, which can blur the x-ray, and so the radiologist can image the entire breast. This also allows for a lower dose of radiation to be used.

**What do doctors look for on the x-ray?**
Abnormal spots or growths will appear white on an x-ray. This is because they block the x-ray particles from reaching the film and turning the film black. This is the same reason bones appear white. The more dense the tissue, the whiter it is on the x-ray film.

**So a white spot on the mammogram means cancer?**
Not necessarily, and this is one of the problems with the test. Any dense tissue will appear as a white spot on the x-ray, not just tumors. Some women have naturally dense breasts, and younger women have denser breasts than older women. Other things can appear white too, like cysts. The mammogram isn’t *specific* enough to differentiate these things. These things are known as **false positives**. A positive mammogram does not mean the patient has cancer.

**What does a patient do if they have a positive mammogram?**
As with the testing for most cancers, a **biopsy** is performed. The surgeon uses a scalpel or a needle to remove part of the growth and examines it under a microscope to determine if it is cancer.

**Does a negative mammogram mean the patient does not have cancer?**
Unfortunately, that is also not necessarily true. A patient may have a negative mammogram and actually have breast cancer. This is known as a **false negative** and, although rare, can happen. This might happen because a cancer is too small to detect with an x-ray. This means the x-ray machine isn’t *sensitive* enough to detect early-stage, or small, cancers.

**Case Study: The Doctor's Office**
Elizabeth Johnson is a 46-year-old female following up on a routine yearly physical exam. Read the following interactions between Elizabeth and her doctor and examine the mammogram results to answer the questions.

**Elizabeth:** Hi, Dr. Smith. How are you today?  
**Dr. Smith:** I’m doing well, Elizabeth. How are the children?
Elizabeth: They are great. Kira just turned 13, Celeste is expecting with my very first grandchild, and Jennie is getting ready to go to college next year! I’m not sure how we are going to afford that, but you know how important education is.

Dr. Smith: Wow, they grow up so fast. Tell them I said hello.

Elizabeth: How were my results?

Dr. Smith: Let’s take a look.

![Mammogram image](Government.wikipedia.org/wiki/File:Mammo_breast_cancer.jpg)

**Figure 1.4:** Mammogram image

**Questions for Discussion**

1. What type of test is this?

2. How is this test performed?

3. Is Elizabeth's test normal or abnormal? How do you know?

**Case Study: The Diagnosis**

Dr. Smith: Do you see that bright white spot?
Elizabeth: Yes, is that bad?
Dr. Smith: Unfortunately, this is an abnormal mammogram.
Elizabeth: Oh, my, does that mean I have cancer?
Questions for Discussion

4. What does an abnormal mammogram indicate? Does Elizabeth have cancer?

5. What steps should be taken to confirm your answer to question 1?

![Normal and Abnormal Mamogram](Government.wikipedia.org/wiki/File:Mammo_breast_cancer.jpg)

**Figure 1.5:** Normal and Abnormal Mamogram
**ACTIVITY 1-1  Cancer: A Dicey Situation**

**Objective:** To simulate the steps in the process for cells to become cancerous.

**Materials:**
- Dice (two per group)
- Cancer FAQ
- Handout IT-H1: Cancer Activity Worksheet
- Red and black licorice sticks

**Note:** This activity is designed to familiarize you with the steps in cancer development. It is **not** intended to simulate the actual probability of getting cancer.

**Part I**
1. Each group selects two students to roll the dice. The two students rolls one die each; one to represent a proto-oncogene and the other a tumor-suppressor gene. The two other students record the results of each roll.

2. Each roller has 10 tries to roll a 1 (indicating a gene mutation). The recorders will keep track of the rolls.
   - Once a roller has rolled a 1, the gene has mutated and “waits” to see if the other gene mutates (rolls a 1).
   - If after 10 rolls both rollers do not obtain a 1, neither gene mutates.
   - If time permits, perform another set of 10 rolls.

3. Once both genes have mutated (both rollers have rolled a 1), or after 2 sets of rolls, stop and answer all of the questions in Part I (questions a-d) on the activity worksheet.

**Part II**
4. Continue the game with the recorders becoming rollers and the rollers becoming recorders.

5. Rollers now simultaneously roll the dice and if rolling the same number (doubles) angiogenesis factors are released. The rollers will have 10 tries to roll doubles.
   - If after 10 rolls doubles are not simultaneously obtained, the cells are cancer-free.
   - If time permits, perform another set of 10 rolls.

6. Once angiogenesis factors are released (rolled doubles), or after 2 sets of rolls, stop and answer all of the questions in Part II (questions e-g) on the activity worksheet.
   - Raise your hand to have teacher check responses a-g.
Part III

7. Continue the game and pick two rollers and two recorders. Rollers will have five tries to simultaneously roll doubles.

