

The American Institute of Stress

# HEALTH AND STRESS

Your source for science-based stress management information

Volume 28 Issue 4

October 2015

## WHAT WILL Medical Care BE LIKE IN 2050?





**The mission of AIS is to improve the health of the community and the world by setting the standard of excellence of stress management in education, research, clinical care and the workplace. Diverse and inclusive, The American Institute of Stress educates medical practitioners, scientists, health care professionals and the public; conducts research; and provides information, training and techniques to prevent human illness related to stress.**

**AIS provides a diverse and inclusive environment that fosters intellectual discovery, creates and transmits innovative knowledge, improves human health, and provides leadership to the world on stress related topics.**

# HEALTH AND STRESS

**We value opinions of our readers.**

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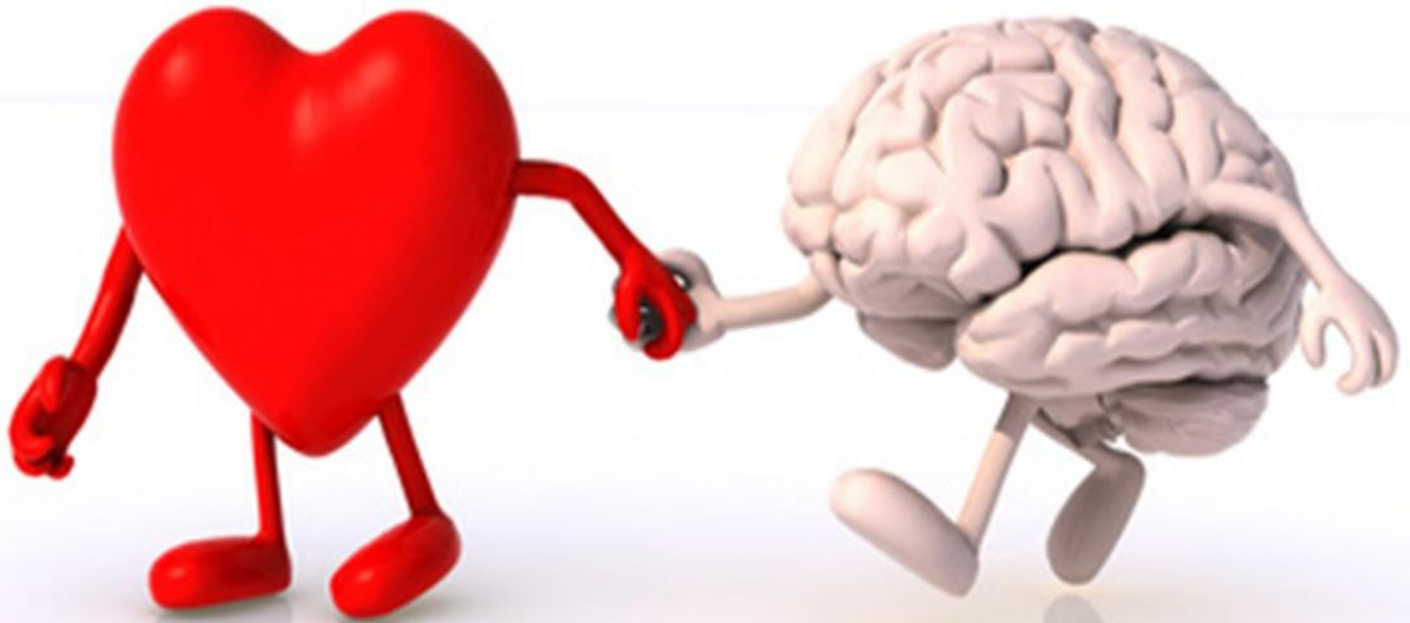
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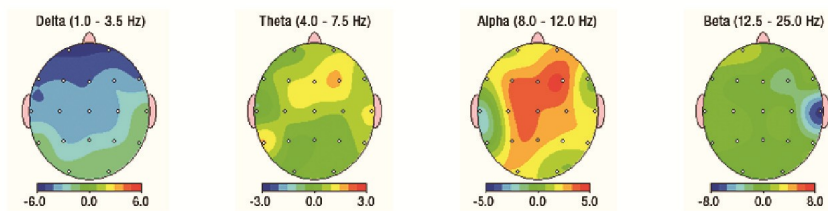
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\*Kennerly R. Changes in quantitative EEG and low resolution tomography following cranial electrotherapy stimulation. PhD Dissertation, the University of North Texas. 2006; 529 pp., 81 tables, 233 figures, 171 references.





# Rise of the Centarians



## What is the Future of Healthcare?

By Paul J. Rosch, MD, FACP

What major changes in health care are we most likely to see over the next few decades? A wish list might include eradicating or reducing cancer, coronary disease, diabetes, depression, Alzheimer's and other debilitating disorders. Another high priority would be correcting problems such as the escalating costs for drugs, professional services, and medical insurance, as well as rampant fraud in Medicare and disability reimbursements.

