3 A Case Study: A BRCA Genetic Testing Dilemma

Adapted from a true story.

It was the decision of a lifetime.

Her latest doctor visit showed nothing was wrong. But Deborah Lawler, age 33, was tired of constantly looking for the lump in her breast. Ever since she had learned about the DNA test that could help predict her risk of developing breast cancer, Deb had agonized over whether to have the test, and what to do about the results.

Deb didn't want history to keep repeating itself: Deb's mother had fought breast cancer when Deb was in high school, and Deb's maternal grandmother died from the disease before Deb was born. Deb's uncle Bob, her mother's only brother, had been diagnosed just after his 50th birthday. One of Deb's first cousins, Katherine, had detected breast cancer at the age of 33. The coincidences were too much to ignore.

"It could be growing inside of me right now," she told her mother on the phone in February, pacing in the living room of her Chicago apartment. "We could find it any time." Waiting for an encouraging word, she added, "I could take the test this week." Her mother, not sure what to say, remained silent.

Deb was referring to the breast cancer susceptibility tests—the BRCA tests. Doctors would isolate DNA from Deb's blood and sequence the Breast Cancer Susceptibility 1 and 2 genes to determine whether known cancer-causing mutations are present. *BRCA1* and *BRCA2* mutations account for about 5% of all breast cancer. The remaining cases are caused by mutations in other genes, environmental exposures, and other unknown factors.

Factors such as excess weight, lack of exercise, having her first period at a young age, and not having children can increase the risk of breast cancer in all women. If the test finds that Deb carries a cancer-causing mutation in her BRCA genes, her risk of breast cancer would increase dramatically – from 12% (the average lifetime risk for all women) to anywhere between 50-85%. A mutation would also increase her risk of ovarian cancer from the average of 2% to between 16-60%.

Few things in biology are 100%.

If she tested positive for the mutations known to be associated with cancer, she could have both of her ovaries surgically removed before cancer could strike. This would reduce her risk of cancer substantially, but not completely. She could also have her breasts surgically removed through a procedure known as a mastectomy, but even after a mastectomy, there would still be a 10% chance that tiny cancer cells might be hiding in her otherwise healthy tissue. She could try regular doses of drugs that block estrogen and help prevent the development of breast cancer, but these drugs induce a form of menopause. She and her doctors could practice increased surveillance to try to catch the cancer early by using twice-yearly **mammograms** (x-rays of the breast to detect breast cancer), breast self-exams, and blood tests, and at least yearly physical exams with her doctor and other tests to detect potential ovarian cancer.

For every **1,000** women…

120 (12%) will get breast cancer.

6 of them inherited mutations in *BRCA1* or *BRCA2* (5% of all cases of breast cancer).

This may seem like a small number, but for a woman who inherits a cancer-causing *BRCA1* or *BRCA2* mutation, her ***risk of developing breast cancer is up to 85%.***

As they seek to avoid the potentially lethal consequences of a mutant gene, many people turn to relatives who may share the burden of having such a gene. But at a moment when a genetic test can make family ties even more tangible, they are often most strained. Parents who fought cancer might not understand the choices that confront their children, and guilt over giving their children a harmful allele might color their advice. Siblings and cousins who may carry the risky allele might try to persuade others to confront the problem just as they do, while those relatives who inherited functional forms of the genes may seem unqualified to judge those who did not.

Even as she searched for her own answer, Deb, a doctor, found herself navigating her family's strong and conflicting opinions on the imperfect options lying before her. Her father, who once feared he would lose his wife to cancer, encouraged her and her siblings to have the test. Her brother John felt ambivalent about the knowledge the test would bring, even though the risk of breast cancer in men carrying BRCA mutations is also high. Her sister Lori was also undecided, though she thought that the results may benefit her two young children some day. Deb's Aunt Sue said she hated to see her niece embrace a course of action that was "upsetting the whole family for her own personal gain." Another cousin, Katherine's sister Lynn, declined even to talk about the DNA test—she did not have health insurance and the test was too costly to pay for out-of-pocket, so why even consider it? But for Deb, even with her family's mixed reactions, it was her mother's blessing that she most eagerly sought.

"I have the potential of this amazing gift, of knowing my risk," Deborah told her mother over the phone that winter night. "How can I not do anything about that?"

But biology is rarely a simple thing, and her risk of cancer, even should she test positive for cancer-causing mutations, was far from certain. Should Deborah take the test?

Credit: Adapted from Harmon, Amy. "The DNA Age: Cancer Free at 33 but Weighing a Mastectomy." *The New York Times*. September 16, 2007. Print.

Homework Questions: Answer these questions in your lab notebook or on a separate sheet of paper.

1. One important principle of ethics is ***Respect***. Part of Respect acknowledges a person's right to make choices, hold views, and to take actions based on personal values and beliefs. Describe one way that the principle of Respect applies to this case study.

2. Another principle of ethics is ***Maximize Benefits/Minimize Harms***, which states that there is an obligation not to inflict harm, to provide benefits to persons, and to contribute to their welfare. Describe one way that the principle of Maximize Benefits/Minimize Harms applies to this case study.

3. Would you ever consider having a genetic test done? Why or why not?

4. Under what circumstances would you not want to have a genetic test done?

3 Focus on the Principles

Do these principles apply? In your lab notebook or on a separate sheet of paper, discuss how each of these bioethical principles applies to the ethical question, "Should Deb Lawler have BRCA genetic testing?" You may use the questions below each principle to guide your answers. Some principles may apply more than others for a particular situation.