8. Each roll simulates DNA replication and whether or not telomerase cells are reactivated.
   - Each time you do not roll doubles, eat a small piece from each end of the red licorice and place it in front of you. If after five rolls doubles are not simultaneously obtained, your red licorice is very small and the game is ended. Cells are cancer-free.
   - Each time doubles are rolled, one student puts a full-length black licorice in the center of the playing area.
   - After 5 rolls, stop and answer the final questions in Part III (h-k) on the activity worksheet.
Lesson 2  
Drug-Test Simulation

To better understand the meaning behind the results of Elizabeth's mammogram, we are going to complete an activity simulating drug testing. Imagine that last week every one in your class took a drug test for steroid use. Let's analyze the possible results.

Drug Test Results

We begin with a set of data indicating the results of a steroid test. Some of those tested received positive results, while others received negative results. Within those groups, some results were accurate, while others were not. The following results are possible:

- **True Positive** – person tested positive and does use steroids
- **False Positive** – person tested positive, but does not use steroids
- **True Negative** – person tested negative and does not use steroids
- **False Negative** – person tested negative, but does use steroids

**ACTIVITY 2-1  Class Simulation**

**Objective:** Conduct a test simulation and present data on a tree diagram.

**Materials:**
- Test Cards
- Handout IT-H2: Class Simulation Worksheet

1. Collect data for your class through a simulation. Each student in your class receives a test result card from your teacher. The cards represent each of the four test results. After counting the number in each result group, use the following procedure to construct a simulation tree diagram to determine the probabilities of these results.

2. Fill in the chart at the top of the simulation tree diagram page from your data. Find the sums of the rows (total positives and total negatives) and the columns (total users and total not users), as well as the total size of the tested group.

3. As a class complete the upper tree diagram.
   a. Use the values in your chart to fill in the boxes.
   b. Find the probability that a student tests either positive or negative and write this probability on the lines marked “+” and “-“.
   c. Determine the probabilities of each branch of the tree diagram by dividing each consecutive box value by the value in the box before it. For example, find the probability of a person testing positive by dividing the number of total positives by the total number tested.
   d. Determine the probabilities of each of the four results by multiplying the probabilities of the branches leading to that result, or by dividing the number of persons with that result by the total number in the tested group.
4. In your small group complete the lower tree diagram.
   a. Use the values in your chart to fill in the boxes.
   
   b. Determine the probabilities of each branch of the tree diagram by dividing each
      consecutive box value by the value in the box before it. For example, find the
      probability of a person testing positive by dividing the number of total positives by
      the total number tested.
   
   c. Determine the probabilities of each of the four results by multiplying the probabilities
      of the branches leading to that result, or by dividing the number of persons with that
      result by the total number in the tested group.
Drug-Test Simulation Tree Diagram

<table>
<thead>
<tr>
<th>Steroid User</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

Test positive
- User
  + User and +
  - Not and +

Test negative
- Not
  + User and -
  - Not and -

Total
- + and user
- User and test positive
- − and user
- User and test negative
- + and not
- Not user and test positive
- − and not
- Not user and test negative
Questions for Discussion

1. Why do we need two trees and not just one?

2. Which numbers on the tree represent probabilities? Give any example of one of these probabilities and explain what it represents.

3. Let’s say your class simulation data is from an actual drug test. If you test another group of the same number of people, would you expect the same probabilities as you found in your class? Why or why not?

Extension

1. To conduct your own simulation, shuffle a deck of cards and then randomly choose a set of 20 – 30 cards. Determine the number for each result using the following guide.
   - True Positive – Red card with 2 -10
   - False Positive – Red card with Jack, Queen, or King
   - True Negative – Black card with 2-10 or any Ace
   - False Negative – Black card with Jack, Queen, or King

2. Complete a simulation tree diagram to analyze your test.
Practice

Complete the following two tree diagrams using the information provided in each diagram.

**Practice Tree 1:** Use the table to fill in the tree and determine probabilities.

<table>
<thead>
<tr>
<th>Steroid User</th>
<th>User</th>
<th>Not User</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>42</td>
<td>12</td>
<td>54</td>
</tr>
<tr>
<td>Negative</td>
<td>7</td>
<td>51</td>
<td>58</td>
</tr>
<tr>
<td>Total</td>
<td>49</td>
<td>63</td>
<td>112</td>
</tr>
</tbody>
</table>

Test Diagram:

```
[Diagram]
```

Imperfect Testing  Student 17
**Practice Tree 2:** Use the information supplied to complete both trees and the table. Add appropriate labels.

### Steroid User

<table>
<thead>
<tr>
<th>Test</th>
<th>User</th>
<th>Not User</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

```
Total
100

+ User | + 20
+ Not | + .25
- User | -
- Not | -
```

```
User

+ User
- User | 10

Not

+ Not
- Not
```
Lesson 3  Breast Cancer Screening Data

As we consider Elizabeth Johnson’s case, something you might want to know about is the likelihood of getting breast cancer.

