

## **Case Study: A BRCA1 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%. 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%.

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.

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 someday. 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. (via NWABR).