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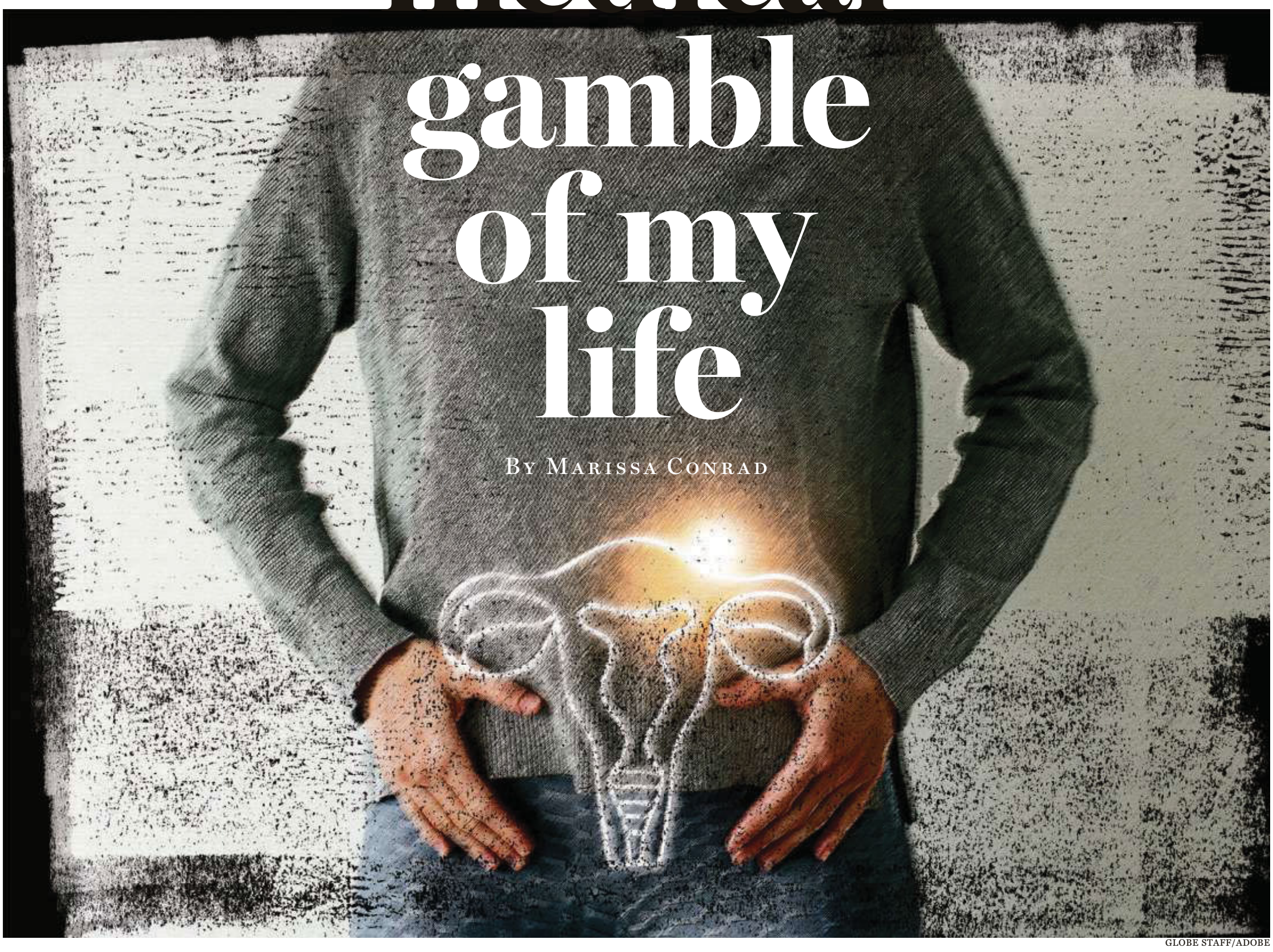
The medical gamble of my life

By Marissa Conrad



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In animation, there's a trope called the piano drop: A character looks up, sees a shadow, and realizes a falling piano is about to flatten them into cartoon roadkill. The day I arrived at the hospital to have my fallopian tubes removed, I figured the piano was coming for me — that I would look up and see all the fear and uncertainty I hadn't yet felt, about to hit me in the face. I do that sometimes with feelings, push them away until they crash all at once, like a plummeting baby grand.