**Probability**

**Probability** is a measure of the likelihood or chance of some event occurring. For example, say that after many years of data collection on women, researchers have found that in a population of 1,000 women, about 100 of them will have breast cancer sometime in their lifetime. Given this data, you can calculate the probability of the event (having breast cancer sometime in one’s lifetime) by determining the number of women in a given population who have breast cancer and dividing it by the total number of women in the given population.

So, the probability of having breast cancer, given the data, is:

\[
P(\text{breast cancer}) = \frac{100}{1,000} = 0.1
\]

In general:

probability of having a certain trait = \( \frac{\text{number of people in a group with a certain trait}}{\text{total number of people in the group}} \).

The notation generally used to denote probabilities is \( P(A) \), which is read “the probability of \( A \)” or “the probability that event \( A \) occurs.”

Recall that a probability must be greater than or equal to 0 and less than or equal to 1. A probability of 1 means that an event is certain to happen, while a probability of 0 means that an event is certain not to happen. For example, when drawing a marble from a bag of blue marbles, the probability of drawing a blue marble is 1 and the probability of drawing a green marble is 0.

Once you know the probability of an event, you can find the probability of the complement of that event. Since the sum of the probability of an event and its complement is 1, the probability of the complement of an event is \( 1 - P(\text{event}) \).

Therefore,

\[
P(\text{not having breast cancer}) = 1 - P(\text{breast cancer})
\]

\[
= 1 - 0.10
\]

\[
= 0.90
\]
Probability Tree Diagrams

Tree diagrams like the one you used in the drug-testing activity are useful when identifying choices. When a tree represents a situation involving two or more traits and their probabilities, it is called a **probability tree**. The probabilities are shown on the branches while the count data are shown in the boxes.

Conditional Probability

Sometimes the probability that an event occurs depends on whether another event occurs. Such events are called **dependent events**. For example, in the tree diagram you just completed, the numbers in the second boxes along each branch depend on the numbers in the first boxes. Notice that along the top branch of the Drug-Test Simulation the number of students who use drugs is a subset of the number of students who test positive. The notation $P(B|A)$ is often used to denote **conditional probability** and is read as “the probability that $B$ occurs given that $A$ occurs.”

The notation $P(\text{use drugs}|\text{test positive})$ indicates that the calculation depends on the number of students who test positive, not on the total number of students in the class.

**ACTIVITY 3-1 Mammogram Data**

**Objective:** Use data to create a probability tree diagram.

**Materials:**
- Handout IT-H3: Mammogram Data Set 1 Solution
- Blank paper

The following data on mammography screening for breast cancer were collected as part of a large study of mammograms. Use these data to make a table, and then draw and fill in the two types of probability trees you’ve learned about.

**Data Set 1**

<table>
<thead>
<tr>
<th>Data Set 1*</th>
</tr>
</thead>
<tbody>
<tr>
<td>The total number of women who had a positive mammogram was 11,523.</td>
</tr>
<tr>
<td>Of the women with a positive mammogram, 831 had breast cancer.</td>
</tr>
<tr>
<td>Of the women with a positive mammogram, 10,692 did not have breast cancer.</td>
</tr>
<tr>
<td>The total number of women who had a negative mammogram was 88,477.</td>
</tr>
<tr>
<td>Of the women with a negative mammogram, 169 had breast cancer.</td>
</tr>
<tr>
<td>Of the women with a negative mammogram, 88,308 did not have breast cancer.</td>
</tr>
</tbody>
</table>

*Adapted from real data[^1]
Questions for Discussion

Use your breast cancer screening data probability trees (or trees provided by your teacher) to answer the following questions.

1. What is the probability that a woman with a negative mammogram actually had breast cancer? Do you think this is low or high?

2. What is the probability that a woman with cancer had a negative mammogram? Do you think this is low or high?

3. What does it mean to have a negative mammogram?

4. What is the probability that a woman with cancer had a positive mammogram? Do you think this is low or high?

5. What is the probability that a woman with a positive mammogram actually had breast cancer? Do you think this is low or high?

6. What does it mean to have a positive mammogram?

7. If I am a patient with a positive test, which number do I care about most? Why?

8. If I think I have a disease, and am thinking about going to get tested, which number(s) do I care about most? Why?

9. What one value would you like to see improved in this mammogram test? Why?

Practice

A positive mammogram can cause a lot of anxiety. Suppose that you were able to change the mammogram so that it gives fewer false positive results. The following data on mammography screening for breast cancer were collected as part of a large study of your new “improved” mammogram.