There is little on the horizon to suggest that any of the above goals will be achieved by the mid-century mark, so what can we look forward to? Predicting the future of medicine is difficult because there are always new discoveries that can have profound influences, such as curing peptic ulcers with antibiotics. More importantly, the popularity of drugs often depends more on their commercial po-

tential rather than proof of greater efficacy or safety. Many, like statins, the most profitable prescription drugs ever, are based on theories accepted as dogma for decades that have now been discarded. The cardiologist Charles Burwell, Dean of Harvard Medical School from 1935 to 1949, warned his students, "*Half of what we are going to teach you is wrong, and half of it is right. Our problem is that we don't know which half is which.*" More recently, John Ionnadis has demonstrated that "*41% of the 49 most influential research studies in medicine have been convincingly shown to be wrong or significantly exaggerated*", and up to 90% of medical publications doctors rely on is flawed.

It is important to keep these caveats in mind when attempting to forecast what medical care and life will be like in

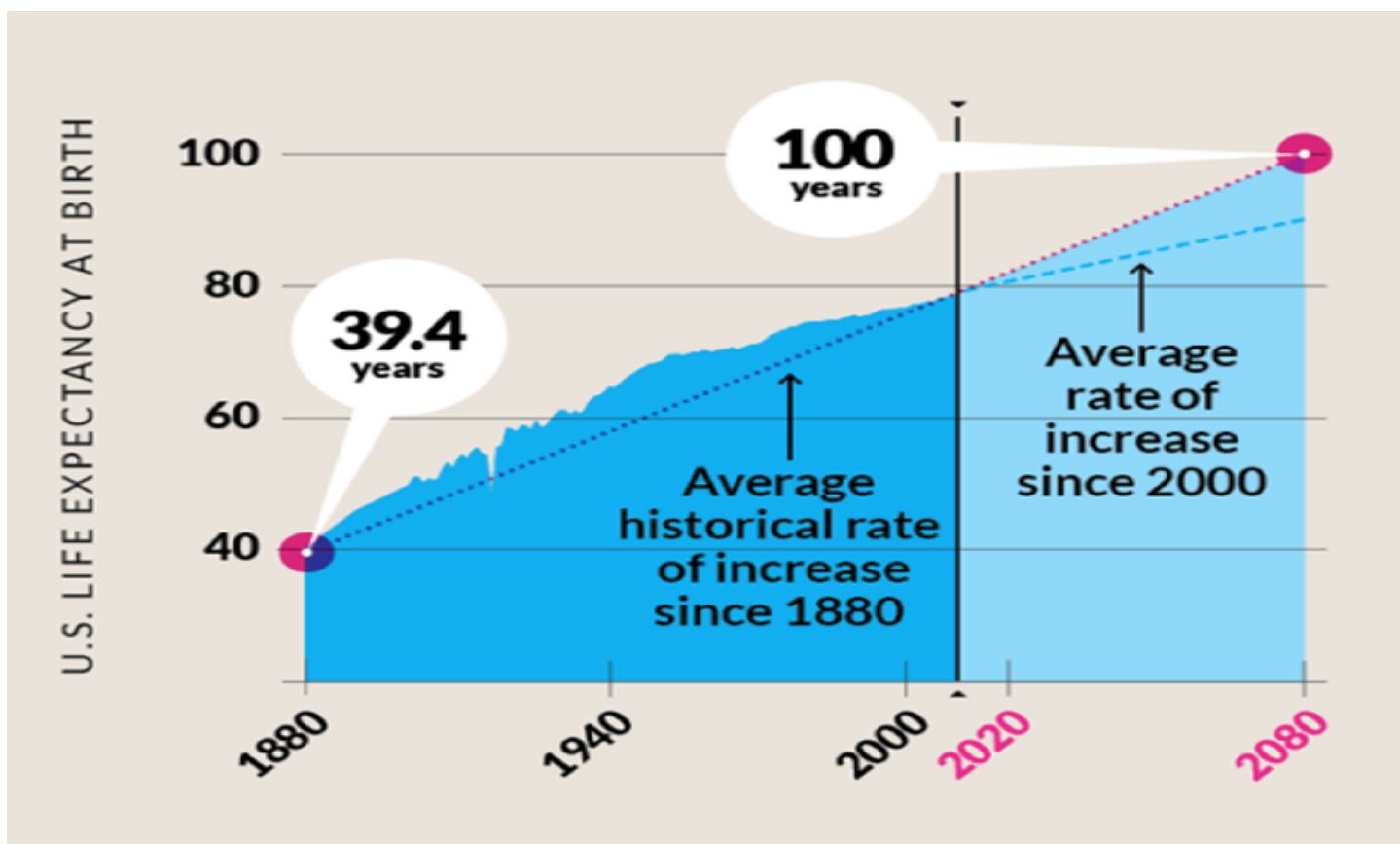
the future, since those who do not learn from the mistakes of history and its numerous shibboleths are doomed to repeat them. The only prediction that can be made with some confidence is to echo Benjamin Franklin's observation that, "*nothing is certain but death and taxes*". With respect to 2050, this means that if current trends continue, we will be living much longer. In 1900, American life expectancy at birth was 47 years but newborns are now expected to live an average of 79 years. If about three months continue to be added with each passing year, life expectancy at birth will be 88 years by 2050, and by the end of the century, life expectancy may be 100, as illustrated below.