Strapped to the operating table, I admired the anesthesiologist's glasses and thought about how the mask she suctioned to my skin smelled like Halloween. Then I was asleep, and then awake again, still feeling nothing but slight disappointment at not being offered the chance to see my snipped-out tubes. They had been segmented into tiny pieces that pathologists would examine for signs of cancer.

A genetic mutation predisposes me to ovarian cancer. Rather than have my ovaries removed, I opted for a less-invasive procedure that, if it proves effective, will revolutionize cancer prevention. It's a big if.

I was born with a BRCA1 mutation, which means that one of my genes that's supposed to create cancer-fighting proteins doesn't do its job. My chance of developing high-grade serous ovarian cancer (the "classic, deadly kind," one oncologist told me) is about 40 percent over my lifetime, or

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Escape plans of the rich and famous

By Evan Selinger

A widespread sense of anxiety grips our society. Climate change, economic upheaval, or another pandemic loom as catastrophes.

In the new book "Survival of the Richest: Escape Fantasies of the Tech Billionaires," Douglas Rushkoff contends that many of the richest and most powerful people are not immune from this anxiety. They are also scared and feel vulnerable, because they see the same problems that we do. The difference, Rushkoff argues, is that they have fueled these problems and intend to deal with them by leaving the rest of us behind.

Even more tragically, Rushkoff says, many of us have internalized their self-centered worldview, which he calls The Mindset — a desire to use technology to escape a reality that technology is making worse.

Rushkoff is a professor of media theory and digital economics at CUNY/Queens, hosts the Team Human podcast, and is the author of several highly acclaimed books on technology and media theory. In "Survival of the Richest," he explains how The Mindset gained traction and

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IAIN MARCKS

Douglas Rushkoff argues that Elon Musk, Mark Zuckerberg, and other tech moguls intend to separate themselves from the rest of humanity.

Inside

With cancer screening, earlier isn't necessarily better

BY H. GILBERT WELCH

When the two Republican senators from Mississippi cosponsor legislation with the two Democratic senators from California, something intriguing must be going on. In fact, there appears to be an outbreak of bipartisanship: 20 Republicans, 25 Democrats, and one Independent in the Senate are cosponsors, along with a bipartisan majority of 99 Republicans and 134 Democrats in the House.

What do these Republicans and Democrats agree on? That Medicare should be compelled to pay for liquid biopsies, which test for multiple cancers using a single vial of blood, even though no one is sure whether they work or not.

Talk about putting the cart before the horse.

The cosponsors would probably respond that their bill, the Medicare Multi-Cancer Early Detection Screening Coverage Act, would go into effect only if the Food and Drug Administration approves the tests. But unlike with drugs and vaccines, the FDA does not have a particularly high bar for medical tests. The agency's focus is on the safety of tests, not whether they help people. One liquid biopsy test, CancerSEEK, has already obtained FDA status as a breakthrough device, which signals an expedited review process. Another, Galleri, has avoided the FDA approval process altogether under a waiver for tests that are performed in a single laboratory and are not sold to other labs. Instead, Galleri is being sold directly to consumers at $949 a pop.

