

From the HEART

A newsletter from Saint Luke's Cardiovascular Consultants

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A Safe Drug That May Slow Aging and Improve Life Expectancy

James H. O'Keefe, MD

Remember when you were a kid and you could eat all of the ice cream, candy, or junk food you wanted and never gain an ounce? Or when you could swim, run, climb, and play all day without feeling like you'd done more than go for a walk? Then, as childhood waned and adulthood crept in, so did the pounds, grays, creaky joints, and numerous health issues.

We all wish for a Fountain of Youth, a mythical spring that can reverse aging and bequeath longevity to people who drink its waters. Legends of such a fountain have been recounted by cultures around the world for at least 2,500 years. Folklore says Spanish explorer Juan Ponce de León, following a tip from a Native American in 1513, thought he might find the Fountain of Youth on Bimini, an island in the Caribbean. He never discovered the magical water with the ability to restore youth, and through the ages, every version of the Fountain of Youth has turned out to be a hoax.

That is . . . until now? In a new scientific paper, we proposed that a drug class called **sodium-glucose**



cotransporter inhibitor (SGLTi) may be the first-ever real-life therapy that *slows the aging process*, thereby improving lifespan.

SGLTis block the sodium-glucose cotransporter, tricking the body into thinking it's starving and/or doing a lot of exercise, somewhat like fasting, but more effective. This triggers autophagy—cellular housekeeping that rejuvenates the cells and makes the whole body and brain younger and more resilient. As discussed further herein, SGLTi seem to slow aging on a cellular level.

Modifying the Aging Process

Aging is associated with erosion of structural integrity of our tissues

and loss of function starting at the cellular level. Eventually, this culminates in musculoskeletal frailty and an increased risk of developing chronic cardiovascular (CV) disease, diabetes, obesity, dementia, infections, and cancer.

The pace of aging varies widely across species due to a combination of genetic, environmental, and evolutionary factors. For example, the domesticated dog (*Canis lupus familiaris*), when just 7 to 10 years old, begins to develop age-related diseases such as cataracts, arthritis, impaired hearing, congestive heart failure, and kidney disease, while a 10-year-old human is still a youthful, exuberant kid with no hint of chronic disease. Meanwhile, the oldest known living land animal is a Seychelles giant tortoise named Jonathan who remains healthy, despite having hatched in 1832. This variability in the pace of senescence, or biological aging, among animals suggests that the aging process may be modifiable. In fact, as we have begun to understand the biological mechanisms of aging, it appears that the rate at which we grow older is malleable. Scientists working with animal models have found the best way to make mice, worms, and yeast cells live longer is to cut their calorie intake by about one-third and keep them in a semi-starvation state. While that might work for mice, humans tend to get cranky when you do that.

The Holy Grail of Lifespan: Delaying Aging

Slowing or reversing the process of aging is a long-sought-after Holy Grail for reducing chronic disease and improving human longevity. According to experts in the field, therapies that delay aging would translate into greater gains in life expectancy and quality of life than would advances in treating or

preventing specific diseases such as cancer or heart disease. The innate aging process is by far the most important risk factor for most serious chronic diseases and death. As you age at the cellular level and become frail, immobile, and disabled, if one disease doesn't get you, another one will.

Accordingly, an October 2023 study in the journal *Health Affairs* by Jay Olshansky, MD, found that shifting the focus of medical research to delaying aging instead of targeting specific diseases could lead to substantial gains in physical health and overall well-being for the current population and future generations. These experts reported that major advances in treatment of cancer or heart disease would improve overall life expectancy by about just one year. By comparison, a therapy that delays aging even modestly would double this to two additional years—and those years would likely be enjoyed in good health.

Healthspan versus Lifespan

Thanks to breakthroughs in preventing and treating potentially fatal conditions like infections, atherosclerosis, and malignancies, the average U.S. life expectancy rose by more than thirty years during the last century. However, in 2019, U.S. life expectancy began to fall and is now down to a 30-year low of 76 years. What's more concerning, though, is the prevalence of people living a disabled life—being alive but not fully functional. This change means the average American can expect to be alive and in good health for fewer years than the previous generation.

If we can uncover ways to age more slowly, we could delay death as well as increase the years of *living* life. We could simultaneously improve lifespan as well as healthspan—the length of time a person is healthy with full mental and physical capabilities.

Lifestyle habits such as maintaining social connections, getting regular exercise—both aerobic and strength training, decreasing time spent sitting, getting seven to eight hours of high-quality sleep most nights, eating a nutritious diet, and fasting for at least 12 hours each night all contribute to an improved healthspan.

SGLTi: A Magic Bullet Against Aging?

While SGLTi drugs, such as Jardiance® (empagliflozin), Farxiga® (dapagliflozin), and Inpefa® (sotagliflozin), have been used for the treatment of type 2 diabetes for more than a decade, a massive and rapidly growing body of data shows that these remarkable drugs also appear to reduce risks for many of the most common conditions of aging, including hospitalization for any cause, heart failure, chronic kidney disease, atrial fibrillation, cancer, heart attack and stroke, Alzheimer's disease, Parkinson's disease, fatty liver, gout, emphysema, and infections. SGLTi also significantly improves overall life expectancy and reduces risks of CV death and cancer death. In short, SGLTis may be the first “anti-aging” class of drugs with compelling data to show they improve longevity.

Our scientific paper in the December 2023 issue of *Progress in Cardiovascular Disease* is the first ever to propose SGLTi as a therapy to slow aging, prevent or delay many of the common age-related diseases, and improve lifespan as well as healthspan. Currently, these drugs are FDA-approved for the treatment of type 2 diabetes, heart failure, and chronic kidney disease, and to decrease risk of CV death.

How Does SGLTi Slow Aging?

How SGLTi bestows these unprecedented benefits has remained largely a mystery until recently. We know

that SGLTi treats type 2 diabetes by blocking reuptake of filtered glucose in the kidney. This relatively simple action leads to extraordinary downstream actions in preventing and treating many of the most common and serious age-related diseases in individuals with or without diabetes. Normally, we

shouldn't have any sugar in our urine—but even healthy people on SGLTi will lose about 60 to 80 grams (about 300 calories) of glucose per day in the urine, triggering a mild diuresis that eliminates excess water. Consequently, these people show subtle improve-

ments in weight, blood pressure, and blood glucose. Yet, the mechanisms behind the astonishing health benefits of SGLTi are largely inexplicable considering their modest improvements in standard CV risk factors. It's as if one plus one equals 10.

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Mick's Gift

In our Saint Luke's Charles & Barbara Duboc Cardio Health & Wellness Center and Saint Luke's Michael & Marlys Haverty Cardiometabolic Center of Excellence, we have been prescribing SGLTi drugs frequently and for several years. In September 2015, the EMPA REG study results were officially released in Stockholm showing empagliflozin, one of the SGLTi drugs, produced an astounding 38% decrease in risk of CV death compared to placebo. Significant benefits were already apparent after just two weeks of starting treatment.

Based on these results, I began using this drug immediately. Mick Haverty was one of the first of my patients for whom I prescribed empagliflozin. He has never had diabetes but had severe coronary disease at a distressingly young age.

Mick was born and raised in Atchison, Kansas, where four generations of his family worked on the railroad, a common undertaking for Irish immigrants. As a teenager, Mick signed on with Missouri Pacific to work summers as a train service brakeman/switchman, often working 16 hours a day. One summer, he worked as a laborer on a track gang, repairing track in heat often in the 90s. He went off to college and upon graduation in 1967, went into a MoPac management training program, then became a first-line manager. He switched to the Atchison, Topeka, and Santa Fe

Railway in 1970, where he moved up through the management ranks, thanks to his determination and no-nonsense approach to the railroad business.