Women tend to live a few years longer than men and there are racial and geographical differences. As will be dis-

cussed, life expectancy may also be influenced by global warming, other weather related or meteorological disturbances, as well as artificial electromagnetic pollution. If life extension continues to increase, it could be the most crucial determinant of what the future will be like because of effects on food, water and financial resources, as well as physical and mental health.

### The Escalating Eldercare Crisis And Its Toll On Health And Finances

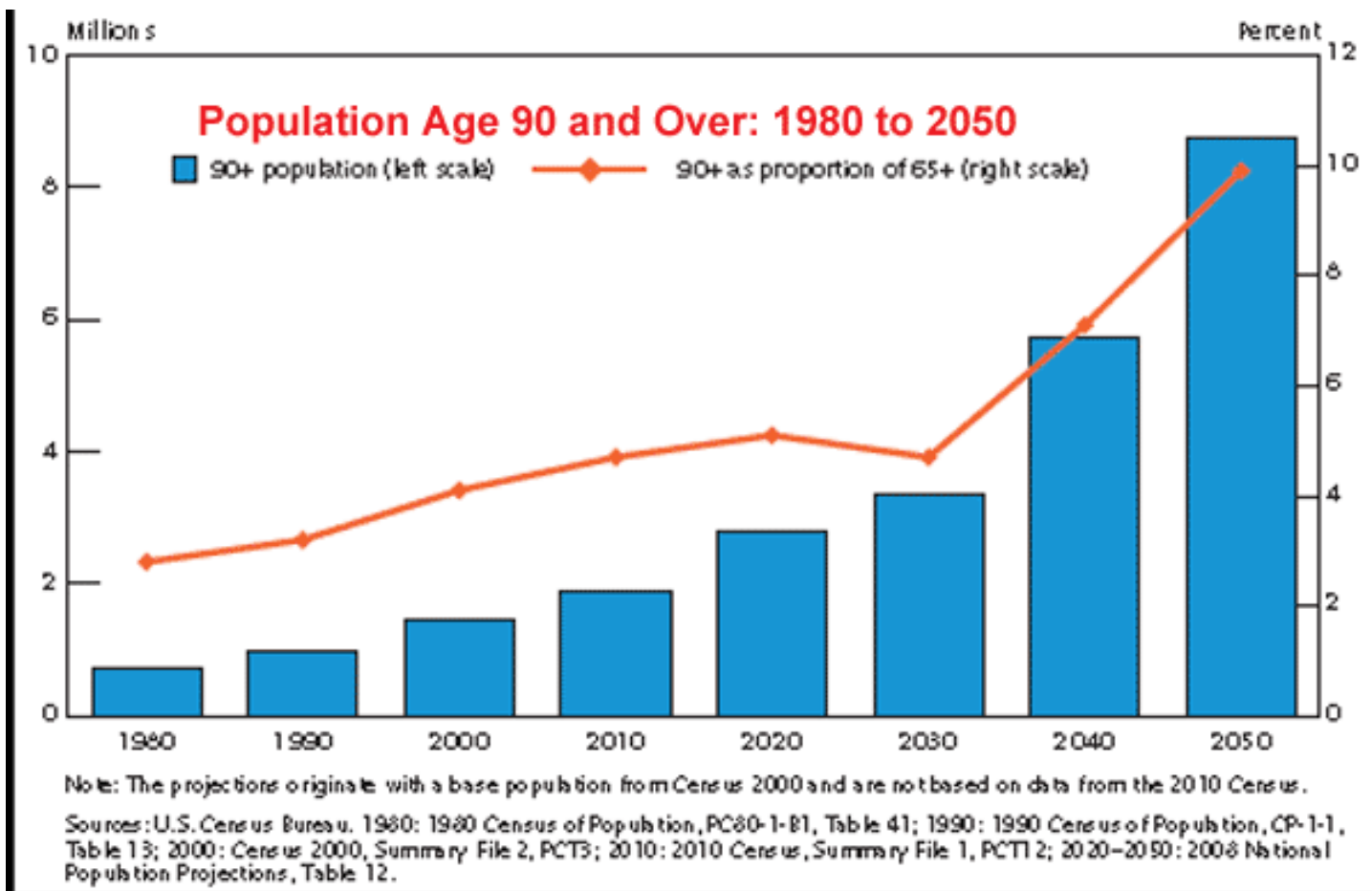
Increased longevity may be more of a burden than a blessing because the longer senior citizens live, the sicker they will be and the sooner Medicare, Social Security and Medicaid will run out of money. Two thirds of Medicare recipients over the age of 65 have multiple disor-



ders such as diabetes, asthma, heart failure, depression, hypertension, chronic obstructive pulmonary disease, Alzheimer's disease, orthopedic or kidney complaints. More than 4 million (15 percent) have six or more long-term conditions and this sickest group accounts for over 41 percent of the \$324 billion/year spent by Medicare. Patients with 5 or more chronic conditions see an average of 13 doctors and have 50 prescriptions filled every year and in some sites, 85 percent of all Medicare funding is spent on the 10 percent of those with multiple ailments. This is a growing concern since Medicare beneficiaries with multiple chronic disorders have increased 20 percent since 2008 in many locations. The reason for this is that 90 and over is the

fastest growing age group in the U.S. It was 720,00 in 1980, 1.9 million in 2010 and is projected to quadruple from 2010 to 2050, compared to a doubling of the 65 to 89 age group, as illustrated below.

