

SEEING DOUBLE:

DISEASE IN MULTIPLE TWINS

When one sibling of quadruplet brothers is diagnosed with cancer, what's the risk for the others?

BY Jamie Valentino



AS CHILDREN, MY QUADRUPLET BROTHERS AND I HAD A KNACK FOR GETTING COLLECTIVELY SICK WHENEVER ONE PERSON WOULD FALL ILL. GERMS TRAVELLED AT THE SPEED OF LIGHT BECAUSE, WHENEVER THE WORDS LEFT SOMEONE'S MOUTH, THE REST WOULD IMMEDIATELY IDENTIFY WITH THE SAME SYMPTOMS. WHO KNEW EXHAUSTION OR HEADACHES WERE SO CONTAGIOUS?

Of course, the possibility of getting to skip school might have had something to do with it. But, since the inception of my memory, I've felt bonded to my brothers—our existences aligned, and I felt deserving of every item or experience they had. Growing up, we were like four cells crowding around the same nucleus, known as Mum.

But happenstance and adulthood cemented our individuality. I always had a tingling about our innate differences, but I fully stepped into them when I came out as gay. Years later, when one of my brothers was diagnosed with testicular cancer, he was also forced to grapple with the different trajectories of our genetics—respective humanities.

"Does that mean I should get tested?" was regrettably my knee-jerk reaction. But I suppose it was easier than facing my real fear of what that meant for him. Thankfully, my brother caught it early and had surgery to replace the problematic testicle with a prosthetic. He was recently deemed cancer-free for the second year in a row.

However, I still wondered if being a multiple increases your risk of cancer if one of the others gets diagnosed. After all, if a family history of cancer is said to increase your risk, wouldn't your twin's health be the closest reflection of your heritability?

DR LORELEO MUCCI, Professor of Epidemiology at Harvard TH Chan



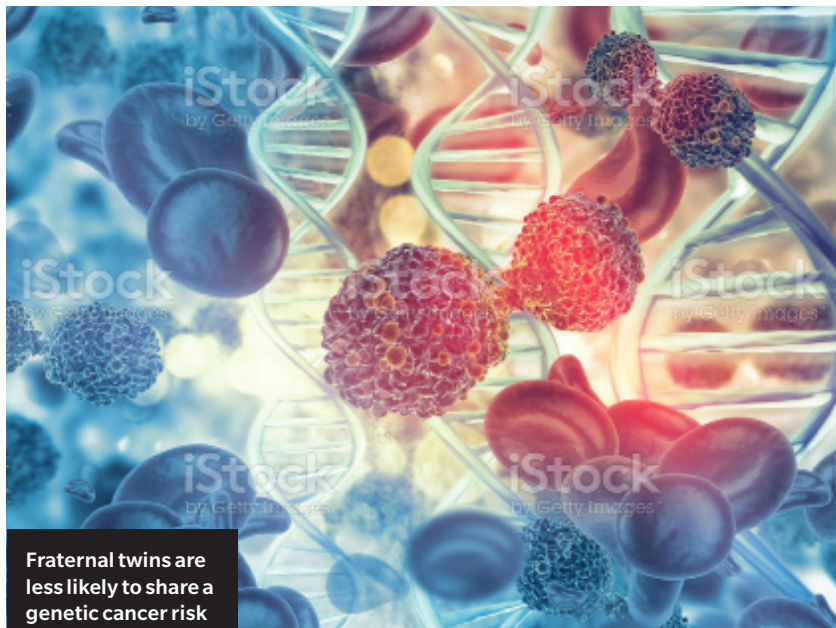
Jamie (first from right) with his quadruplet brothers, and younger brother (second from right)

School of Public Health, says my brothers and I share no more genetic similarities than regular siblings. Fraternal twins, triplets and quads share an average of 50 per cent of their inherited genomes, unlike their identical counterparts, which share 100 per cent. "The familial risk is higher in identical twins than fraternal twins, meaning that if their twin developed cancer, their own risk of cancer would be higher if they were identical," says Dr Mucci.

She was the first author of the Nordic Twin Study of Cancer publication in the *Journal of the American Medical Association* and

THE FAMILIAL RISK OF CANCER IS HIGHER IN IDENTICAL TWINS THAN IT IS IN FRATERNAL TWINS

one of the original members of the cohorts executive committee. The study collected data on cancer occurrence among 80,309 identical and 123,382 fraternal twins over 30 years within the population-based registers of Denmark, Finland, Norway and Sweden.



Fraternal twins are less likely to share a genetic cancer risk

"The study of cancer occurrence in twins is critical in estimating the relative contribution of genetic and environmental factors to cancer development," says Dr Mucci. "It also provides important information about the familial risk of cancer, which may help in targeted prevention, screening and early detection."

The risk varied by cancer type, but for most, there were significant familial risks, and the study found the estimated cumulative risks were five per cent higher in dizygotic (not identical) and 14 per cent higher in monozygotic (identical). Although it measured all cancer types, specific

cancers such as testicular and skin cancers showed substantial excess risk, particularly among identical twins.