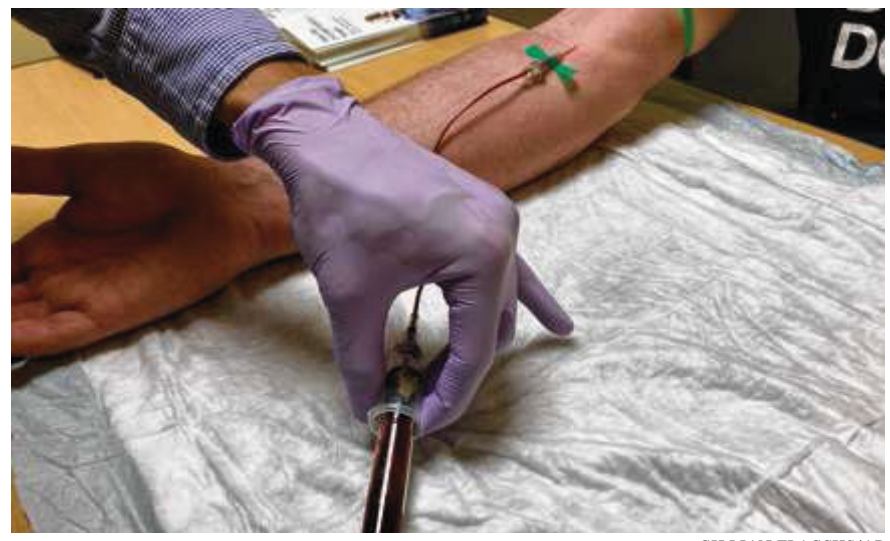
The company that sells Galleri recommends that people test once a year. So let's do the math. Given that there are some 60 million Medicare beneficiaries, that would be approximately $60 billion per year. It would represent a 7 percent increase in total Medicare expenditures — to be passed on to taxpayers and/or to Medicare beneficiaries in the form of higher premiums.

All for one test. And no one knows whether that test helps people live longer or live better.

Nonetheless, enthusiasm for cancer screening abounds. As one opinion piece in The Daily Beast put it, "Early Cancer Screening Saves Lives. Congress Needs to Act," which appears to capture the thinking of more than 400 medical organizations and advocacy groups that support the legislation. They seem to be forgetting the great prostate cancer screening mistake — when men were indiscriminately screened and put through debilitating treatment for a disease that would have killed very few of them.

Advocates of liquid biopsies apparently assume that multi-cancer screening can only help. But screening can hurt people. Some will be overdiagnosed and treated for cancers that would never have otherwise bothered them. Some of these people will be harmed by treatment; a few may even die from it. Others will be found to have advanced cancer at a time when they have no symptoms, yet the earlier detection may have no effect on when they die. These people will be subjected to the toxicities of treatment at a time they would otherwise feel well.

Still others will be told by a liquid biopsy that they have a "cancer signal" — triggering fear and more testing — only to be told later it was a false alarm because subsequent imaging tests (like a combined PET/CT scan) found no abnormalities. But was it truly a false alarm or does it mean they have a cancer that can't be found with current technology? Imagine having a cancer signal detected, yet your doctors can't find the cancer.



GILLIAN FLACCUS/AP

Blood is drawn from a person participating in a clinical trial of liquid biopsy technology at the Oregon Health & Science University.

There is only one way to know whether a new cancer screening test helps more than it hurts: Perform a randomized trial in which participants are divided into two groups. One gets regularly screened; the other does not. The participants are then followed for a decade or so, counting the number of deaths in each group. It's the time-honored standard used in tests that screen for breast, colon, lung, and prostate cancer. Such studies have shown, for example, that early screening for lung cancer in heavy smokers does save lives.

The National Cancer Institute is actually planning a randomized trial of liquid biopsy screening now. Ironically, passage of the Medicare Multi-Cancer Early Detection Screening Coverage Act would impede the trial because of a dynamic we have seen before. In the 1990s, many doctors and patients believed that a transplant of a patient's own bone marrow was an effective treatment for metastatic breast cancer. Press reports focused on young women dying from aggressive cancer without access to the "lifesaving" procedure. Insurers were sued for not covering it. Fifty-four members of Congress wrote to the Office of Personnel Management demanding that it cover the procedure for federal employees. The presumption of benefit was so strong that investigators had great difficulty finding volunteers to enroll in studies to see if the procedure worked. Everyone already assumed it did.

But it didn't. Although enrollment was painfully slow, the randomized trials ultimately demonstrated bone marrow transplants didn't help women live longer. And they most certainly did not live better. Tens of thousands of women were subjected to an arduous procedure often complicated by anemia, infection, and diarrhea. And some died from it.