However, when Mick needed emergency coronary artery bypass graft (CABG) surgery at age 33, and a second CABG at age 37, his promising career seemed like it might be derailed. On both occasions, his competitors wrote him off as finished. Despite the adversity, Mick roared back and was named president of Santa Fe Railway at just 44 years old. Since then, Mick has had 15 coronary stents and minor heart attacks, but throughout it all, he has maintained a productive and rewarding life.

In 2018, though, he began experiencing worrisome swelling, shortness of breath, and reduced stamina. We diagnosed him with heart failure, which in the past would often be lethal within 5 years of diagnosis. His heart's pumping efficiency, or ejection fraction (EF), had deteriorated to 32% (>50% is normal).

I started Mick on empagliflozin and other effective heart failure therapies, which resulted in a remarkably quick and robust recovery. His EF came back up to normal, and he regained his energy and physical strength. Over the last nine years, Mick has needed no further stents. He is retired now and will celebrate his 80th birthday this



June. He still travels internationally (Ireland is his favorite destination) and thoroughly enjoys an active life with his wife Marlys, their three children, and 11 grandchildren.

In gratitude for his recovery, Mick and Marlys donated \$2 million five years ago to start the Haverty Cardiometabolic Center of Excellence, the first such center in the world devoted to using these drugs to improve health and longevity for CV patients. In the Haverty Cardiometabolic Center, we standardly use SGLTi often in combination with other new therapies including semaglutide (Wegovy®, Ozempic®) or tirzepatide (Mounjaro®, Zepbound™) to help patients to lose weight and regain their health and well-being. We have published papers in scientific journals detailing how these medications confer unique health benefits. Mick's gift and these life-saving medications are making a real difference for getting our patients on track for longevity with vigor.



Taylor Swift and the Chiefs: Why You Need to Belong to a Tribe

James H. O'Keefe, MD

The world in which I grew up was a kind of mono-culture. Grafton, North Dakota, is a town of 4,000 people nestled against the borders of Canada and Minnesota. Everyone drove a Ford or Chevy, went to one of two churches, and watched Walter Cronkite on the evening news. *Ubuntu* is an ancient African concept that is often translated as, "I am what I am because of who we all are." But today, our society is splintered into a million factions, and there is less shared culture, leaving many people feeling empty and lonely. I believe the evolving crisis with drug overdoses, depression, record-high suicides and falling life expectancy in America is in part due to an unmooring of our traditional social connections to each other.

When Taylor Swift's Eras Concert came to Kansas City, my daughter, Kathleen, and I were among the 70,000 Swifties packing Arrowhead Stadium that Friday night in July. Joan and the rest of our gang—Jimmy, Darren, Evan, Mary Kate, and Caroline—were on hand for the show the next night. We had the time of our lives with Taylor Swift that weekend. Like everybody in the stadium, we received a light-up bracelet when we arrived at the venue. Taylor says that she likes to give out the bracelets before shows so that she can see every person through their flashing lights. After the sun went down and the sky grew dark, the music started. The bracelets flashed, sometimes a rainbow of colors rolling in waves around the stadium. Other times, they would light up simultaneously, uniting all of us as we sang along and danced to each of the 44 songs during the three-and-a-half-hour show. The whole spectacle had a mesmerizing effect, making it seem like we were all connected, united in our love for Taylor Swift and her music.

The crowd at Arrowhead was mostly young females wearing sparkly dresses and boots, often with their moms. But there were occasional dads too, like a guy sitting next to me, who was also

with his daughter. He and I were high-fiving and laughing together during the concert. As a 60-something male, I'm not a typical Swiftie, but not unusual either. For example, George Stephanopoulos, anchor for *Good Morning America*, is also on the Swift bandwagon. Although the crowd was massive, the concert somehow felt communal and intimate, like we were all immersed in a joyful experience that made us all feel emotionally connected at a deeper level.

When one of our favorite songs would start, Kathleen and I would glance at each other and cheer loudly. At the very beginning of the concert, Taylor explained, "My songs are about things that happened in my life, but I hope this night will be about making memories for you and the friends and family who are here with you." That's exactly how we felt. We made lifelong transformative memories dancing and singing along with Taylor Swift that night. Meanwhile, the Eras tour has become an economic and cultural phenomenon.

You Belong with Me

Swifties have a global connectedness. They are seemingly immune from the divides of race, class, age, and gender—a nice change from the

divisiveness that permeates nearly all other areas of our society. This TSwift social connectivity is more beneficial than we may realize. The defining features of *Homo sapiens* are intelligence and our intensely social nature. We humans have a deep need for a sense of belonging. This social connectedness is essential if we are to thrive.

Taylor reminded her fans before the start of the show, "You're not making memories when you're on your phone the whole time," taking pictures, texting, posting to Tik Tok, etc. Hers is a tangible connection—from friendship bracelets to cryptic messages and clues that Taylor hides in her music and videos, she makes her fans feel like they belong to a special group.

Today, Taylor Swift is a powerful force for intergenerational bonding. Many females grew up with Taylor; her music has been the soundtrack to their life through their teens, 20s, and now 30s. As in my family, generations often share an appreciation of Swift and her music. When I was a kid, my parents and I had very different tastes in music, and it contributed to an infamous generational gap between Baby Boomers and their parents and grandparents. The Eras Concert was a unique event for Kathleen and me that will always be a shared memory we cherish.

Psychology Class: Taylor 101

It's been a rough past few years, and many people have become isolated and despondent. We desperately need to connect with each other—our lives depend upon it. Psychologists and professors have been writing articles and teaching college courses on how Swift's music and lyrics serve as a source of comfort for many and can augment emotional well-being.

In her article for *Psychology Today* titled "Taylor Swift May Be Good for Mental Health," Alli Spotts-De Lazzer wrote,

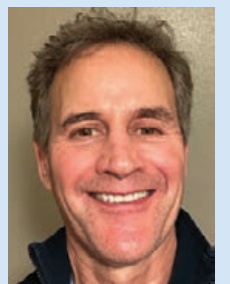
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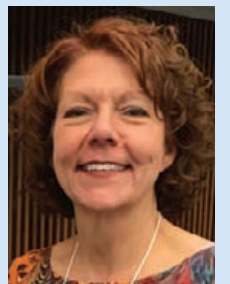
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Taylor Swift and the Chiefs *continued from page 5*

“Swift’s songs are often brilliant storytelling; her music and lyrics offer comfort and coping for many.” Brian Donovan is a professor who teaches a course called *The Sociology of Taylor Swift* at the University of Kansas. Unsurprisingly, it’s hard for KU students to get into this extremely popular class. Donovan says Taylor is a unique musical genius, and the community of Swifties is large, international, and diverse. “It’s immense, on a scale that I think is much larger than, say, Beatlemania,” says Donovan. “What attracts people to Taylor is that she is able to write in a way that seems like it’s speaking to their own personal autobiography.”

Chiefs Kingdom

Until recently, a Venn diagram of Swifties and NFL fans would show very little overlap, although I would be one person squarely in that shared middle ground. Now that Taylor and Travis

are dating, Professor Donovan says, “Swift and Kelce are combining forces of two of the most energetic fan bases in the United States.” This synergy makes for a worldwide phenomenon, and astoundingly, the center of all that attention is right here in Kansas City. Allegedly, Travis and Taylor recently bought a home together in town. Some experts predict that Kansas City could possibly morph into a boomtown like Austin, Texas, in coming years.

On the topic of belonging, the Kansas City Chiefs fanbase is another group of diverse people who share a fierce loyalty to their beloved team. Being a member of the Chiefs Kingdom is a major source of camaraderie and joy for millions. Coach Andy Reid and quarterback Patrick Mahomes, like Taylor Swift, are superstars with down-to-earth personalities who are authentic, likable people and great role models. Being emotionally

committed to the Chiefs fosters a sense of belonging to a large community of like-minded individuals. Fans bond over shared experiences and moments like Superbowl parades, leading to a sense of increased social connection.