Data Set 2

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total women with a positive mammogram</td>
<td>6,523</td>
</tr>
<tr>
<td>Of the women with a positive mammogram, breast cancer</td>
<td>731</td>
</tr>
<tr>
<td>Of the women with a positive mammogram, did not have breast cancer</td>
<td>5,792</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Category</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total women with a negative mammogram</td>
<td>93,477</td>
</tr>
<tr>
<td>Of the women with a negative mammogram, breast cancer</td>
<td>269</td>
</tr>
<tr>
<td>Of the women with a negative mammogram, did not have breast cancer</td>
<td>93,208</td>
</tr>
</tbody>
</table>
1. Use these data to make a table, and then draw and fill in the two types of probability trees you’ve learned about. Then answer the questions that follow.

2. What is the probability that a woman with a positive mammogram actually had breast cancer? Is this an improvement over the mammogram data you saw in class?

3. What is the probability that a woman with a negative mammogram actually had breast cancer? Is this an improvement over the mammogram data you saw in class?

4. What number of women with a negative mammogram actually had breast cancer? How does this compare to the old test?

5. Is the new mammogram better or worse than the original mammogram? Why?
Lesson 4  Properties of a Test

How can you evaluate various available tests? What are the properties of the tests that allow you choose among them and how do you choose the best test?

Predictive Properties

There are four properties of a test that one must consider when evaluating that test. These four properties are: positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity. PPV and NPV can be found as probabilities on the top trees in our examples while sensitivity and specificity can be found as probabilities on the bottom trees. Again, this is why we need both trees in order to evaluate a test.

PPV is the probability that a positive test means you actually have the disease/condition. In other words, what is the probability you have the condition, given a positive test: \( P(\text{disease}|+\text{test}) \)?

NPV is the probability that a negative test actually means you do not have the disease: \( P(\neg \text{disease}|-\text{test}) \). These are the numbers a patient would often be interested in because they are usually first presented with a positive or negative test result. PPV and NPV tell you how good that test result is at predicting the actual answer of disease or no disease. These numbers are found on the top trees in the handouts.

What are the PPVs for the two data sets in Lesson 3?
What are the NPVs for the two data sets in Lesson 3?

Specificity relates to a test’s ability to differentiate like objects or substances. In our drug-test example, that would mean that the test did not mistake any other substance for the drug the test was trying to detect. In a mammogram, it means that the test would not mistake another condition (like a cyst) for cancer. A test with a low specificity will give more false positives because it will mistake other things for the item in question. The value of a test’s specificity can be found on the bottom trees in the handouts. It is the probability of testing negative, given no disease: \( P(-\text{test}|\neg \text{disease}) \).

What was the specificity of the mammography test from data sets 1 and 2 in lesson 3?

Sensitivity relates to a test’s ability to detect smaller and smaller amounts of the “disease.” In our drug-test example, that would mean that the test could detect very low levels of the drug in someone’s system. The less of the drug you need present for the test to detect it, the higher the test’s sensitivity. In our mammography example, this means you could detect cancer with only a few cancerous cells present. A test with a low sensitivity will result in more false negatives because it will miss people who actually have the disease when the test did not detect it. Sensitivity is found in the bottom trees. It is the probability that you test positive, given that you have the disease: \( P(+\text{test}|\text{disease}) \).
What are the sensitivities for data sets 1 and 2 in Lesson 3?

Look at the chemical structures in the following diagram. What problems might you have if you are testing a person for the presence of methamphetamine?

<table>
<thead>
<tr>
<th>Antidepressant: Wellbutrin</th>
<th>Ephedrine</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Wellbutrin" /></td>
<td><img src="image2" alt="Ephedrine" /></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metabolites of Wellbutrin</th>
<th>Methamphetamine</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image3" alt="Wellbutrin metabolites" /></td>
<td><img src="image4" alt="Methamphetamine" /></td>
</tr>
</tbody>
</table>

*Figure 4.1: Similar Structures in Drugs*
One other important property of a disease (not the test) is the concept of **prevalence**. Prevalence is the number of people with the disease out of the total population, e.g., 10,000/1,000,000 or 1/100 or .01. Prevalence gives the probability that a random person in that population would have the disease. The population can be defined for specific purposes. For example, the population can be the total population of the world, or a country, or a subset of the country, such as only women who report a lump in their breast. Prevalence can be seen in the first bifurcation on the bottom tree as the probability that leads to the box showing the number of people with disease. The prevalence of a disease affects the test results. It is important to realize that even if a test only has a 1% false negative rate it may be affecting thousands of people, depending upon the population size.