Regarding how far apart cancer occurrence happened when both twins got it, Dr Mucci says that for most types of cancers, the age difference was about eight to nine years. For prostate cancer, however, the age difference was much smaller, falling at about four years for identical and six years for fraternal twins.

DR MICHAEL MURRAY, a geneticist at the Yale Cancer Centre, says that with a triplet birth and higher multiple

births, you can have all identical, all fraternal, or both identical and fraternal, so the risk varies.

He says there are two different categories of genetic cancer risk. "There's what we call monogenic (or single gene) genetic risk, which means that one out of your 20,000 genes can be broken in a way that predisposes you to genetic risk for cancer. The example that many people are familiar with are the BRCA genes (BRCA1 and BRCA2). If one of these are broken, it predisposes someone with that to cancer, but it doesn't cause cancer."

The BRCA-related gene risks include breast, ovarian, prostate and pancreatic cancer. Dr Murray explains that if two siblings are fraternal twins or born at different times, and one of their parents carries a broken gene, then there's a 50 per cent chance that each one would inherit that broken gene from the parent. So they may both get the broken gene, or both miss the broken gene, or one gets it, and one doesn't. In contrast, identical twins either both get it or both miss it.

"When you have these elevated single gene risks which only occur in one to two per cent of the population," Dr Murray says, "then the cancer occurs in 75 to 85 per cent of individuals over a lifetime. Still, never a 100 per cent disease occurrence."

The other genetic cancer risk Dr Murray references is called a polygenic risk score or PRS, which

every person has that arises from a combination of changes in different genes. This new kind of analysis looks at the hundreds, or thousands of gene changes that each increase the risk for a certain cancer a little bit and combines them into scores that may be high, average or low.

"It's worth stepping back for a second and thinking about the risk for cancer in general," says Dr Murray. "It is a combination of environmental and

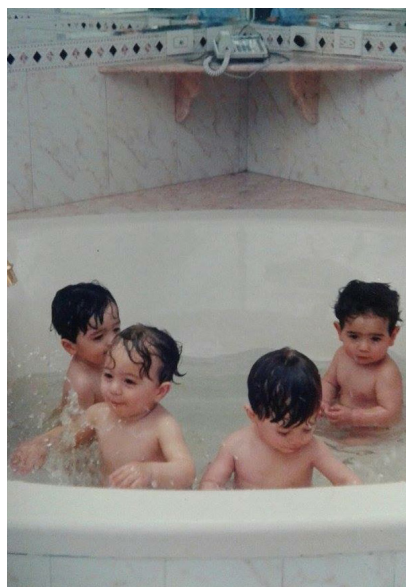
BRCA-RELATED GENE RISKS INCLUDE BREAST, OVARIAN, PROSTATE AND PANCREATIC CANCER

genetic factors. And so twins and larger birth groups share a lot of the same genetics and a lot of the same early environment, at least until they grow up and move away from each other."

For example, my history of smoking cigarettes (until recently quitting) might put me at a higher risk for lung cancer than the rest of my brothers, who were wise enough never to start. But Dr Murray emphasises you can have a risk for cancer and never get it. There are events at the molecular level as a cancer develops, and a person may have a predisposition, but the follow-on events never happen, so



Jamie's brother found a strong support network in his family



they don't get cancer. In other words, twins may have increased risk when one gets diagnosed, but it doesn't mean there is a reason for the other to panic. What's important during this challenging moment is to be there for the sibling diagnosed and be emotionally available for them to express themselves. A family member's diagnosis will undoubtedly scare you, but your sibling should feel supported without the burden of carrying anyone else's emotional baggage.

Don't assume you know what they are feeling or project your own fears. You don't need to have the "right" answer—or any for that matter—but just let them know you're there.

YOUR SIBLING SHOULD FEEL SUPPORTED WITHOUT CARRYING ANYONE ELSE'S BAGGAGE

My brother was fortunate that his situation was relatively easy, as far as cancer goes. His real worry manifested the night before the surgery regarding whether future romantic partners would be able to tell he has a prosthetic. As his only gay brother with field experience (testicular cancer is more common than you think), I was happy to let

him know it's hardly noticeable. His testicles would still be as gorgeous as testicles could possibly be!

THE REALITY OF THE MATTER is that cancer will probably affect most of us if we're lucky enough to live a long and fruitful life.

"Across the entire population, age is the number one risk factor for cancer, period," says Dr Murray. "If we all live long enough, we'll probably all have to face cancer of some sort. And that's because the body's machinery for fixing mistakes in the DNA as we get older seems to break down over time."

Luckily, with regards to the common cancers, he says there are

strategies for prevention and screening, which can be enhanced for those with elevated risk.

If you're worried about your risk, both experts suggest that your doctor will always be the best professional to consult. Asking your parents or grandparents about your family's history regarding cancer will also be useful information for your doctor. After you have the facts, you can always count on friends, family or local resource groups for support.

I'm lucky to have three other individuals to share experiences with and learn from their own journeys—the good, the bad and everything in-between in the spectrum of life. ■

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