

WHO BECOMES A SUPER-AGER?

Genetics play a part, but there's a lot more to it than that.

BY LESLIE GOLDMAN

MY GRANDFATHER was 90 when he retired from his forensic accounting career. Morty, who died in his 90s, attributed his enduring health to a glass-half-full attitude, a lifetime passion for exercise (he swam laps until a ripe old age), the love of his wife of 71 years, a daily handful of blueberries, and a nightly shot of Jack Daniels. Grandma Jeannie, 98, now lives in a long-term care facility with physical challenges but still lectures on religion—she taught Sunday school until age 85—and has a quick wit that belies her years. (My brother recently surprised her after an admittedly too-long stretch. Nearly blind, she asked, “Who’s there?” “Your grandson,” he said. Her reply, with feigned surprise and perfect comedic timing: “I have a grandson?”)

My grandparents are what many researchers of aging, known as geroscientists, call super-agers. The exact definition varies by institution—at Northwestern University Feinberg School of Medicine’s SuperAging Research Program, they’re 80-plus-year-olds with exceptional memory on par with people two to three

decades their junior; in the SuperAgers Family Study, cohelmed by the American Federation for Aging Research, the Albert Einstein College of Medicine, and Boston University School of Medicine, they’re 95 or older and have either evaded most age-related diseases or at least maintained general good health and can live independently. One thing everyone agrees on: These folks do aging extraordinarily well.

“These are the Betty Whites of the world,” says Emily Rogalski, PhD, a neurology professor and director of the Healthy Aging and Alzheimer’s Research Care Center at the University of Chicago. “They’re your friend or neighbor or grandparent whom you describe by saying, ‘You’d never believe they’re 85.’ They’re the people defying the current expectations out there for aging.”

Genetic resilience plays a key role

The combination of a maturing population and a growing interest in prioritizing healthspan (the number of years spent in good health) over lifespan (number of years alive) has fueled an upswing in centenarians—



approximately 108,000 Americans, primarily women, are 100 or older, a number that’s expected to quadruple over the next three decades. Some (but not all) of these longevity champs are considered super-agers thanks to their tendency to escape some or all of the big four age-related illnesses: Alzheimer’s disease, diabetes, cardiovascular disease, and cancer. Cognitive super-agers, in particular, “have managed to avoid dementia, even though they have the number-one risk factor for dementia—age—and they have preserved much better memory function than expected,” says behavioral neuroscientist Stacy Andersen, PhD, codirector of the New England Centenarian Study (NECS).

Thriving through old age depends on a mix of healthy habits and genetic luck, though the ratio shifts as you move from 90 to 100 and beyond.

About 75 percent of living to age 90 in good health is behavior—and it’s not just about eating salads and doing yoga. Andersen says cognitive super-agers tend to be outgoing, with a large social network. They enjoy learning new things, she adds, which “keeps the brain engaged and builds new connections between brain cells while keeping existing connections healthy. They have a purpose and feel engaged in life.” These characteristics “are just as important as diet and exercise.” (That said, nutrition and exercise are VIP players when it comes to extending one’s healthspan.)



THE WRITER'S GRANDPARENTS,
JEANNIE AND MORTY SCHUR.

The other 25 percent of reaching age 90 in good health? Genetics. If your parents lived to a ripe old age, you've got some longevity baked into your DNA.

But the story changes as you add more candles to your birthday cake. "When you look at extreme ages, like 95 and 100, that's where genetics tend to play a much bigger role," says Sofiya Milman, MD, a professor of medicine and genetics at Albert Einstein College of Medicine and director of human longevity studies at Einstein's Institute for Aging Research.

Attaining centenarian status is about 50 percent genetics, and supercentenarians (age 110 and older; odds are 1 in 5 million) can attribute almost all of their longevity to receiving the right DNA lottery ticket. Many of these people "haven't necessarily been the poster children" for healthy living, Milman says, a nod to the stories that abound of pack-a-day smokers who insist that burgers, martinis, and avoidance of exercise helped them reach the century mark. For these longevity unicorns, their genetics are essentially so protective that "they seem to defy the odds."

In the past, researchers believed super-agers thrived because they lacked critical disease-causing genes.

Indeed, data from the NECS indicates that about 15 percent of centenarians are "escapers," meaning they've managed to avoid diseases like the big four.

As it turns out, most exceptionally long-lived people have just as many potentially harmful genetic variants as the general population. "But they also have a lot of protection built into their genes that counteracts the disease variants," Andersen says. Some of these genes work their magic by repairing DNA damage that would lead to cancer in most people or by maintaining above-average levels of high-density lipoprotein (aka "good" cholesterol), shielding super-agers from heart attacks and dementia.