**Activity 4-1**  Imperfect Word Search  
**Objective:** Investigate the idea of specificity.  
**Materials:** Handout IT-H5

**Directions:** Find the word **IMPERFECT** in each of the following puzzles.

<table>
<thead>
<tr>
<th>Puzzle 1</th>
<th>Puzzle 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>I I B N I M P E R F E T C I M</td>
<td>A R D Z A Q J R L F T Z B Z H</td>
</tr>
<tr>
<td>C M Q U B M L M U T A H I M M</td>
<td>Z R R P M C V L T X R E V C E</td>
</tr>
<tr>
<td>X R Q R A K M E I N R Z L E T</td>
<td>Q M K E Z V C E C G W F L X E</td>
</tr>
<tr>
<td>R F H B F T F N F M X H T R C</td>
<td>Q L S X W M B K C S P B T X H</td>
</tr>
<tr>
<td>T E V A H E P G T R R C O F E</td>
<td>T R J H V W V N Q C O F H V B</td>
</tr>
<tr>
<td>W T E P R M M T E R I C A T R</td>
<td>X A N I H T X Z E C Q L W U K</td>
</tr>
<tr>
<td>A Q M F I P V D F C H H T C E</td>
<td>K I N A J M Q Q H E X K L R B</td>
</tr>
<tr>
<td>Q I E E R T I E R U B Y G U M</td>
<td>A S D F T K G B F S M I K Z</td>
</tr>
<tr>
<td>H C Y F F E P B E T D Y F F P</td>
<td>H T T D Z N L B Y R S H L F A</td>
</tr>
<tr>
<td>Q C P S I Q W M N S P D V F R</td>
<td>X D Q U S R T H P D L V J E</td>
</tr>
<tr>
<td>T C E F E R P M I P V M I I N</td>
<td>O H Z V H K G X X M V D E Q I</td>
</tr>
<tr>
<td>T Q Z I M P E R F E T I W W</td>
<td>C K A E U B X X V I L J M W C</td>
</tr>
</tbody>
</table>

1. In which puzzle was it easier to find the word **IMPERFECT**? Why?

2. Did you start to circle the wrong word in puzzle 1? in puzzle 2?

3. Let’s say your “test” for finding the word **IMPERFECT** is to find the letters **IMP**. How many do you find in the first puzzle?

4. What if your test is finding **IMPER**?

5. Is the test for **IMP** or **IMPER** more specific? Why?

6. How does this relate to medical testing for drugs and mammography?
What Does a Positive Test Really Mean?

What does it mean if your test result for a disease (e.g., mammogram for breast cancer [BC]) is positive? What is the probability you actually have the disease, given that the test was positive (positive predictive value)? You must know the answer to this question before you can respond intelligently to a positive test result. In the examples you’ve seen so far, we had all of the information on who had the disease (or used drugs) and who did not have the disease. We need that information to develop a test, but the goal is to use these tests in groups where we don’t know who has the disease and who doesn’t. The probability that the positive test result is correct depends on three other probabilities that are commonly associated with disease testing: prevalence, sensitivity, and specificity. To explain these three probabilities and how they are used to determine the probability that your positive result is correct, we consider the case of testing a single woman for BC. You can also explore other diseases and populations with the formula developed in this section.

Prevalence is a proportion: the number of people with the disease out of the total population. This can be expressed as a fraction or as a decimal. For instance, one estimate of the prevalence of breast cancer in women coming in for mammography screening is $P(BC) = 1/100 = 0.01$ or 1% (assuming no prior knowledge of BC disease risk).

Sensitivity is the probability that the test will be positive when the individual really has the disease. The sensitivity of the mammography varies. Let’s assume the sensitivity is $P(+|BC) = 0.85$. The vertical bar between “+” and “BC” can be read as “assuming” or “given”; the probability of a positive mammogram given the woman has breast cancer is 85%.

Specificity is the probability that the test will be negative, given the individual does not have the disease. Poor specificity may be caused by errors or difficulties in the testing procedures. The specificity of a test can be estimated by following those who test negative to see if they later develop the disease. We will suppose that the specificity of mammography is $P(−|no BC) = 0.9$. Because a person who does not have BC must have either a positive or negative mammogram, another way of saying the same thing is $P(+|no BC) = 0.1$. In other words, only 10 out of 100 individuals who do not have BC would test positive.

Now we put together prevalence, sensitivity, and specificity to compute $P(BC|+)$, the probability of having BC, given a positive mammogram (a.k.a. positive predictive value).

$$ \text{Positive Predictive Value} = \frac{\text{Sensitivity} \times \text{Prevalence}}{\text{Sensitivity} \times \text{Prevalence} + (1 - \text{Specificity}) \times (1 - \text{Prevalence})} $$
Bayes’ Rule

The general formula for calculating $P(BC|+)$ is called Bayes’ Rule, an important topic in probability and statistics:

$$P(BC|+) = \frac{P(+|BC)P(BC)}{P(+|BC)P(BC) + P(+|\text{no BC})P(\text{no BC})}$$

$$= \frac{.85*.01}{.85*.01+.10*.99} \approx .079$$

Bayes’ Rule tells us that, for this example, if you have a positive test for BC, there is only about an 8% chance that you actually have BC. This seems surprising, since the test is fairly sensitive (0.85) and specific (0.90).