Liquid biopsy proponents want to bypass the time-honored standard of a randomized trial, which would make clear whether these tests are truly worth doing. They want to bypass review by the US Preventive Services Task Force — the panel authorized by Congress to review the evidence and make recommendations about clinical preventive services like screening. They want multi-cancer liquid biopsy screening to become part of routine medical practice before it is rigorously evaluated. They argue we can't afford to wait.

In fact, the opposite is true: We can't afford *not* to wait. Congress must let the National Cancer Institute and the task force do their work.

H. Gilbert Welch, senior investigator in the Center for Surgery and Public Health at Brigham and Women's Hospital, is the author of several books, including "Less Medicine, More Health: 7 Assumptions That Drive Too Much Medical Care."

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40 times that of the average person with ovaries. This cancer often starts in the fallopian tubes, so it makes sense to get rid of them. Think of it as the old movie trick of cutting the rope bridge before the enemy can come across.

That's the theory, anyhow. I'm a test case, part of a clinical trial designed to investigate whether this simple outpatient surgery actually does keep ovarian cancer at bay. Specifically, does it work as well as removing both ovaries, which is currently what doctors recommend for high-risk patients? My ovaries, like me, are only 37, spring chickens really, still working hard to regulate my mood, metabolism, and sleep cycle. I'd like to hang on to them for as long as possible. This trial may establish that choice as a safe one for patients under 45 — a revolution in preventive care.

Or the story could end another way. Researchers could find that tubal removal does not significantly reduce cancer risk. I could develop ovarian cancer and wonder if I should have removed my ovaries after all. That space, between theory and proof, between what researchers hope will be and what is already proven, is the windowsill where the piano teeters.

The long road to a clinical trial

We're all born with four BRCA genes, a little squad of goalies guarding the net so cancer doesn't kick one in. About 1 out of every 400 people carries a mutation on one of these genes, often unknowingly. "Not enough people get genetic testing," says Joan Walker, a gynecologic oncologist at the Stephenson Cancer Center at the University of Oklahoma. BRCA mutations also spike risks of breast and prostate cancers, but ovarian cancer can be the trickiest disease. Even the best screening methods available don't catch it until it has grown to an advanced stage. The five-year survival rate is less than 50 percent.

Anyone with ovaries who tests positive for a BRCA mutation is at risk. Most oncologists advise these patients to consider ovarian removal as early as age 35, before cancer typically strikes. Statistically, this surgery, called a risk-reducing salpingo-oophorectomy, or RRSO, which also removes the fallopian tubes, is the safest choice a high-risk woman can make. Physically and emotionally, the side effects can be brutal.

"We're asking 35-year-olds to become menopausal, and that's detrimental," Walker says. It's not just that putting the body through a major change about 15 years ahead of schedule can mess with the mind, although that's a big part of it. Menopause induced by RRSO is immediate, a shock to the system. Picture one sharp crank to the garden hose of estrogen and progesterone versus letting the stream gradually slow. These patients "get osteoporosis, they get depression, they get mood disorders, they get sexual dysfunction, they have painful intercourse," Walker says. "It's not a good quality of life."

Roughly a decade ago, Walker and colleagues began to map out the trial that I would eventually join. It's built on research that dates back almost 40 years, when a team at Roswell Park Comprehensive Cancer Center in Buffalo, N.Y., started to offer RRSOs to women with a family history of ovarian cancer. Taking their microscopes to the extracted body parts, pathologists found something unexpected: Some of these patients' fallopian tubes carried precancerous cells.

By 2011, RRSO had become a routine surgery for cancer prevention, and the data was stacking up. Much of the cancer that clinicians had historically diagnosed as ovarian, potentially 68 percent of it, "is actually cancer of fallopian tube origin," wrote National Cancer Institute geneticists Mark Greene and Phuong Mai and Yale University oncologist Peter Schwartz in an influential paper coauthored for the American Journal of Obstetrics & Gynecology. Walker calls this the seed and soil theory. "The tube deposits the tumor in the ovary, and then it grows," she says. "The ovary is a very, very luscious soil for those seeds to grow in." But what if the seed never reached the soil? "If you take the tubes out," Walker says, "maybe the cancer won't happen."