In his 1798 *An Essay on the Principle of Population*, Reverend Thomas Malthus argued that human populations grow exponentially (doubling with each cycle), whereas our food supply increases at an arithmetic rate by a fixed increment. This meant that we would reach a point when our means of sustenance was inadequate. Based on a hypothetical world population of one billion in 1800, Malthus predicted that the population would increase to 256 billion within 200 years but our food supply could only support nine billion.





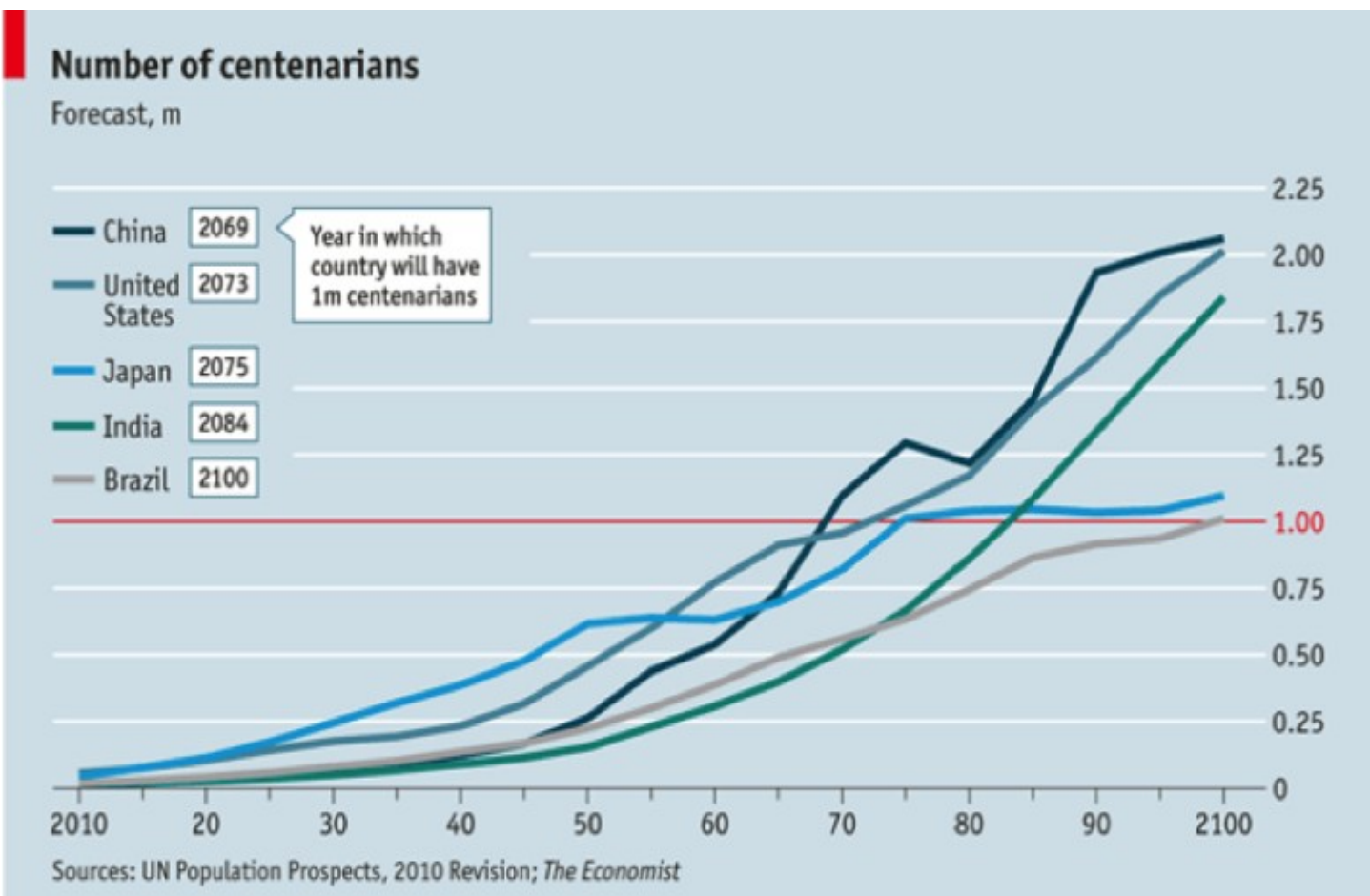
To prevent this catastrophe, Malthus proposed various "preventive and "positive" checks to restrict population growth. The chief preventive check was "moral restraint", the deliberate decision by men to refrain "from pursuing the dictate of nature in an early attachment to one woman", i.e. to marry later in life than had been usual and only at a stage when fully capable of supporting a family. He anticipated this would result in smaller and fewer families, although he was strongly opposed to birth control after marriage. Other checks that shortened lifespan included poor living and working conditions that promoted disease, epidemics, war and famine.