An alternative way to compute $P(BC|+)$ might help you understand Bayes’ Rule and see why $P(BC|+)$ is so low. Suppose a population of 1 million women is tested for BC. You would expect about 10,000 in this population to have BC for our example that assumes 1% of women screened have BC. Of these 10,000, you would expect only 8,500 (10,000*0.85) to test positive. On the other hand, of the 990,000 without BC, you would expect about 99,900 (990,000*0.1) to test positive. Thus, 107,500 (8,500+99,000) women had a positive mammogram, but only about 8% (8,500/107,500) of them actually have BC. Of course, randomness in the population means that none of these numbers are exact, which is why Bayes’ Rule uses probabilities instead of population counts.

Why is Prevalence Important?

As you may know, the current recommendations don’t say that all women should get regular mammograms. Only women who have reached a certain age (i.e., 40 years) or have reason to think they might have a higher risk of BC disease (including, but not limited to, family history, finding a lump, experiencing symptoms) are encouraged to get a mammogram. The reasons for the recommendations are complex, but are due in part to the important role that prevalence plays in determining the probability that an individual has BC, given a positive mammogram.

Example: Assume that the prevalence of BC in women coming in for mammography because of symptoms is 5%. Again use 1 million as our population size so that we can see how the numbers change in our example.

With a prevalence of .05, we would expect that 50,000 women in the population have BC. Of these, we predict that 50,000*.85 = 42,500 will have a positive mammogram. We would also expect that of the 950,000 women without BC, about 950,000*.01 = 95,000 will have a positive mammogram. Thus, 42,500 + 95,000 = 137,500 women had a positive mammogram, and about 31% (42,500/137,500) of them actually have BC. This is a big improvement over the performance of the same test (with 85% sensitivity and 90% specificity) by increasing the prevalence in the group of women screened. This property is part of the rationale behind targeting screening tests to groups of individuals who have higher disease prevalence.
Questions for Discussion

1. Compute the positive predictive value, $P(BC|+)$, when sensitivity is 0.6, specificity is 0.99, and prevalence is 5%.

2. Compute the positive predictive value (PPV) if the specificity is .80, but the sensitivity is still 0.6 and prevalence is still 5%.

3. What is the negative predictive value (NPV) for the scenario in question 1?

4. What is the NPV for the scenario in question 2?

5. Is NPV=(1-PPV)?

6. Were you surprised by how the PPV and NPV changed based on changing the specificity? Why or why not?

7. What property of a test would you change to have a greater effect on NPV than PPV?

Extension

In order to explore the effects of changing aspects of the test and/or population, use a computer or calculator program to determine the PPV and NPV with various inputs. A sample program for a TI calculator is shown below.

Calculator Program

Choose a name for the following predictive value program and enter it into your calculator.

```
Disp “SENS:”
Input A
Disp “SPEC:”
Input B
Disp “PREV:”
Input C
(A*C)/(A*C+(1-B)(1-C)) -> D
Disp “The PPV is”
Disp D
(B(1-C))/(B(1-C)+(1-A)C) -> E
Disp “The NPV is”
Disp E
```

Note: The $\rightarrow$ is typically created by hitting the Store button. In other words, you are telling the calculator to store the result of the first equation as D and the second equation as E.
**Challenge Questions**

Use your calculator program or a computer program to answer the following questions.

1. Explore the effect of sensitivity on testing by computing $P(BC|+)$ when sensitivity is between 0.6 and 0.99, keeping the prevalence 0.01 and the specificity 0.999.

2. Explore the effect of specificity on testing by computing $P(BC|+)$ when specificity is between 0.9 and 0.9999, keeping the prevalence 0.01 and the sensitivity = .85. Which had a greater effect, changing sensitivity (in question 1) or changing specificity?

3. Which do you think should be a higher policy priority: increasing the sensitivity or decreasing the false positive rate (increasing the specificity) of mammography? Explain your answer.

4. Explore the effect of prevalence on the positive predictive value by computing $P(BC|+)$ when prevalence is between .5% and 5% for a test with .85 sensitivity and .90 specificity. Suppose you were screening:
   
   a. All women over the age of 20 (prevalence=.5%).

   b. All women over the age of 40 (prevalence=1%).

   c. All women over the age of 40 who have symptoms (e.g., pain, lump; prevalence=5%).

5. Why are screening programs targeted at specific groups rather than the whole population?
Lesson 5    Pharmacogenetics

Let’s return to Elizabeth and her doctor.