This genetic leg up is on full display during post-mortem autopsies of cognitively healthy centenarians, as their brain often harbors just as much amyloid plaque—a sticky, toxic compound long considered a hallmark of Alzheimer's disease—as the brains of patients who suffered from the dreaded form of dementia. But other factors at play in their brain are making them resilient.

Besides boasting brains that age at half the pace of regular agers, super-agers are also the proud owners of robust immune systems. This may help explain why many centenarians sailed through their infections early in the COVID-19 pandemic. (My grandma was asymptomatic when she tested positive at 95.)

Remaining more or less disability-free for 100 years, then, boils down, at least in part, to DNA-rooted resilience—super-agers' bodies often contain evidence of an age-related condition, but their genetic hardwiring neutralizes it so effectively that they never fall ill. Either that or they do experience a typically devastating illness, such as cancer or a stroke, but their body copes with it so well that they not only survive but go on to live independently and in good health for years or even decades. (About 40 percent of those enrolled in the NECS are "survivors," meaning they developed one or more age-associated diseases before turning 80, and another 40 percent are "delayers," for whom this happened after age 80. So yes, a cancer survivor can absolutely one day join the super-ager club.)

As for supercentenarians, disability tends to be postponed until around age 106 and only lasts a few years. As Andersen's colleague, NECS codirector Thomas Perls, MD, MPH, often says, "The older you get, the healthier you've been."

A common trait of super-agers: resilience. Many have endured significant trauma, "but they've bounced back from what life has thrown at them," says Rogalski. "They see what they can learn from it and thrive."

Healthy habits matter a lot, too

Golden genomes aside, champion agers tend to share other common features, most of which, unlike choosing our parents, are under our control. Social support is paramount, with reams of data underlining the protective health benefits of having partners, friends, family, and even colleagues to whom you feel connected. These relationships help us buffer stress and reduce the system-wide inflammation responsible for a litany of chronic illnesses, including diabetes, arthritis, depression, and heart disease.

Another common super-ager trait: emotional resilience. "We don't find that these are individuals who have had life handed to them on a silver platter," Rogalski says. Many successful agers have endured significant trauma, including losing a child (as my grandparents did) or being forced from their homeland, "but they've bounced back from what life has thrown at them. They see what they can learn from it and thrive."

Super-agers also tend to be curious (when Rogalski worked at Northwestern's SuperAging Research Program, where she helped coin the term "SuperAger," she interviewed an 89-year-old who, realizing his grandkids weren't familiar with Frank Sinatra, would ask them about Taylor Swift and Chance the Rapper) and embrace lifelong learning, which can take the form of attending seminars or book clubs, picking up a new hobby, reading books outside your comfort zone, and updating your Spotify playlists to include trending bands. Stimulating your mind with new, challenging information strikes a match that fuels new neuron-to-neuron connections in the brain.

The bright future of aging

Milman's research has found that those who live to age 95 or older are seven times more likely to have had a parent who lived to 90 or beyond, and that children of

super-agers enjoy significant protection from heart disease, regardless of their personal risk factors. Andersen adds that children of centenarians experience aging-related diseases at half the rate of those whose parents had average lifespans.

Some of those genetically blessed offspring may very well ride their long-lived loved one's coattails into a centenarian sunset. But what about the 99.9 percent of us who didn't luck into longevity genes? The ultimate goal, Milman says, is to study super-agers and leverage those discoveries to develop "treatments and drugs that mimic the beneficial effects" of their genes, delaying the onset of age-related diseases in the general population "so people don't only live longer, but live healthier."

Milman is utilizing a National Institute on Aging grant to do just that, working with colleagues to determine whether levels of certain growth hormones may help prevent dementia and other age-related diseases. Other geroscientists are studying Ashkenazi Jews, who tend to live exceptionally long, healthy lives (again, my grandparents), for fountain of youth clues; investigating the potential use of the diabetes drug metformin in delaying aging by collectively targeting the big four; and creating stem cells using blood samples from centenarians to see how their neurons react in a lab setting when exposed to Alzheimer's disease proteins. All told, Milman says, "I wouldn't be surprised if we see, in the next decade, a treatment that can delay aging."

Until then, Rogalski hopes people lean into the lessons of super-aging to create a new outlook on growing older. "If your expectations involve being frail, then the first time you forget your keys, you'll think, 'Ugh, I guess forgetting is just part of my life now.'" Help avoid a self-fulfilling prophecy by instead thinking about all the steps you can take to live long and strong, such as getting better sleep, meeting a friend for dinner, or even enjoying an occasional martini. In other words, ask yourself: "What would a super-ager do?" ■