Many fans also have rituals and routines linked to watching the Chiefs play, which can add structure and meaning to their week. Following a team, understanding strategies, and diving into statistics can be cognitively stimulating. Yet, watching sports can be an emotional roller coaster of highs and lows, especially for those who are deeply emotionally invested. Indeed, some of my patients worry their hearts can’t take the stress, especially during big games. My standard advice is to move your body before, during, and after the game. Adrenaline primes your system to fight or flee—exercise is the natural and healthy way to burn off those stress hormones. I often go to the gym to work out during Chiefs games, or play pool with my son Evan and grandson Grant while the Chiefs are on.

Being a Swiftie at her concert or while watching the Eras Tour movie or being a Chiefs fan during an epic Superbowl season can be a hypnotic communal experience. These days more than ever, we need to rally around people and wholesome causes that unite us and make us feel connected. It’s crucial for your well-being that you find your people and develop real-world relationships that make you feel like you belong. We humans tend to feel most alive when we are tightly woven into a fabric of connections with other life around us. At the deepest level you need your tribe. This is who you are, and bonding with a group over a shared passion can bring joy, even ecstasy, to your existence.

How to Connect with a Tribe

- Join a book club.
- Find a church that resonates with your spirituality and attend services regularly.
- Feed the birds in your yard.
- Get a dog and/or a cat. Take your pooch to your local dog park regularly.
- Start playing pickleball. You will meet a whole group of friendly people immediately.
- Join a gardening club.
- Volunteer at a hospital, school, or daycare.
- Do group exercises at a gym or a community center.
- Take an adult education class on a topic that fascinates you.
- Socialize with your neighbors.



Tree Nuts: A Cheat Code for Longevity

W. Grant Franco, MD, Preventive Cardiology Fellow
UMKC/Saint Luke’s Health System, Kansas City



As a kid, I loved playing video games. Those that required perseverance, skill, and strategy were my favorite. I love

the feeling of accomplishment that comes with overcoming a challenging quest. Other times, I like games to just be easy. As a kid, I would search the internet and find the literal cheat codes that might make my character invincible or unlock all items. In games that didn’t have cheat codes, I would try to find the best items in the game that could trivialize any challenges I would face in the future.

For the last five years or so, when I have returned to my childhood home, I have seen an old familiar crystal jar sitting on my parent’s kitchen counter. In my childhood, it would be filled with jellybeans or candy corn. Now, however, it’s always filled with almonds, and I see my dad grabbing a handful of nuts multiple times a day. I recently asked him why he’s been eating so many. “I believe they are good for my health,” he replied. “My cholesterol came down about 40 points, and the only thing I did differently was regularly eating nuts. I’m not sure if that was why, but it seemed connected.” I thought, sounds kinda like a cheat code!

The more I have learned, the more obvious it is that consuming tree nuts regularly constitutes one of the health cheat codes. Common tree nuts include almonds, Brazil nuts, cashews, hazelnuts, macadamias, pecans, pine nuts, pistachios, and walnuts. Peanuts are technically a legume, but they can be considered in the same class as tree nuts due to their nutritional similarities.

Nuts have been a central part of the human diet throughout the world. They were a mainstay of our diet until about the last century, when nut consumption was markedly reduced. Especially in the winter months, our ancestors subsisted on a diet chock-full of nuts. An Oxford University study reported that our ancient ancestors who lived in East Africa about two million years ago survived mainly on a diet of nuts.

The nutrient profile of tree nuts provides several benefits. Nuts are rich in healthy fats, such as monounsaturated fats and polyunsaturated fats. Walnuts are particularly high in a plant-derived essential omega-3 fatty acid alpha-linolenic acid. These healthy unsaturated fats are beneficial for both lowering cholesterol and reducing appetite. Their fat, protein, and fiber content leave us feeling full longer.

Tree nuts are an important source of vegetable protein, containing a large amount of L-arginine, a key building block of nitric oxide, a key molecule in our body for blood pressure regulation. They also contain a large amount of dietary fiber which is helpful with gut health, and contain molecules called phytosterols that help prevent the absorption of cholesterol in the gut. Nuts also support better fertility in both sexes.

Tree nut consumption has been strongly associated with several positive health outcomes, including: 15% decreased risk of cardiovascular disease, 23% decreased risk of cardiovascular mortality, 15% decreased risk of hypertension, between 8% and 18% reduced risk of cancer mortality, and 19% decreased risk of all-cause mortality! In randomized controlled trials, tree nuts have been shown to reduce weight and improve lipid profiles, diabetes control, and blood vessel function. There is considerable evidence that nuts help preserve cognitive function and prevent Alzheimer’s disease due to their neuroprotective nutrients. They also decrease stroke risk.

Some people may see the caloric content of a handful of nuts and worry about weight changes. Tree nuts are high in calories, but their effects on appetite reduction and sugar absorption translate into significant reductions in both weight and waist circumference, as well as better blood levels for cholesterol and glucose.

In terms of health and longevity, adding a few servings of nuts to your diet, like my father does each day, can be a tailwind that keeps you sailing along smoothly. And it’s simple and delicious enough that it may feel like a cheat code for good health.

Semaglutide for Obesity: Largest Benefit Ever for Heart Failure with Preserved LVEF



Mikhail Kosiborod, MD, a cardiologist and Vice President of Research at Saint Luke's Health System, recently presented a landmark study showing that the weight-loss drug semaglutide was a potentially game-changing therapy

that significantly improved breathing, exercise ability, and quality of life in patients with heart failure and obesity.

Worldwide there are 64 million people living with heart failure, and it is the most common cause for hospitalization in the U.S. The STEP-HFpEF study enrolled 529 people with obesity and a common and potentially lethal condition called heart failure with preserved ejection fraction (HFpEF), the most common type of heart failure. Patients who have HFpEF have a heart pump that is not weak, but instead too stiff, so it doesn't fill properly between beats. HFpEF patients typically experience symptoms like shortness of breath, fatigue, swelling, and difficulty doing even light physical activity. This type of heart failure accounts for more than half of all cases in the U.S. and is rising in prevalence due to increasingly common predisposing risk factors in our country like obesity, diabetes, sleep

apnea, advanced age, and high blood pressure.

Study participants were randomly assigned to take weekly injections of either a placebo or a 2.4 mg dose of semaglutide, which is marketed as Wegovy®, for one year. Semaglutide produced significantly larger improvements in symptoms and physical limitations, with better stamina while walking and greater weight loss compared to the placebo injection, as detailed in the *New England Journal of Medicine*.

In August 2023, Dr. Kosiborod presented the STEP-HFpEF study at the European Society of Cardiology—the largest cardiology meeting in the world. He said, “The improvements in heart failure-related symptoms and physical limitations that we observed with semaglutide are impressive, and the largest that we have ever seen with any pharmacologic intervention in patients with this type of heart failure.”

Semaglutide Reduced Obesity and Improved Quality of Life

People on semaglutide lost on average about 31 pounds (13.3% of their body weight) during the year-long study. The trial used the Kansas City Cardiomyopathy Questionnaire (KCCQ), a 100-point scale devised and validated by John A. Spertus, MD, Clinical Director of Outcomes Research at Saint Luke's Mid America Heart Institute. KCCQ is the gold standard

tool for measuring quality of life in the setting of heart failure, where higher scores indicate fewer symptoms and physical limitations. The semaglutide improved the average KCCQ by 17 points at one year, about twice the results seen in the placebo group.

The STEP-HFpEF study participants completed a six-minute walking test at the start of the study and again one year later to assess change in exercise capacity. In the semaglutide group, people walked an average of 70 feet farther by the end of the study.

Dr. Shauna Levy, Medical Director of the Bariatric and Weight Loss Center at Tulane University Medical Center in New Orleans, said, “These results are incredibly exciting, because the patients only took semaglutide for one year, and it had a profound impact on their health and physical capabilities,” Dr. Levy, who was not associated with the STEP-HFpEF study, said. “Semaglutide is truly a life-saving medication. We are just scratching the surface of all the disease processes that will reduce once we finally start treating obesity.”