Case Study: The Results

Dr. Smith: Well, Elizabeth, the biopsy came back positive
Elizabeth: Oh, my, I have cancer?
Dr. Smith: I’m afraid so.
Elizabeth: What is the next step? Surgery? Oh, my goodness! Do I need radiation?
Dr. Smith: Well, first I would like to do a genetic test for BRCA1 and BRCA2.
Elizabeth: BRCA? What is that? And then what do we do? Is this going to kill me?

Questions for Discussion

1. What is BRCA? What does it mean if you have an abnormal mutation in BRCA1 or BRCA2?

2. List and explain two reasons why someone would get a genetic test after finding out he or she has a particular disease/condition.

3. Now that the doctor knows Elizabeth has breast cancer, what would the doctor do to check the extent or spread of the cancer?

SNP and Pus-Poppin’ Frogs

ACTIVITY 5-1    Pus-Poppin’ Frogs Tree
Objective: Examine various effects of drugs on populations
Materials:
   • Computer access
   • Handout IT-H7: Pus Poppin’ Frogs Tree Worksheet

Pharmacogenetics examines the relationship between an individual’s genetic makeup and his or her response to a particular drug. The hope is to tailor drugs to an individual or group of individuals who are genetically similar. The goal is to increase a drug’s effectiveness while decreasing its side effects.

Read http://learn.genetics.utah.edu/content/pharma/intro/ and http://learn.genetics.utah.edu/content/pharma/snips/
Go to http://pus-poppin-frogs.software.informer.com/1.0/ complete the Pus-Poppin’ Frogs simulation on a computer. The Pus-Poppin’ Frogs program is available on this site and must be downloaded and installed to complete the simulation.
The data below are adapted from the Pus-Poppin’ Frog program shows four different SNP profiles, the population distributions of these profiles across three towns and the effects of three tested drugs.

<table>
<thead>
<tr>
<th>SNP Profile</th>
<th>Town Percentage Distribution</th>
<th>Average</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Croakytown</td>
<td>Hopsterville</td>
<td>Ribbitfield</td>
</tr>
<tr>
<td>5G; 11A</td>
<td>23%</td>
<td>37%</td>
<td>23%</td>
</tr>
<tr>
<td>5G; 11G</td>
<td>39%</td>
<td>34%</td>
<td>43%</td>
</tr>
<tr>
<td>5T; 11T</td>
<td>23%</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>5C; 11T</td>
<td>15%</td>
<td>9%</td>
<td>4%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Choose one of the drugs (or use the one assigned by your teacher) and use the “average” percentages from the table to complete the 2×2 table below.

<table>
<thead>
<tr>
<th>“DRUG NAME”</th>
<th>Effective</th>
<th>Ineffective</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Adverse Effects</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse Effects</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Use these data to create two probability trees for your drug. The trees should look at effectiveness of the drug and whether or not there were adverse effects. After creating your trees, answer the questions below.

1. Outline the steps that a drug company takes when trying to test and market a new medication for a particular genetic profile.

2. What will the pharmaceutical company claim is the rate of adverse effects for your drug across the whole population? (remember, the company wants their drug to ‘look good’)

3. As a patient who is considering taking the drug, what probability on the tree would you want to know?

4. Compare Ribbitra and Zertoadinoxx in terms of effectiveness and adverse effects across the whole population. Which drug would be better to give to patients if you do not know their SNP profile?

5. Explain why SNP profiling can be a useful technology in patient health care.

6. Describe some problems that could arise in society if everyone has an SNP profile on record.
Clarhoppin Answers

Total

- **Effective**: $P(e)$
  - $P(n|e)$ (no adverse effect and effective)
  - $P(a|e)$ (adverse effects and effective)

- **Ineffective**: $P(i)$
  - $P(n|i)$ (no adverse effect and ineffective)
  - $P(a|i)$ (effective and adverse effect)

- **No Adverse Effect**: $P(n)$
  - $P(i|n)$ (ineffective and no adverse effect)
  - $P(a|n)$ (adverse effect)

- **Adverse Effect**: $P(a)$
  - $P(e|a)$ (effective and adverse effect)
  - $P(i|a)$ (ineffective and adverse effect)
Ribbitra Answers

Total

P(e)

- effective
  - P(n|e)
  - adverse effects and effective
    - P(e and n)
  - no adv effect and effective
    - P(e and n)

- ineffective
  - P(n|i)
  - adv effect and ineffective
    - P(i and n)
  - effective and no adv effect
    - P(i and a)

P(i)

- no adverse effect
  - P(e|n)
  - ineffectve and no adv effect
    - P(n and e)
  - effective and adverse effect
    - P(n and i)

P(a)

- adverse effect
  - P(e|a)
  - ineffective and adverse effect
    - P(a and e)
  - P(i|a)

- no adverse effect
  - P(i|a)
  - P(a and i)
Lesson 6  Ethics and Decision-Making

With your knowledge of testing, now consider the following discussion between Elizabeth and her doctor.