The doomsday scenario proposed by Malthus obviously never took place,

and instead of a population of 256 billion in 2000, there were less than 7 billion. Nor could he have anticipated agricultural advances that increased crops and the rearing of livestock or the impressive increase in life expectancy, which averaged age 40 in 1800 and has now nearly doubled. As noted, there is a steady increase in the total population that starts to soar in 2030, along with the percentage over the age of 90.

The number of people aged 100 or more is projected to be over 6 million by 2050, compared to a few thousand in 1950 and 340,000 in 2010.

As shown below, the highest concentration of centenarians is in Japan and the U.S. Their numbers are projected to grow at more than 20 times the rates of the

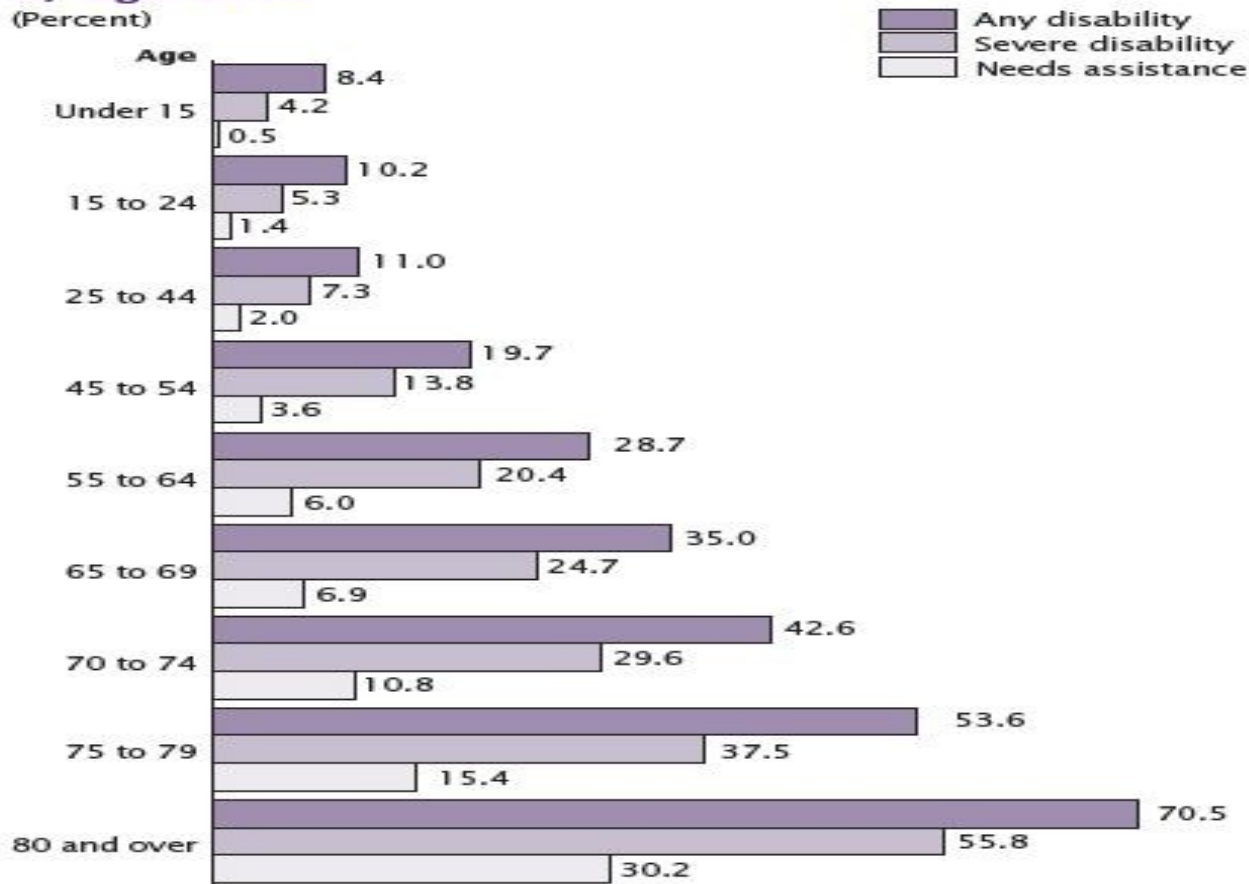


total population by 2050. U.S. centenarians are expected to increase from 75,000 to over 600,000 by 2050 due to surviving baby boomers. This will further increase rising government costs for the already strained Medicare and Social Security programs and a surge in demand for nursing homes, assisted living centers and other special housing. A 2010 census report found that while only 3 percent in their upper 70s were nursing home residents, this rose to 20 percent for those in their lower 90s, and over 30 percent for people in their upper 90s. However, it was 40 percent for centenarians, and half

of these suffer from Alzheimer's or a disabling dementia. Medicare and Medicaid spend \$150 billion/year on Alzheimer's patients, and since their number is projected to triple by 2050, that price tag could exceed our current defense budget. A 2012 survey found that a nursing home private room cost an average of \$248 daily (more than \$90,500 annually) and a semi-private room ran \$222 daily (over \$81,000 per year). These expenses will likely progressively increase since disability rates rise dramatically in senior citizens as illustrated below.