There were fewer serious adverse events in the semaglutide group than in the placebo group, mostly due to fewer heart-related issues. Similar numbers of participants stopped taking semaglutide and placebo during the study, though more patients stopped semaglutide

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Tina's Transformation

James H. O'Keefe, MD

Tina is a bright and earnest medical technician who is devoted to our patients and her coworkers here at the Saint Luke's Charles & Barbara Duboc Cardio Health and Wellness Center (CWC). She has been working with us for five years and is a beloved member of our team.

Even as an active teenager playing soccer for hours a day, Tina had a difficult time keeping her weight under control. Her mother took her to various doctors, but they could find no medical or hormonal reason for the weight gain. Tina struggled to lose the extra pounds around her midsection, no matter how hard she tried with diet and exercise. When her weight ballooned to 262 pounds in her 20s, she developed prediabetes and polycystic ovarian syndrome (PCOS). Her physician started her on metformin, which lowered the blood sugar and helped regulate her cycles but didn't budge the weight.

Then about a year ago our CWC nurse practitioner Tammy Ibanez started Tina on a GLP-1 agonist; at first this was Mounjaro® (also approved for weight loss as Zepbound™), then Ozempic®; currently she is on Wegovy®. In our CWC, we use these four meds interchangeably, depending on which one is best covered by the patient's insurance. Tina noticed mild and transient nausea when she first started the once-weekly self-injections, but this resolved when Tammy discontinued Tina's metformin. Now she occasionally has mild constipation, which she treats with a stool softener pill and psyllium (Metamucil®)—a fiber supplement. She immediately noticed that her appetite was not as voracious, and it was easier to make healthy choices and avoid sweets and junk food.

One year later, at 187 pounds, Tina is 75 pounds lighter and still trending down. At 5' 8" tall, her BMI went from 40 (morbidly obese) to 28 (mildly overweight). More importantly, nearly all the weight came off her mid-section and abdomen; her waist shrunk from 50 inches to 38 inches. Tina beams when she tells me about her off-the-chart high energy levels. Even after working 10 hours, she comes home and is ready to go out with friends or get some exercise. She never feels like she needs a nap anymore and spends much less time watching TV. Her lab values are dramatically improved as well, with no more prediabetes or PCOS.

Nothing succeeds like success. As the weight has come off, she has been more and more motivated to eat right, get her sleep, and be physically active; her mood is consistently vibrant and happy. Increasingly, Tina is hearing compliments from her friends and family about the sparkle in her eyes, her energetic and cheerful demeanor, her fit-looking physique, and her beautiful skin. I have noticed that when I start my patients on these new once-weekly injectable GLP-1 agonist drugs, they don't just lose weight, they also become healthier—not only in appearance but also when we look deeper with blood tests, imaging studies, etc. The fat in their liver melts away, reducing inflammation throughout the system. Their sleep and blood pressure improve, and their lab values are better across the board.

Tina is increasing her intake of healthy protein foods and doing strength training three times per week to maintain her muscle tissue while still

losing fat tissue. All of us should be doing weightlifting twice a week for at least 20 minutes per session to maintain strong bones and muscles, but this is critically important for anyone on these GLP-1 agonist drugs, which tend to reduce muscle and bone mass along with the excess fat tissue.



Tina before



Tina now

A Woman's Heart Is Special: Risk Factors for Heart Disease You Didn't Know You Had

Tamar Ibanez, RN, AGACNP



As February focuses on women's heart health and the anniversary of our Saint Luke's Muriel I. Kauffman Women's Heart Center, we wanted to highlight uniquely female cardiovascular (CV) risks. Heart disease is still the number one killer of women. As females, we face conventional risk factors for heart disease, such as high cholesterol, high blood pressure, tobacco and nicotine use (including vaping!), diabetes, sleep apnea, and obesity. Unfortunately, we have secondary risk factors that you need to be aware of, which are entirely gender-specific.

Polycystic Ovary Syndrome (PCOS)

PCOS affects approximately 10% of women, and is often associated with obesity, high cholesterol, high blood pressure, and insulin resistance. Typically, women with PCOS have higher coronary artery calcium scores and elevated levels of inflammatory/clotting markers, such as C-reactive protein (CRP) and homocysteine. Women with PCOS are three times more likely to develop gestational diabetes and preeclampsia, which are known to increase CV risk as well. Typical treatment options for PCOS have been spironolactone for hormone regulation and metformin to

treat insulin resistance. GLP-1 agonist drugs such as Wegovy®, Ozempic®, Mounjaro®, and Zepbound™ markedly reduce abdominal fat and are emerging as tools for reducing inflammation and improving insulin resistance.

I have a patient that I have been following for quite some time who is in her mid 40s and has PCOS. She was having irregular menstrual cycles. Her obstetrician tested her female hormones and determined she was starting to go through menopause. Several months after starting Wegovy®, she started having regular



Author with daughter, Gracie

menstrual cycles again, in addition to getting benefits of weight loss and seeing improvement in her blood sugar levels. Improving insulin resistance has a tremendous hormonal benefit and might even delay menopause by several years.

Diabetes During Pregnancy (Gestational Diabetes)

Gestational diabetes is defined as any degree of glucose intolerance with onset or first recognition during pregnancy. Increasing rates of obesity and often undiagnosed type 2 diabetes have led to rising rates of gestational diabetes. Individuals who suffer from gestational diabetes have a seven times greater risk of developing type 2 diabetes over the course of their lifetime, which is of course a risk factor for CV disease. If you had gestational diabetes during your pregnancy, you should talk to your primary care provider and make sure you are having annual labs drawn to check for diabetes and prediabetes.

Hypertensive Disorders of Pregnancy

Hypertensive disorders of pregnancy include pre-pregnancy chronic high blood pressure, gestational hypertension, and preeclampsia and eclampsia. These disorders can cause placental

ischemia, meaning blood flow through the placenta is dangerously reduced. This can be a risk factor for long-term blood vessel damage to the mother and make it much more likely for future development of high blood pressure, dyslipidemia, and diabetes. If you had blood pressure issues during your pregnancy, it is very important that you get a blood pressure cuff and monitor this regularly at home. If you have readings consistently greater than 130/80, please talk to your primary care provider about getting treatment.

Autoimmune Diseases

Autoimmune diseases such as lupus, rheumatoid arthritis, Addison's disease, inflammatory bowel disease, psoriasis, scleroderma, and type 1 diabetes increase a person's risk of developing CV disease by 150%. The mechanism behind this is thought to be underlying inflammation. The risks seem to be greatest in women under 55 years of age.

Radiation and Chemotherapy for Breast Cancer

Anyone who has undergone chest radiation or has been exposed to certain chemotherapy agents can be at increased risk for developing heart disease. As our cancer treatments improve, so does the subsequent life expectancy, and we are now seeing cardiotoxicity (heart damage) as much as 30 to 40 years after treatment. If you have had chest radiation or chemotherapy, you should ask to be evaluated with an echocardiogram every five years for surveillance.

Radiation exposure, while successful in treating cancer, can cause both small and large blood vessel damage and valve problems like aortic stenosis and mitral stenosis. This is due to increased inflammation in the coronary arteries and the cardiac

valves. The risk of developing coronary artery disease from radiation is dose-dependent. Getting a CardioScan to look for coronary artery disease is a simple, inexpensive, and valuable screening tool.

Mental Health: Sexual Assault/ Domestic Violence/Depression and Anxiety

Violence against women is widely underreported but can impact women of all ages. This has been well documented to have an adverse effect on psychological health. Without mental health treatment and development of positive coping strategies, women who have experienced violence are at higher risk for depression, hypertension, anxiety, eating disorders, PTSD, and substance abuse.

Have an honest conversation with your primary care provider about your risk. If you are not comfortable discussing a history of violence or abuse, find a mental health care provider with whom you can discuss this comfortably. As women, we twist ourselves into knots taking care of everyone else, but we need to also make time to take care of ourselves, both mentally and physically.