If Walker and her team could prove this hypothesis, it could change the calculus of preventive care. A salpingectomy, or tubal removal, is a fast, low-risk procedure. Unlike ovarian removal, it doesn't induce premature menopause. (One's ovaries remain attached to the uterus and to the pelvic wall via a suspensory ligament.) This procedure does eliminate the option of conceiving a child through sex. But for someone who doesn't want kids, is done having them, or plans to have them another way, there's little downside to the surgery.

Still, it took years to get a clinical trial approved. Walker's study design broke patients into two groups: those who would remove their ovaries and tubes and those who would remove their tubes only. Randomization — having a computer assign participants to one group or the other at random — didn't feel ethical. But letting patients self-select is potentially problematic. For example, those who have watched family members go through ovarian cancer might be more likely to choose ovarian removal, but having that family history might mean their mutations are different in some way from those of study participants with no known ovarian cancer in the family. If the ovarian-removal group is heavy with this kind of patient, it could skew results.

Wary of the pitfalls of self-selection, the National Cancer Institute initially declined to fund the trial. Walker, who had designed questionnaires that ask about motivation for joining one group over the other so her team can incorporate that data into their analysis, pushed back. "I just was so angry, I couldn't stand it," she says. "I had to knock on their heads until they hurt. They finally understood that there's no other way."

With NCI funding in place, the SOROCk trial finally launched in June 2020. Walker and her team, who are still enrolling patients, will collect data from more than 2,000 participants with BRCA1 mutations, all at least 35 years old, to compare the cancer rates of those who choose to remove their ovaries and those who choose tubal removal alone.

Is incidence comparably low? In 15 years, they might have an answer. It will be worth the wait.

"If we can even say it's safe to have a 35-year-old have their tubes out, and their ovaries out at 45, that would be a benefit," Walker says. "We're trying to just give women more choice in making their lives as healthy and happy as possible."

Living with uncertainty

After the surgery, my stomach looked like a sumo orange. They're my favorite citrus, in season from January to April, round with a puffy, wrinkly cap crowning the top of the fruit. I had been warned that the air pumped into me during the procedure would create something like an orange or a beach ball. The little hat, puffed out right around my belly button, was a weird surprise. I avoided looking in the mirror. When I had to look down during showers to make sure I wasn't scrubbing directly on my sutures, I saw that my belly button held a dime-sized disc of tangled, dried blood. My partner named it my blood button.

The bloating went down in a few days. The blood button took a few weeks to fall out, revealing a belly button that looks alien to me, more outie than innie, a coiled snake. I haven't accepted it as mine yet. My eyes pass over it, a skip in the record, a hurried step that doesn't let my brain process and question and accept. Maybe I need to force myself to look at and touch it, sit in its newness.

Maybe I'm obsessing over the belly button so I don't obsess over the harder things. I know I'm still pushing away feelings: that this is all an experiment, that I said no to what might turn out to have been the surest option in favor of a chance. I say those words without really hearing them. I read academic papers and news articles with foreboding statistics without fully absorbing them. "About 80 percent of ovarian cancers are diagnosed in advanced stages when treatment options are few," one reminds me. Tubal removal is "an experimental approach that may reduce the risk of ovarian cancer and is supported by current science, but is completely unproven," another reads.

But one more maybe: Maybe not obsessing over the scary stuff is what keeps us sane through illness, or risk of illness. The beauty of the piano drop in cartoons is that no matter how hard the blow, the character always survives. They come out of it with scrambled eyes, a mouth full of ivory keys, but they walk away. In real life, outcomes are less certain. I could let the uncertainty crash, or I can keep a distance and remind myself what I am certain about. I'm not ready for menopause. Tubal removal was a good interim step, better than doing nothing. I'm helping collect data that could improve next-generation patient care. And I can always change my mind. As part of the trial, I will receive counseling every year that tells me the surgery I have chosen is not the "standard of care," and that I should still consider getting my ovaries out by 40.

As 38 approaches, I'm not sure what the future will bring. Let's hope it's not anything falling from the sky.

Marissa Conrad is a journalist based in New York.