



# AN OUNCE OF PRECISION

The next step in breast cancer research? Hyperpersonalized prevention that could halt the development of cancer in the first place. By Maria Del Russo

SISTERHOOD COLLAGE: ATHENA PETRA TASIPOULOS; REED AND VIRTUE: NICOLE VIRTUE.

When she discovered a small lump in her breast in April 2018, Alyssa Reed was 28 at the time and didn't think much of it. She was just about to graduate from her master's program, and she was planning a wedding. All the research she'd done on the internet told her the lump was likely a benign cyst. But when she finally went to see a doctor that June, Alyssa was given news she never expected—the lump was actually one of several tumors. She had breast cancer.

"That isn't typical, of course," she says. "So my doctor immediately put in a referral for genetic testing for me and my family." Hidden away in Reed's DNA was the BRCA1 mutation. According to Memorial Sloan Kettering Cancer Center, women with an altered BRCA1 gene, on average, have a 50 to 85 percent risk of developing breast cancer by age 70. The gene had come down from her paternal grandfather's line and hadn't been detected until now.

After going in for testing herself, Alyssa's older sister Nicole Virtue, 34, also discovered that she carried the BRCA1 mutation. "As soon as I found out, I wanted to start prevention right away," Virtue says.

Although her screenings thus far have come back cancer-free, Virtue's situation comes with its own set of stressors that are completely different from her sister's—and a lot less definitive. Reed had her breasts removed and underwent chemotherapy and radiation; she was also able to have fertility services covered by insurance because of her diagnosis. Virtue, on the other hand, is left with a handful of vague possibilities for prevention.

She might develop breast cancer or ovarian cancer, so she might want to have her breasts and ovaries removed, but exactly when it's best to do so is somewhat up to interpretation. She might want to consider egg freezing, but since she is undiagnosed, the cost will likely come out of pocket. And since Virtue is unmarried, the conversation around fertility treatments can be tricky. "I'm in this window where there are a lot of options, but these are difficult decisions to make, and I'm constantly worrying whether I'm doing enough," she says.

It is women in Virtue's position, who are left with less-than-ideal and sometimes heartbreaking preventive options, that the Breast Cancer Research Foundation hopes to help with its Precision Prevention Initiative, which launches this October. BCRF was founded in 1993 by Evelyn Lauder of the Estée Lauder Companies, who battled breast cancer herself before she died from ovarian cancer in 2011. The initiative is the first large-scale, coordinated philanthropic effort to apply the principles of precision medicine to breast cancer prevention research. "The initiative has three goals: to identify risk factors that can reliably predict breast cancer, to develop and validate new biomarkers of risk, and to test novel prevention strategies," says Dorraya El-Ashry, PhD, who joined BCRF as its chief scientific officer in 2019.

According to El-Ashry, precision medicine has already been used successfully in the treatment of breast and ovarian cancers. *Precision* is the key word: Doctors look into the specific factors that are causing cancer in a patient, whether they involve genetic mutations, breast density, environment, or lifestyle choices like smoking, alcohol intake, diet, or exercise. They tailor treatment to its cause, choosing whether to administer chemotherapy, radiation, and/or hormonal medication—and in what configuration—based on what's been proven to be most effective for that individual's cancer. In Reed's case, some elements of her care were selected based on her cancer's pathology, but there were no known effective precision treatments available at the time for her specific cancer type, nonmetastatic BRCA1. Clinical trials are currently underway, however.

"Over the last 30 years, we've seen a 40 percent decline in deaths from breast cancer, and that's thanks to the advances we've made in both diagnosis and treatment," El-Ashry says. "But the incidence of breast cancer has remained steady, so the idea behind this initiative is to take what we've learned from precision treatment and apply it to prevention."



ALYSSA REED AND NICOLE VIRTUE AT REED'S WEDDING IN JULY 2018.

Precision prevention is in its infancy. According to the National Cancer Institute (NCI), some of the most significant options currently available for women with BRCA mutations are preventive mastectomy and oophorectomy, both of which are very serious surgeries. Certain hormone-therapy medications have also been shown to reduce cancer development by 56 to 86 percent in women with specific precancerous lesions (however, less than 10 percent of women offered this option take it, due to possible side effects of the drugs). All things considered, the room for innovation is overwhelming. "To research new precision prevention options, you have to combine information from thousands of women over a few decades and see if you can accurately predict their risk," says Richard Wender, MD, chief cancer control officer for the American Cancer Society. "Then you need to feed that into a computer system that can push all that data together to generate near- and long-term risk assessments. It's pretty darn complicated, but the potential is significant."

Promising studies are in the works, like the ongoing WISDOM study at the University of California San Francisco, which aims to personalize screening recommendations. A recently concluded trial at the University of Texas MD Anderson Cancer Center showed that, as a preventive measure against ovarian cancer, removing just the fallopian tubes could help delay eventual ovary removal, mitigating risk while allowing a patient to avoid negative side effects, like early menopause. The research funded by the BCRF Precision Prevention Initiative, says El-Ashry, could include designing artificial intelligence that can analyze an individual's risk data or exploring medications that can target cancer triggers.

And while these developments would certainly be useful for those with genetic risks for cancer, "the vast majority of cancers are not inherited," El-Ashry says (a host of factors including age, ethnicity, age of your first period, and even birth control choice are also at play). "So this treatment could be useful for all women who are at some kind of risk."

Doctors hope that precision prevention will be one of the most effective ways to forestall cancer in women who are at risk, both for breast and other cancers, and reduce unnecessary screening for women who are not. "If we can determine which precancers do or don't progress, we wouldn't be treating women who don't need to be treated and vice versa," says Edward Sauter, MD, PhD, medical officer in the Breast and Gynecologic Cancer Research Group at NCI. "There's more and more evidence we will be able to tailor therapy." It would certainly take the pressure off women like Virtue, who find themselves facing difficult decisions—decisions that compound a stressful time in their lives. Luckily, Virtue has a built-in support system with her sister, Reed. But she's also in a kind of limbo for the time being.

"I wasn't prepared to make these decisions right now," Virtue says. "But just because I have this mutation, it's not as dark as it sounds. I think I'm still going to be able to live the life I want to live, regardless of this risk. When I hear about research like this, I'm hopeful."