Seek out positive coping strategies to deal with stress and anxiety. I have been teaching my three-year-old daughter yoga, and this has come to be our nightly routine after bath time. While I am certainly no yogi, we do basic poses and, most importantly, deep breathing exercises. My goal is to teach Gracie a simple stress reduction technique that she can use throughout her life to help manage all the very big feelings she already has.

In addition to mindfulness techniques, there are many options for medications to treat depression and anxiety that can greatly improve your quality

of your life. Do not be afraid to ask for help from your health care team.

Take Control of Your Health

We can all do better with nutrition. We know highly processed foods and foods high in sugar are not the best choices for our bodies, and being mindful of our intake can be a powerful step in taking control of your health. Dr. James O'Keefe has written prolifically about nutrition in previous newsletters, and there are many free online resources about a heart-healthy diet.



If you have no exercise regimen, start with a daily walk—with a dog ideally. Most people can tolerate at least five minutes a day and then build from there. The goal is to get to 20 minutes of regular physical activity daily, in addition to strength training twice per week.

Seek out proactive preventive care, such as our Saint Luke's Charles & Barbara Duboc Cardio Health and Wellness Center (CWC). This is a great way to assess your personal risk for heart disease and start working on the things you can control. We have a wonderful team here in our CWC clinic, and we are always eager to take new patients.

The Best Time Is Now, Honey

Kathleen Cartier O'Keefe

I recently celebrated a birthday. Twenty-eight, to be specific. And this year, with a fully formed frontal cortex and fewer red solo-cup parties, I've found myself with more time to think. *Really* think. For me recently, some of this deep contemplation has been about my mother. I am now the same age she was a year into her radiation treatment for Hodgkin's Lymphoma. After being diagnosed at twenty-seven, while also pregnant with my oldest brother, Jimmy, she delivered him prematurely, in between cancer treatments, with tumors still encasing her neck and chest. She was then told by doctors that, due to the repeated radiation, she'd never have children again. My late twenties have brought me a startling capacity for gratitude. To exist here and now, alongside the people we love, is a stroke of phenomenal fortune far beyond my comprehension.

I've been watching young adulthood sunset for a while now. Yet, I must admit pulling up to twenty-eight feels like that sun dropped out of the sky. My late twenties arrived quietly. They've been encompassing me in adulthood's obscurity before I felt prepared, or maybe just before I was ready to part with adolescence. Suddenly, I've found myself riding this very jarring, polarizing pivot from childhood to middle age. I have a stable job, a humble savings, a semblance of purpose. My birthday this year didn't bring me to tears as it usually does, but rather, it sort of blurred my nostalgia. My typical fixation on where I've been

and who I've lost has faded, I'd say, from a constant buzzing to a forgettable hum.

I've noticed, recently, that many of my peers' life concerns do not mirror mine like they may have on a younger birthday. We're rapidly branching out into singular directions—personally, geographically, and professionally. Imagine a track race—we all began at the same white, starting line. For a while, we were neck and neck. But recently, I lifted my head up to find that my childhood friends are all running at varying speeds, in individual lanes, with distinct goals in mind. Our positions on the track all shifted, simply because that's always been our destiny. For, hopefully, a long time, we'll all keep circling this track. The weather will fluctuate, and visitors might join us for short sprints, for rest, or for recovery periods. I'm realizing that a major threat to the health of a long-term friendship is just enduring



Kathleen on her 28th birthday

these life stages collecting us at different times—marriage, infertility, layoffs, breakups, loss, abuse, moves, atrocious first dates.

In this way, aging requires us to listen to our friends and sympathize with anxieties that may not be our own. For instance, I have one friend mourning a deceased parent and another disheartened by a never-ending egg donor search—two situations where I, thus far, lack experience. I never know the right thing to say, so instead, I try to listen. *Intently*. Show up and shut up. Dreadful days will come, and when they do, we must walk each other out of darkness, not because we know where to go, but because we know how to hold each other's hand. You see, we're all running in a circle; no one's ahead or behind. Wherever they are on the track, you'll probably be there one day too. With age, our compassion for those we love has to overwhelm our lack of understanding for their problems.

There's no finish line; no winner or loser. In the end, we'll all collapse under the sun. We'll recline into the grass patch in the center of the track that we've been circling for our whole lives. Our mortality has always been there, but at some point, we'll be laying in it alongside one another. We'll be winded from our long run, but we'll be smiling as we look up at a clear, blue sky.

While on the topic of death, I've become painfully aware that what I have now is also what I'll eventually lose. By late twenties, we've all lost something. We've met loss in one way

or another—a job, a pet, a relationship, a loved one. I'm coming to terms with the fact that everything we have known will evaporate. We will change—our haircut, our address, our coffee order, our idols, our best-fitting jeans, our Saturday night plans, our favorite songs. Existence is brief, so nothing can be permanent.

Change is inevitable, so rather than resisting it, shift that energy into welcoming it when it arrives. Emotional flexibility is the name of the game. To have faith, in quite literally *anything* greater than yourself, is to be adaptable. One of my favorite authors, Michael Singer, once wrote, "You naturally begin to center more and more on the spiritual part of your being. You do this not by reaching for the Spirit, but by letting go of the rest." Parting ways with something good because you have conviction in something greater is an act of spirituality.

I used to fear getting older. I'd pluck the grey hairs sprouting from my crown and spend money I didn't have on anti-aging cream for the wrinkle deepening on my forehead. Aging reminds me that time is passing. Like all other great battles in life, I think being okay with aging comes down to accepting *change* more than anything—something my mother is much better at than me. Amid gathering my thoughts for this essay, I asked her a few questions: "If you could go back to one age again, what would it be?"

My mother chuckled and responded, "Oh, I wouldn't go back. This is the best age, right now."

"Sixty-five?" I countered.

"Yep." She retorted. "Sixty-five."

She's not one to lie, but this answer seemed mindless, so I dug further: "What about like... thirty-five? You wouldn't go back?" She rolled her eyes and snickered, as if I was telling jokes.

"Oh no. Are you kidding? Thirties were good, they brought me you, but so much was unclear back then."

"Explain that," I said.

She peeled the red reading glasses off the bridge of her nose and let out a long exhale.

"Ok, well, at thirty-five I was a mother of two who desperately wanted to be a mother of four. Financially, things were rocky. I was only a few years into my cancer remission, deathly afraid it'd resurface any day."

She paused and took a moment to finish.

"I'm proud of how I made it through my thirties, but I'd *never* go back."

Ok fine, thirties were tough for her. I probed again, "What about twenties? Or forties?"

"Twenties were great, but that's the kind of fun you only want for a decade. And forties... my forties were *tough as hell*. I was raising four kids, paying off debt and mortgages, working fulltime then rushing to soccer games and basketball games every night. Like I said, it was the time of my life, but I was just keeping my head above water."

"So, the best decade, you'd say, has been your sixties?"

"Without a doubt; the best time is now, Honey."

I expected her to say twenty-four, fifty-seven—some random age that I deemed ultimate, perfect, or euphoric. However, according to my mother, that age does not exist. And if it did, the closest thing to it is right now. *The best time is now, Honey.*

As my mother spoke, I could feel the boundaries of what I know to be true expanding (miraculous, I know, but don't tell her that). Her words echoed

around in my head for a while. This kitchen table conversation encompassed what I'm starting to understand about aging: supposedly, it only gets better. Life, if you zoom out, has an overall upward trajectory. Yes, with time we lose plumpness in our cheeks and color in our hair, but who cares if in exchange we get to blossom? Age largely liberates us from self-doubt. The grooves of what make us *us* just deepen, and how magical is that? I heard Pamela Anderson recently say, "It's fun getting older. It's a relief." My mother certainly feels the same way. Learning how we interact with this world is remarkable. Embracing our individuality and discovering where we can meaningfully contribute—these are the real indulgences of a lifetime.