Case Study: Genetic Test

Dr. Smith: Hello, Elizabeth. How are you feeling?
Elizabeth: I’ve been very nervous about this BRCA test. Do you have the results?
Dr. Smith: Yes.
Elizabeth: Well, don’t keep me in suspense! Am I positive or negative?
Dr. Smith: You have tested positive for mutations to BRCA 1 and 2.
Elizabeth: Oh, my, what should I do now? Should I tell my children?

Questions for Discussion

1. Should Elizabeth tell her children that she has the BRCA mutations and that they may have them also? (Remember, Kira is only 13, Jennie is about to start college, and Celeste is about to have her own daughter.)

2. If Elizabeth does tell her three daughters, do you think they should get tested? Why or why not? Is the answer different for each? Read the article on the pros and cons of testing at http://www.breastcancer.org/symptoms/testing/genetic/pros_cons.jsp.

Read the following guidelines from the U.S. Preventive Services Task Force on genetic counseling and/or genetic testing for BRCA1 and BRCA2. http://www.uspreventiveservicestaskforce.org/uspstf05/brcagen/brcagenrs.htm

3. Given this article and everything you’ve learned about testing, why is it so important to have genetic counseling before making a decision about whether to get tested?


4. What were the important issues for this woman?

5. Was the information presented well by the author? Why or why not?

6. Would you change the way the author presented the data regarding risk and the interpretation of the genetic test?
Glossary

Angiogenesis – a physiological process involving the growth of new blood vessels from preexisting vessels.

Bayes’ Rule – a mathematical theorem that provides a way to calculate the probability of having a disease, given a positive test.

Benign tumor – a group of cells that is very slow growing and typically well defined.

Biopsy – a procedure that involves the removal of cells or tissues for examination.

BRCA1 and BRCA2 – genes that can have mutations that are associated with breast cancer.

Cancer – a condition in which cells in the body grow in an uncontrolled way.

Carcinogens – things that may cause a cell to become cancerous.

Chemotherapy – the treatment of disease by chemicals that kill cells, specifically those of microorganisms or cancer.

Complement (of an event) – the set of all outcomes in the sample space that are not included in the outcomes of the event.

Conditional probability – the probability of some event $A$, given the occurrence of some other event $B$.

Dependent events – events such that the occurrence of one affects the likelihood of the occurrence of any of the others.

False negative test result – a test result that does not appear to detect a disease or condition when in fact it is present.

False positive test result – a test result that appears to detect a disease or condition when in fact it is not present.

Gold standard – the best test currently available, which may not be definitive, depending on the disease or condition for which we are testing. New tests are compared against the gold standard to determine sensitivity and specificity. If the new test is better, it may become the new gold standard.

Haplotypes – the combination of the different SNPs in a particular region of your DNA that tend to be inherited together. Also known as SNP profile.

Malignant tumor – a group of cells that invades the surrounding tissue.
**Mammogram** – An x-ray of a patient’s breast.

**Metastatic cancer** – cancer that spreads to other parts of the body.

**NPV** – negative predicted value; the probability that a negative test actually means you do not have a disease or condition.

**Oncogenes** – mutated proto-oncogenes.

**Pharmacogenetics** – a discipline that studies the relationship between genetic makeup and response to a particular drug in an effort to tailor medical treatments to the individual.

**PPV** – positive predicted value; the probability that a positive test means you actually have the disease or condition.

**Prevalence** (of a disease) – a proportion: the number of cases of the disease out of the total population.

**Probability** (of an event) – a measure of the likelihood that an event will occur.

**Probability tree** – a diagram that shows the possible outcomes and probabilities of a series of events.

**Proto-oncogenes** – normal genes that help regulate cell division.

**Radiation** – energy in the form of waves or moving subatomic particles emitted by an atom or other body as it changes from a higher energy state to a lower energy state.

**SNP** – Single Nucleotide Polymorphism – a single nucleotide substitution in a DNA sequence that is found in a significant proportion of the population.

**SNP profile** – the combination of the different SNPs in a particular region of your DNA that tend to be inherited together. Also known as *haplotype*.

**Sensitivity** – relating to a test’s ability to detect smaller and smaller amounts of the “disease.”

**Specificity** – relating to a test’s ability to differentiate like objects or substances.

**Telomeres** – noncoding, repeating nucleotide sequences (TTAGGG) at the ends of DNA strands.

**Tree diagram** – a diagram that branches, showing all the possible outcomes of a process that is carried out in several stages.

**True negative test result** – a test result that does not appear to detect a disease or condition when in fact it is not present.
True positive test result – a test result that appears to detect a disease or condition when in fact it is present.

References