**Figure 2. Disability Prevalence and the Need for Assistance by Age: 2010**

(Percent)



Note: The need for assistance with activities of daily living was not asked of children under 6 years.

Source: U.S. Census Bureau, Survey of Income and Program Participation, May–August 2010.

Although not shown in this graph, disability rates escalate dramatically in 90 to 94-year-olds and the proportion of disabled people in this age group is over 13 percentage points higher than in 85 to 89-year-olds. A subsequent 2013 survey found that the need for assistance in walking, bathing or climbing was present in 44% of 90–94 year olds, 66% of 95–99 year olds and jumped to 92% for centenarians. A July 2015 report predicted that in 2016, the Medicare program's trust fund will run out of money and that Social Security would be unable to pay full benefits. Depletion of the Medicare and Social Security trust funds does not mean that all benefits would stop. At the current rate of payroll tax collections, Medicare would be able to pay about 86 percent of costs in 2030 and 80 percent by 2050. Social Security would be able to pay about 81 percent of disability benefits starting in late 2016, but by 2033, could only cover 75 percent of the current pensions since it will be paying out more than it takes in. The Medicare hospital trust fund is projected to run out of funds in 2026.

### **The Graying Of America And Its Political And Economic Ramifications**

This situation is worsening because in 2010 the baby boomer generation age ranged from 46 to 64 and only 40 million Americans were 65 or older. By 2030, all baby boomers will be eligible for Medicare and Social Security retirement benefits and senior citizens will represent 20 percent of the population, compared to 13 percent in 2010. By 2050 there could be 106 million senior citizens and over 10 million will be 90 and older. Unless finan-

cial support can be provided to the millions of family members or others caring of disabled or chronically ill patients, the government will have to assume this expense. This will cause astronomically higher health care costs, as more people have to be placed in nursing homes and hospices. We need more of these and other qualified assisted living facilities, and since they are also understaffed, certified training programs for geriatricians and allied health care personnel will have to be devised and implemented. Caregivers are aging along with everyone else, and because of declining birth rates, there will be fewer family members to provide support for chronically ill elderly relatives. It can be comforting for middle-aged people to learn they will likely live past 80, but caregiving is extremely stressful for 70-year-old "kids" who must provide constant care for their parents.

Legislators are also more elderly and a graying Congress tends to preserve the status quo since incumbency provides a political advantage because chairs of congressional committees tend to be senior members of the body's majority party. Both houses of Congress are the oldest in history, with the average age of senators at 62 and 57 for representatives. Five senators are now over 80 and 7 are in their late seventies. Six representatives are over 80, 41 are over 70, a dozen have served more than 35 years and one has served over 50 years. This breaks Strom Thurmond's record as South Carolina's senator for 48 years, and he was over 100 years old when he decided to retire in 2003. Members of Congress receive an annual salary of \$174,000 although the majority minority leaders are paid \$193,4000 and it rises



to \$223,000 for the Speaker of the House. However, each member of Congress has an average allowance of \$1,255,909 for expenses such as staff, travel, district office rental, office equipment and supplies, in addition to free furniture and furnishings. There are also liberal retirement benefits, health insurance and other perks.

The nine justices on the first Supreme Court sat an average of nine years whereas the last nine to leave served an average of 27 years. John Paul Stevens, the most recent to retire, was a justice for 35 years. If Clarence Thomas lives to the actuarial life expectancy of a male his current age, he could be a Supreme Court justice for 40 years. When the Constitution was written, no one could have anticipated how much life span would increase, or how much power the Supreme Court would wield. The Judiciary Act of 1789 created a Supreme Court with six justices and also established the lower federal court system. Since then, Congress has altered the number of seats on the Supreme Court from a low of five to a high of 10, but after the Civil War, it was fixed at nine, one for each judicial circuit. Today, there is one Chief Justice and eight Associate Justices of the United States Supreme Court. Like all federal judges, they are appointed by the President and confirmed by the Senate. They hold office for life and their salaries (\$255,500 for the Chief Justice and \$244,400 for Associate Justices) cannot be decreased to insure their independence from political pressures. Most are millionaires since they make an additional amount or more from outside activities such as books, lectures, investments or realty revenue. Each justice is

also entitled to four law clerks (usually a graduate from a leading law school), two secretaries and a messenger.

The Court has jurisdiction over suits between two or more states, those involving ambassadors or other public ministers and certain other special situations. It can hear an appeal on almost any other case that involves a point of constitutional or federal law and its decision is final. However, it can reject a request and usually agrees to hear only 100 to 150 of the more than 7,000 cases it is asked to review each year. Its decisions set precedents that all other courts must then follow, and not even Congress or the president can change, reject or ignore a Supreme Court decision. The reason for this is that our legal system operates under the doctrine of *stare decisis*, which means that prior decisions must be maintained and lower courts must abide by the prior decisions of higher courts. This is designed to insure that our government remains relatively stable and predictable even if it means that a ruling is now unjust because of unanticipated changes.