This doesn't mean, however, that the obstacles that come with female ripening aren't daunting—fertility decline, greying hair, permanent stretch marks, looming Botox, discovering pesky spider veins on our legs and sunspots on our chests. I could cry just listing it all. For better or for worse, as females we're taught from birth to contribute beauty, and by definition, youth, to this world. Our society worships the zest of youth, that inquisitive drive that seems to slip through the fingertips of grown-ups. But maybe this adoration is just envy of their spontaneity or naïveté. The bottom line is that our glorification of youth is dangerous.

continued on page 17

It turns out that inhibiting the SGLT1 channel changes the way the body senses the amount of available nutrients. SGLT1 deceives the body into thinking that it's not getting enough food, triggering upregulation of nutrient deprivation signaling and downregulation of nutrient surplus signaling, somewhat like starvation or endurance exercise training.

This fasting mimicry activates a key process called autophagy—a fancy word for cellular housekeeping. This is a primal response that is normally turned on during difficult conditions like insufficient food, intermittent fasting and/or strenuous exercise. Autophagy cleans up and rejuvenates cells by breaking down and recycling damaged organelles, particularly mitochondria—tiny powerplants that churn out energy. Autophagy reuses these recycled proteins to rebuild brand new

mitochondria that crank our energy levels back up to youthful levels.

This revitalizes old worn-out cells and restores optimal function to tissues and organs throughout the whole system. These vital mechanisms of action help provide the biological plausibility to explain how and why SGLT1 seem to slow aging, prevent myriad diseases, and improve life expectancy. They confer anti-aging effects at a cellular level.

SGLT1 Safety and Tolerability

Any compound being considered for use for decades by healthy people should meet the *Primum non nocere* (first do no harm) maxim and must have very low risk for serious adverse effects. SGLT1 is a safe and well-tolerated, once-daily pill, with discontinuation rates that are similar to placebo. A meta-analysis of 47,000 patients in randomized controlled trials reported that SGLT1 compared to the placebo caused no significant increase in risk of adverse events, including low blood sugar, urinary tract infection, bone fractures, or low blood pressure. Other studies show that SGLT1 users report improved quality of life.

I have been prescribing this drug frequently for my patients over the past nine years, and they routinely come back feeling and looking better. Even so, because

SGLT1 causes sugar in the urine, this drug increases the risk of fungal infections in the genitalia or groin regions. A large meta-analysis found that SGLT1 use was linked to a statistically significant 3.3-fold increased risk of genital yeast infections, which occurred in 6.3% for SGLT1 users versus 1.7% for placebo. This problem can usually be avoided with careful urinary hygiene, including wiping any excess urine off skin/genital surfaces after urinating and bathing/showering once or twice a day. SGLT1 may also slightly increase risk of urinary tract infections and can very rarely lead to dangerous infections in the perineal region or cause ketoacidosis.

Conclusion

SGLT1 mimics starvation and promotes cellular housekeeping, which rejuvenates cells and organs, thereby improving overall health and longevity on a cellular level. Clinical studies show SGLT1 lowers risks for premature death and many of the diseases of aging. Of the potential drugs to slow aging, SGLT1 has the most compelling data for safety and efficacy in humans. Importantly, further randomized studies to assess SGLT1 for reducing age-related disease and improving life expectancy in otherwise healthy people are warranted to objectively confirm this hypothesis that we've put out there based on experimental data, clinical trials and results we've seen in our patients.

In the meanwhile, if you are curious about whether you might be a candidate for SGLT1 therapy, talk to your health care provider.

Disclosure: Dr. James O'Keefe has done scientific presentations for Boehringer Ingelheim, the company that makes Jardiance.

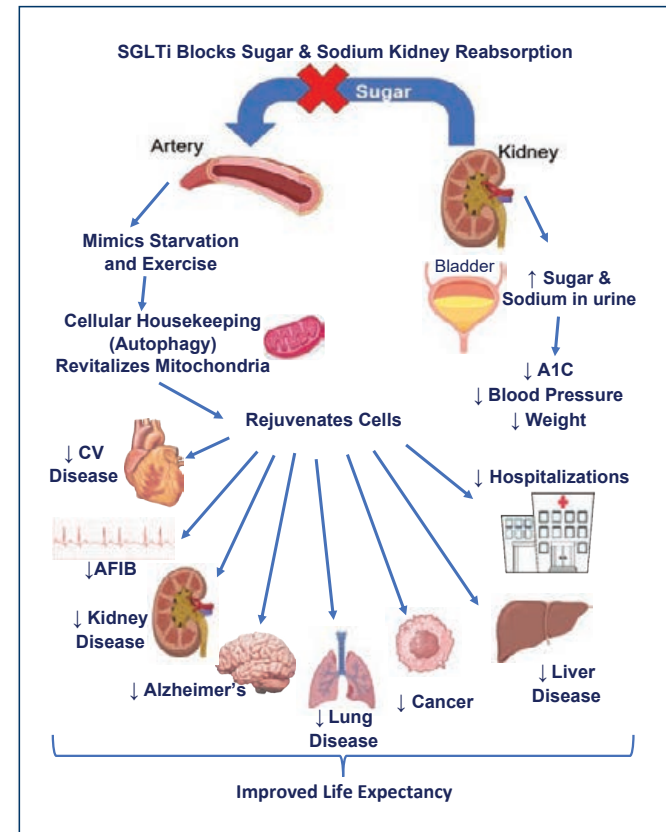


Figure 1



Living Wholeheartedly

You only live once, but if you do it right, once is enough.

—Mae West

Politicians and diapers must be changed often, and for the same reason.

—Mark Twain

When I was growing up, I always wanted to be someone. Now I realize I should have been more specific.

—Lily Tomlin

Never regret anything you have done with sincere affection; nothing is lost that is born of the heart.

—Basil Rathbone

When I hear somebody sigh, "Life is hard," I am always tempted to ask, "Compared to what?"

—Sydney Harris

Before you marry a person, you should first make them use a computer with slow internet to see who they really are.

—Will Ferrell

Does it disturb anyone else that "The Los Angeles Angels" baseball team translates directly to "The Angels Angels"?

—Neil DeGrasse Tyson

Normality is a paved road: it's comfortable to walk, but no flowers grow.

—Vincent van Gogh

Have you ever noticed that anybody driving slower than you is an idiot and anyone going faster than you is a maniac?

—George Carlin

Cal: You are really pushing my buttons today.

Becky: Which one is 'mute'?

Hating people is like burning down your own house to get rid of a rat.

—Harry Emerson

Men marry women with the hope they will never change. Women marry men with the hope they will change. Invariably they are both disappointed.

—H.M. Harwood

Never go to a doctor whose office plants have died.

—Erma Bombeck

It is not enough to be busy. So are the ants. The question is: What are we busy about?

—Henry David Thoreau

Life can be hard; but it will surely get harder if you are careless with your health.

—James O'Keefe

There comes a point where we need to stop just pulling people out of the river. We need to go upstream and find out why they're falling in.

—Desmond Tutu

The secret to happiness isn't falling in love; it's staying in love, which depends on what psychologists call "companionate love"—love based less on passionate highs and lows and more on stable affection, mutual understanding, and commitment.

—Arthur C. Brooks

Why don't doctors trust atoms? Because they make up everything.

—Grant Wiggins, Grandson

Always try to see the good in others, even when it's well hidden.

—Gregory Haskamp

Don't pray for an easy life. Pray for the strength to endure a difficult one.

—Bruce Lee

All success is a lagging indicator. So too is wisdom and insight. Nothing comes from nowhere. Not success. Not awards. Not strength. Not greatness. Everything is a lagging indicator. Of years and years of working, trying, and failing, of enduring. Of whether or not you keep going when most would give up. That's what you're going through right now. So keep going.

—Ryan Holiday

An apple a day keeps the doctor away if you throw it hard enough.