RESPECT for PERSONS

Definition: Individuals have inherent dignity and worth and deserve to be treated accordingly. Each person has the right to self-determination and to make his or her own decisions and choices. Individuals from vulnerable populations should also be respected.

Questions related to RESPECT for PERSONS:

- *What would be respectful to the people (or other stakeholders) involved?*
- *How can we respect people and their right to make their own choices (autonomy)?*

MAXIMIZE BENEFITS/ MINIMIZE HARMS

Definition: Individuals should try to directly help others, acting in others' best interests. Individuals should not intentionally inflict harm on others.

Questions related to MAXIMIZE BENEFITS/ MINIMIZE HARMS:

- *How can we do the most good (beneficence) and the least harm (nonmaleficence)?*
- *What kinds of harms and benefits might arise from different solutions?*

ETHICAL QUESTION

Should Deb Lawler have BRCA genetic testing?

JUSTICE

Definition: Individuals who are equals should qualify for equal treatment. Risks, resources, and costs should be distributed equally.

Questions related to JUSTICE:

- *What would be fair?*
- *How can we treat others equitably?*

OTHER

Are there any other ethical considerations?

Name _____ Date _____ Period _____

3 Structured Academic Controversy Worksheet

This Issue: *Should Deb Lawler have BRCA genetic testing?*

Team Members ***FOR***

1. _____
2. _____

Team Members ***AGAINST***

1. _____
2. _____

Relevant facts:

Individuals or groups who have a stake in the outcome ("stakeholders") and their concerns:
(Who is affected by Deb's decision? Why do they care?)

Main arguments ***FOR***: 1. 2. 3.	Main arguments ***AGAINST***: 1. 2. 3.
List of possible solutions:	
Areas of agreement:	Areas of disagreement:

3 Structured Academic Controversy FOR Position Statement

FOR Arguments: (Deb ***should*** proceed with BRCA genetic testing).

If Deb takes the test and the result is negative (meaning she does not have a mutation in her *BRCA1* or *BRCA2* genes that would increase her risk of breast and ovarian cancer), she will likely feel relieved and be less anxious about her future. She will also not have to worry about passing the mutation on to future children.

If Deb takes the test and the result is positive (meaning she does have a mutation in her *BRCA1* or *BRCA2* genes that would increase her risk of breast and ovarian cancer), she can begin to make some lifestyle and behavioral changes to reduce her risk, such as:

- Having physical exams more frequently to try to detect breast or ovarian cancer early.
- Increasing her number of medical screenings, such as mammograms (x-rays of the breast used to find cancer).
- Beginning **chemoprevention** medications, which are drugs that are taken regularly to help prevent cancer from developing.

She could also reduce her risk by having surgery to remove her breasts and/or ovaries.

Ethical Arguments Supporting the *FOR* Side Include:

Respect for Persons

Deb has the right and responsibility to make decisions and take action based on her values and beliefs. She appears to value the knowledge that would come from the test results. Deb is a competent adult, fully able to understand the results and take action on those results. Whether or not her mother supports her decision to take the test, Deb can make her own autonomous decision about her own health and care. It is her body and her decision.

Maximize Benefits and Minimize Harms

The benefits that come from knowing her BRCA status outweigh the harms that may result.

If the test is negative, the benefits (relief, less anxiety) far outweigh any harms that come from the knowledge.

If the test is positive, Deb will benefit by being able to be proactive about her health care. Being able to take action (see the bullets above) will outweigh the anxiety that may result from a positive test result.

3 Structured Academic Controversy AGAINST Position Statement

AGAINST Arguments: (Deb ***should not*** proceed with BRCA genetic testing).

- Not all people with a mutated *BRCA1* or *BRCA2* gene will develop breast or ovarian cancer as a result.
- Inherited mutations in *BRCA1* or *BRCA2* genes only account for about 5% of breast cancer.
- Not all family members may want to know the results of this test. A positive or negative result for Deb also informs family members who have a similar genetic makeup.
- There is a possibility that testing results may not remain entirely private.
- There is a possibility of discrimination from insurance companies based on results.
- While there are some behavioral changes Deb could make, there is really no "cure" and treatment options are limited.

Ethical Arguments Supporting the *AGAINST* Side Include:

Respect for Persons

While Deb has the right to make her own decisions and choices about her health, her test results also affect her family. A positive result for Deb identifies her mother as also having the mutation. This information has strong implications for both of Deb's siblings and her maternal cousins. If a family member does not want to know his or her BRCA status, that individual's right to make his or her own choices may be violated by Deb's test results.

Maximize Benefits and Minimize Harms

The harms that come from knowing her BRCA status outweigh the benefits that may result.

Nothing in biology is 100%, and knowing that her chances of breast/ovarian cancer are increased does not mean that Deb will develop the disease. Acting on positive test results (meaning she does have a BRCA mutation that would increase her risk of breast and ovarian cancer), Deb may choose to have her breasts and/or ovaries removed. While there might be some unknowable benefit to this procedure, she would be intentionally inflicting harm on herself in the pursuit of health.

Many of the lifestyle changes that reduce the risk of breast cancer in all women (such as keeping a healthy diet, exercising regularly, and maintaining a healthy weight) have widespread benefits, regardless of BRCA status. Deb does not need to take the genetic test to benefit from embracing these health and lifestyle choices.