Historically, the Supreme Court cannot make laws, it can only determine if an action violates the Constitution, Bill of Rights or a subsequent amendment. While its decision is final, it can be overturned in three ways. If the decision is based on a law that Congress has passed, Congress can simply change the law to correct this. If the decision is based on the Constitution, such as the ban on school-sponsored prayer, the Constitution can be amended. However, this requires approval by three-quarters of the state legislatures, which is difficult and costly to obtain. The most common

method is for the Supreme Court to overrule itself, which it has done many times, particularly when a point of law conflicts with a decision made decades previously that needs to be revoked because of societal or other changes. There are also some gray areas, such as the June 26, 2015 5 to 4 ruling that same sex marriage was now legal in all 50 states. Some members of Congress have questioned whether the Supreme Court has the final say on whether this violates the Constitution. One quoted Abraham Lincoln, who, in his First Inaugural address, warned that if citizens and the president accept the Supreme Court's wrong decisions they will have "*practically resigned their Government into the hands of that eminent tribunal.*" Another, who is currently a candidate for the presidency said, "*The stakes are too high and the issue too important to simply cede the will of the people to five unaccountable justices.*"

If there is a referendum on this, the outcome may depend on the opinion of senior citizens because of their political clout. Elections are decided by those who vote and older people are the most likely to show up at the polls because they have a vested interest in protecting the numerous benefits they receive. Over 60 percent of senior citizens voted in the 2010 election and in some states, it was more than 75 percent. In contrast, merely 37 percent of 25 to 44-year-olds voted in 2010, and only about 21 percent of those under 25. Older people are also more apt to vote because they don't have to squeeze a visit to the polls into their work schedules. The voter registration process is another reason older people vote in greater numbers than

younger people. Every time a person moves to a new address, they must re-register to vote and people who forget to do this may be kept from voting. People over 65 tend to live at the same address for longer periods of time, have more ties to the community and more likely to be mobilized by political parties for election campaigns. Voters who are away at college or a distant temporary work location are at a severe disadvantage.

AARP (American Association of Retired Persons) is a very powerful advocate and lobbying group for the elderly. Founded in 1958, it has grown to include approximately 38 million members over the age of 50 and has a \$1.8 billion operating budget. AARP is credited with helping pass the Medicare Modernization Act of 2003 that added prescription drug coverage to the program, rejecting President Bush's Social Security privatization plan in 2005, getting the Affordable Care Act approved and successfully opposing any reductions in benefits to Social Security or Medicare. It derives income from endorsing certain products and services and earns more from selling insurance to members than it does from membership dues. AARP is not an insurer and does not pay insurance claims but allows its name to be used by insurance companies to sell all types of insurance products and receives a commission just as any insurance agent would.

No other demographic group has such a powerful proponent. There is no similar advocacy group for children, recipients of Pell Grants, student loans or food stamps, all of whom depend on governmental assistance. In his second inaugural address, President Barack Obama said:

We, the people, still believe that every citizen deserves a basic measure of security and dignity. We must make the hard choices to reduce the cost of health care and the size of our deficit. But we reject the belief that America must choose between caring for the generation that built this country and investing in the generation that will build its future.

That sounds admirable but a recent survey showed that his administration spends almost \$7 for seniors for every \$1 spent on children. This disparity is likely to increase for several reasons. Senior citizens currently represent only 14% of the population but since 10,000 people join their ranks every day, this will rise to 22 percent by 2040. However, their political clout is much greater than this number suggests since a much larger proportion will actually show up at voting booths. And they also have a tremendous influence on legislators since AARP spent almost \$9 million last year on lobbying. Many believe the U.S. is rapidly becoming a gerontocracy, or political system designed to benefit the elderly, and there are concerns they might vote themselves even more benefits that younger workers would have to pay for.

### **Everyone Wants To Live Longer, But Nobody Wants To Look Or Feel Old**

Although there is no Fountain of Youth, there are ways to diminish wrinkles and other stigmata of aging, which explains the current explosion of interest

in cosmetic plastic surgery. American spent about \$2.5 billion on Botox injections in 2014. Cosmetic surgery is no longer limited to movie stars and the wealthy since 1 in 20 U.S. women have undergone this and half are repeat customers. Approximately 13 percent of all cosmetic procedures are done in men, who are also responsible for 40% of Google searches for cosmetic surgical procedures, particularly breast reduction. TV and print media are replete with advertisements for wrinkle removers and other ways to restore a youthful look, grow hair on your head, remove it from other parts of the body, breast augmentation and various types of liposuction. Tanning salons abound despite their dangers. There were almost 1.7 million cosmetic operations performed in 2014, the top five being breast augmentation, nose reshaping, liposuction, eyelid surgery and facelift. With respect to the top five non surgical procedures, compared to 2013, Botox injections increased 6 percent in 2014 (6.7 million procedures), soft tissue fillers were up 3 percent (2.3 million procedures), chemical peels increased 7 percent (1.2 million), laser hair removal was up 3 percent (1.1 million), but microdermabrasion fell 9 percent (881,905 procedures.)