—Grant Wiggins

Lifestyle Changes That Prevent AFib

Ellen Murray, MD



In my first year of medical school, I had barely heard of atrial fibrillation (AFib), other than from the occasional commercial for blood

thinners. Little did I know then how it would impact both my personal and professional life and even guide my future career. A year ago, my dad was experiencing AFib and had to undergo an electrophysiology procedure called ablation—he now participates in a masters ice hockey league several times each week! And I am currently a third-year cardiology fellow, about to start training in electrophysiology, the type of cardiology specializing in management of electrical heart issues like AFib.

AFib is a condition that affects millions of Americans, with symptoms such as racing heart, uneven pulse, and heart palpitations and fluttering. AFib can cause heart failure, stroke, and death if not properly treated. This is an abnormal and irregular heartbeat in the atria—the upper chambers of the heart. When “fibrillating,” the atria are quivering rather than beating regularly, which results in sluggish blood flow in these upper heart chambers, predisposing to blood clots that ultimately can cause devastating strokes even in healthy people. This was something

I experienced personally, when my long-term boyfriend’s father had a fatal stroke just a few months after we had gone on a family trip to Mexico together. Traditional AFib treatments can be long-term, invasive, and even potentially toxic, sometimes entailing catheter-based procedures such as the one my dad underwent. Thankfully, there are many non-drug and non-invasive ways in which we can prevent and reduce risk of AFib in our daily lives.

One of the most well-known and preventable risk factors for AFib is alcohol use. The term “holiday heart” dates back to the 1970s, when it was first described by Dr. Phillip Ettinger. He noticed that the day after holidays like New Year’s Eve, July 4th, Memorial Day, Thanksgiving, and Christmas, patients showed up frequently with rapid AFib and even heart failure. Alcohol can have a direct toxic effect on the muscle cells of the heart that is dose-dependent—the bigger the dose the more heart irritability. Alcohol can also cause indirect damage to the heart by raising stress hormones and blood pressure, which in turn can increase likelihood of AFib.

Several recent studies clearly show that cutting way back on drinking—or ideally, abstaining from alcohol altogether—will markedly decrease the number and duration of AFib spells. We now tell our patients with AFib to

try to avoid alcohol entirely, or if they do drink, to limit it to not more than one beer, one glass of wine (5 ounces), or one shot (1.5 ounces) of distilled spirits per day, and not more than 3 drinks per week. Even if you only have AFib risk factors like high blood pressure, sleep apnea, tall stature (6’2” or taller for males and 5’10” or taller for females), or heart disease, you should keep your drinking to a minimum or avoid it entirely. It is especially important to avoid binge drinking (more than 4 drinks in a day). So, to avoid ending up in the ER with holiday-heart, celebrate special occasions with light or modest drinking rather than heavy drinking.

Omega-3 fatty acids found in fish/seafood have long been heralded for their health benefits, with many doctors, nutritionists, and wellness professionals recommending multiple servings of fish per week and/or a daily fish oil supplement. Omega-3s can improve brain and heart health, lower blood pressure, heart rate, triglycerides, and inflammation, and reduce risk of heart attack, stroke, and early death. However, studies have shown that in high doses, omega-3 concentration in the blood has been associated with an increased risk of AFib. Omega-3 increases stimulation of the vagus nerve—the “rest and digest” arm of the autonomic nervous system. This balances out the fight or flight autonomic response in a yin-yang relationship. Lower doses of omega-3 modestly stimulate vagal activity, which reduces risk of AFib, but higher daily doses—greater than 1200 mg of EPA + DHA (the 2 most important omega-3s)—can increase the likelihood of developing AFib.

Similar to omega-3, aerobic exercise is unquestionably good for your heart health. U.S. guidelines recommend at least 150 minutes of moderate cardiovascular exercise (about 30 minutes, five days a week) with some added

weight training weekly to improve optimal mental and physical well-being. A physically active lifestyle with moderate exercise has been shown to reduce AFib risk. But some take this recommendation to the extreme, training and competing in ultra-races like marathons and grueling long-distance triathlons. Chronically doing very high-dose strenuous exercise can markedly increase the risk for AFib. The mechanism is thought to be related to increased cardiac workload and stretching of the atria size. This risk goes away if the person moderates their exercise load.

Sleep apnea—intermittently not breathing while asleep—is one of the most common causes of AFib. Treating this with a CPAP machine is a proven strategy to reduce episodes of AFib. If a person is obese and/or using excess alcohol, substantial weight loss, or abstinence from drinking will improve both sleep apnea and risk of AFib.

I come from a tall family. For example, my father is 6’5” tall. Taller people have a predisposition to AFib, probably because their atria are naturally bigger and harder to keep “electrically organized.” For these families, recommendations like avoiding alcohol, using modest amounts of omega-3, treating sleep apnea, and doing moderate exercise should be followed. African Americans tend to have AFib less frequently, but are at higher risk of bad outcomes like stroke and heart failure if they develop AFib.

AFib is a disease that affects one in four American adults at some time during their life. While we have plenty of medical therapies and invasive procedures to manage this condition, there are also many lifestyle changes you can make to prevent AFib on your own, even if you have a history of prior AFib spells.

The Best Time Is Now, Honey *continued from page 13*

I’m learning now that beauty is not synonymous with being young.

So, what is aging then? Aging, as I understand it, is the opportunity to *keep on learning*. Maturing will only make our world smaller if we allow it. If we stop chasing curiosity and allow familiarity to lull us into apathy, that is the byproduct of complacency, not the passing decades. Every trip around the sun is just another chance to get it right, to leave this place better than we found it. That is all. To attach any meaning to growing older beyond that is counterproductive.

One of the best ways to keep learning, I believe, is through inter-generational investment. Spending time with people decades apart from you is an invaluable investment. Deeply engaging with our parents, grandparents, teachers, mentors, children, grandchildren, students, nieces/nephews, or even neighbors garners a well-rounded outlook for healthy development at all ages. Psychologist Gabor Mate has talked about this concept:

“For so many people, their world begins and ends with their own age group. Which is a developmental disaster. We evolved as creatures in touch with multiple people of multiple ages, and we’ve spent time around people with multiple ages. When you isolate people by age, as this culture lately does, there’s subgroups within subgroups within subcultures within subcultures within a society all based on very shallow identification with age. It just limits our development and our possibilities.”

If we only surround ourselves with the same age group, we’re drastically curbing how we see the world. It is only when we consult someone in another stage of life that we can expel some of the misjudgments in our narrow, isolat-

ed minds. For example, when I shared the forecast that thirty would be my best decade with my sixty-five-year-old mother, she laughed at me. She downright cackled. The decade that I romanticize now is one that she would never go back to. Don’t get me wrong, idealizing future life chapters is imperative; we all need to dream. But do yourself a favor and think more about today. Our elders and our children are some of our finest advisors, and if we try to understand the world as they see it, we just might stumble upon joy.

As I close in on thirty, I like to think that I’ve spent my twenties exactly how sixteen and sixty-year-old me would have wanted me to—experimenting a lot—trying on various hobbies, hairstyles, cities, and boyfriends. Some people, things, and habits have stuck around, but most have come and gone. Twenty-eight is an age that sits on the cusp of change, approaching what just might be the precipice of real adulthood. However, unlike previous cusps in my life, I have a small confidence in my durability. There’s a quiet, underlying faith in my abilities that wasn’t there a year ago. Whatever heartbreak or disappointment or loss occurs, I’ll recover. I’ve done it before, so I’ll do it again. I care less about what people think than I did two years ago. I like myself noticeably more today than I did at seventeen or even twenty-five. I’ll keep going, because I sort of know how to now.

So, I suppose, twenty-eight has sweetened the moment. It’s underscored what I have right now, and as my mother brought to light, what may lie ahead. The years keep passing, and for the first time, that’s thrilling to me.

So, the reports are in. The trend is strong. It turns out that getting older is a gift.

Green Exercise Magnifies Benefits— Get Out There!

James H. O’Keefe, MD



photo by Rocky Mountain Joe®, Boulder, Colorado

If you want to calm your mind and sharpen your attention, go for a walk in a park, along a wooded sidewalk or path, or around a lake, even for just 15 minutes. Scientific studies consistently report that doing your exercise outdoors is a reliable way to magnify the benefits of moving your body, not only for sharpening your thinking but also for improving sleep, and boosting well-being, joy, energy, and motivation.

I have found that even when the temperatures plummet and the leaves have fallen from the trees, we come back from a brisk outdoor walk or a game of basketball outside with my grandson Grant happier and more relaxed than if we did indoor exercise. Lisa Nisbet, PhD, psychologist from Trent University says, “You can boost your mood just by walking in nature, even in urban nature. And the sense of connection you have with the natural world seems to contribute to happiness.”

A recent study published in the prestigious journal *Nature* found that green exercise—defined as physical activity done outside in natural surroundings—confers better improvements in brain function than the same dose and type of exercise done indoors. This study showed that a brief walk among trees, gardens, and grass improved working memory and concentration significantly better than doing a similar short walk inside.

Leafy-Walk Meetings

Katherine Boere, a PhD student at the University of Victoria in Canada, said, “This all started with our walking meetings,” when she her neuroscientist colleagues strolled while they chatted about their ideas and projects. It dawned on her that these outdoor walking meetings were much more energizing and cognitively stimulating than indoor meetings done sitting around a table. Katherine suspected the campus walks along the tree-lined sidewalks and paths were more productive than staying inside but needed confirmation.

Previous research showed walking, indoors or out, reliably increased blood flow to the brain and helped people focus better after the exercise. However, the walks in most prior studies lasted at least 30 minutes. For her new study, Boere and colleagues enrolled college undergraduate students and had them walk for about 15 minutes, either indoors or outside on leaf-canopied trails, then tested memory and ability to focus immediately afterwards. The outdoor walk soundly trounced the indoor version; the students concentrated better, remembered more, and responded faster after strolling outside.

Mother Nature: Our Ancestral Home

The natural world predictably relaxes our whole system, slowing the non-stop internal ruminations and calming

down the monkey-mind. Being out in nature provides what scientists refers to as “soft fascination,” which holds our attention yet doesn’t demand continual intellectual analysis. Our overburdened brain gets to rest and reset, so that when we come back inside, we can concentrate better and reason more clearly.

Exercise, no matter where it’s done, will augment the brain’s blood flow and increase oxygen levels, but those benefits are magnified if the physical activity is done outdoors, especially in a natural milieu. Only for the last several generations have humans lived as predominantly indoor creatures. During the vast majority of *Homo sapiens’* 300,000-year existence, the great outdoors has been our home. The biophilia hypothesis argues that our instinctive drive to connect with nature is our genetic destiny because our ancestors evolved in wild settings and relied on the natural world for survival.

Outdoor Exercise Can Make Demanding Workouts Seem Easier

A recent study from China randomly assigned a group of inactive, obese young adults to regular walks either in a park or a gym. After the outdoor walks, the participants reported that the \exercise reduced their stress better and was more enjoyable compared to the indoor walks. Similar results were reported from a study of older people; those who walked outside exercised for

about 30 minutes more per week compared to people who walked indoors.

Even when exercise is strenuous, people generally find it easier and more pleasant when out in nature. A study done in Austria found that volunteers who hiked along a trail in the mountains for three hours felt happier and more relaxed compared to volunteers who did a similar walk on an inclined treadmill. Heart rate monitors revealed that while the hikers exerted themselves more during the outdoor alpine trek, the effort felt less strenuous and left them feeling more elated and relaxed than walking in the gym.

Physical activity done in urban outdoor environments like downtown commercial areas and warehouse districts with extensive pavement and concrete and few trees or other natural elements appears to be less beneficial for a person’s mental health than similar exercise in greener environ-

ments like parks, ponds, fields, and forests. The duration and intensity of green exercise matters, too. Study participants reported feeling more tranquil and relaxed after walking or slowly jogging for 15 minutes through parks, but less so when the workout lasted for more than 40 minutes and/or was physically exhausting. One study reported that a four-mile run through a park calmed women participants, whereas, a nine-mile run was not nearly as soothing and restorative.

Bottom line: Fifteen minutes of green exercise is highly beneficial for health. Even shorter outdoor excursions, such as taking a five- or 10-minute stroll during a work-break, can improve mood and cognitive performance. I do this myself during the workday because it energizes and relaxes me at the same time. But whether you get your physical activity indoors or out, in green spaces, blue spaces (around bodies of water), or grey spaces (in a



concrete jungle), illuminated by sunshine or fluorescent lighting, exercise is very good for you. As researcher Claire Wicks from the University of Essex in England said, “You may experience greater mental health benefits if you are able to be active outside in a natural environment. But since physical activity is extremely important for our physical and mental health no matter what you do or where you do it, just keep being active.”

Semaglutide for Obesity *continued from page 8*

because of gastrointestinal issues like nausea and constipation, which are frequent but usually transient side effects with this GLP-1 agonist class of medicines.

The new study adds to a growing body of randomized controlled trial data showing that semaglutide improves cardiovascular (CV) health even in people without diabetes. The SELECT study randomized 17,604 patients from 41 countries who were overweight or obese with established CV disease but no history of diabetes. During the five-year study, the patients assigned to receive semaglutide (a weekly injection of 2.4 mg) had a 20% lower risk of CV death, heart attack, or stroke compared with the placebo group.

Semaglutide and a newer similar (and possibly even more potent) drug

called tirzepatide (Mounjaro® and Zepbound™), that is also an injection patients give themselves once a week, are transforming our approach to weight management—especially for patients with obesity and risks for CV disease. These drugs may be helping in ways beyond simple weight loss, possibly by decreasing inflammation and congestion. Dr. Kosiborod says, “Clearly, we cannot continue to treat obesity just as something that accidentally happens to occur in these patients,” he said. “It’s likely a root cause of the complications and should be treated as such.”

Semaglutide is FDA-approved for diabetes and weight loss and now will also be used commonly as a treatment for the most common form of heart failure, expanding the demand for this already wildly popular drug. Charles

Barkley, NBA Hall of Fame broadcaster, recently disclosed that he lost 62 pounds after he started taking tirzepatide. Barkley joins a number of celebrities, including Elon Musk and Chelsea Handler, who have used semaglutide or tirzepatide to lose weight. Barkley said, “I feel so good physically I’ve got to make sure I don’t get fat again. You don’t even realize how crappy you feel until you start losing weight,” Barkley said on the *Dan Patrick Show*.

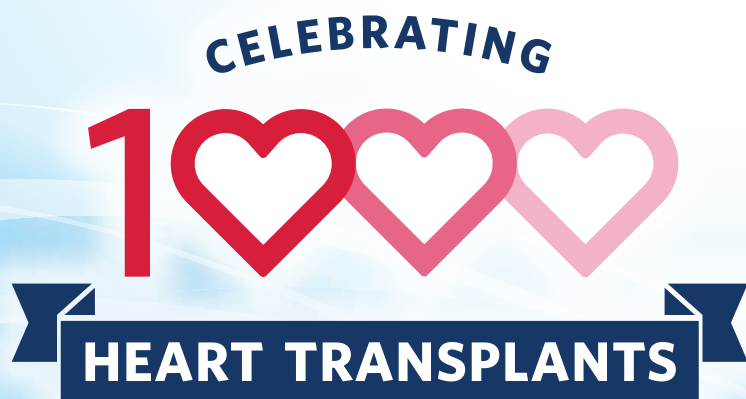
Dr. Kosiborod said that as a doctor caring for patients, he found the results “extremely gratifying, because what I now can tell them is that we have pretty definitive evidence that if we prescribe this medication, you will feel better and be able to do more, and it’s going to have a significant impact on your quality of life.”



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