People want to not only improve the way they look, but to also feel and act younger. One illustration of this is the increased popularity of artificial knee and hip replacements. Over 7 million Americans now have an artificial knee (4.7 million) or hip (2.5 million), the majority of which are paid for by Medicare. To put these numbers in perspective, there are one and a half times as many people in the U.S. with a hip or knee replacement



than people living with heart failure. The prevalence of total hip replacement in adults 50 and older is 2.3 percent and for knee replacement it is 4.6 percent. But by age 80 this increases to 6 percent for hip and almost 10 percent for knee replacement. It is estimated that by 2030, the number of total knee replacements will increase to nearly 3.5 million a year due to rising obesity rates and the need for revision surgery to correct complications from a previous procedure.

An equally impressive example is the growth of exercise and fitness centers to promote health and improve appearance. Jogging and running were popular in the 1970s and 1980s but were usually performed alone and outdoors, weather permitting. Health and fitness centers began to attract increased interest in the 1990s because they supplied attractive equipment to facilitate aerobic and anaerobic exercise on a regular schedule even when it was snowing or raining. In 2000, there were 16,938 fitness centers with 32.8 million members but by 2013, this jumped to 53 million members enrolled at 32,150 such facilities. Fitness center income was \$22.4 billion in 2013, almost double the 2000 revenue, and continues to rise. It was \$24.2 billion in 2014, a 7.4 percent over 2013. Over 54 million Americans belonged to one of the 34,460 fitness/health facilities in 2014 and more than 63 million people utilized their services, up 2.3% over 2013.

These services vary, but there is usually a main workout area with dumbbells, barbells, strength training and exercise machines. This area often has mirrors so that exercisers can monitor and maintain correct posture during work-

outs. A cardio area includes various types of cardiovascular training equipment such as rowing machines, stationary exercise bikes, elliptical trainers and treadmills. Such areas frequently include TVs and audio-visual displays on the walls or integrated into the equipment to keep exercisers entertained during long workouts. Some exercisers time their visits so they can watch their favorite TV programs.

Group exercise classes based on aerobic conditioning are increasingly popular. These vary from spin-cycle workouts, boxing and martial arts instruction and high-intensity-interval training, to Pilates, Zumba, regular and hot (Bikram) yoga and muscle training. Some offer self-defense classes such as Brazilian jiu-jitsu and Krav Maga. Brazilian jiu-jitsu is based on the premise that taking the fight to the ground, and then applying certain joint-locks and chokeholds can subdue a larger and stronger assailant. Krav Maga (Hebrew for contact combat) is a self-defense system developed for the Israeli military that consists of a combination of techniques derived from aikido, boxing, judo and wrestling along with realistic fight training. It is famous for its success in real-world situations since students learn to respond immediately and effectively to any type of physical attack. Health clubs with swimming pools may offer aqua aerobics classes taught by a certified instructor to insure participant safety.

The main surge of increased interest comes from Millennials (aged 18-34), since 82 percent exercise regularly. They are particularly fond of group activities, especially fitness classes with music. Baby Boomers and the elderly tend to

exercise to improve cardiovascular health, shorten recovery from orthopedic surgery, and to lose weight or avoid gaining it. Many also have a stationary bicycle or treadmill at home and use a personal trainer. There were 267,000 personal trainers in the U.S. in 2012, almost a 50% increase from 2001, and it is projected that this will grow to 338,000 by 2018. Economists from the Bureau of Labor Statistics believe that occupations like fitness instructors and personal trainers are the driving force in the success of the fitness industry and that the number of people in these occupations will increase 31.7% by 2020.

### **Extending Health Spans And Why Calico Will Soon Be A Household Word**

The focus of 21st century medicine will be on adding life to years by increasing the health span of seniors. Some authorities view certain signs of aging as a disease entity that might be mitigated or even prevented by appropriate intervention. Others suggest that since every cell in our body contains the DNA template of a healthy younger version of itself, it should be possible to activate this to increase our health span. There are numerous efforts here and abroad to prevent or retard the aging process with stem cells, telomerase and diverse pharmaceuticals.

One of the most impressive is Calico, an independent research and development biotech company established by Google in late 2013 to combat aging by focusing on "health, wellbeing and longevity." Calico stands for California Life Company, and its founder and CEO is Dr.

Arthur Levinson, who succeeded Steve Jobs as chairman of the board of Apple Inc. He has received numerous awards for his research on cancer and is also chairman and former CEO of Genentech, which focuses on discovering and developing new medicines for significant unmet medical needs, especially malignancies and currently has 20 novel drugs in its pipeline. In addition, he serves on the board of directors of Broad Institute (affiliated with MIT and Harvard), Board of Scientific Consultants of the Memorial Sloan Kettering Cancer Center, the Industrial Advisory Board of the California Institute for Quantitative Biosciences (QB3), and the Advisory Council for the Princeton University Department of Molecular Biology and has previously been a member of the board of directors of Google, Hoffman-La Roche, Amyris Biotechnology and NGM Biopharmaceuticals. The significance of these affiliations is apparent from the following dazzling Calico achievements over the past 12 months.

September 3, 2014 - Calico, partnered with AbbVie, a global pharmaceutical company that was formerly a division of Abbott Laboratories, to establish an R&D facility to focus on the prevention and treatment of aging and age related diseases. Each company will invest an initial \$350 million to start with an option to add another \$700 million for a total investment of \$1.4 billion.

September 11, 2014 - Calico also announced a partnership with the University of Texas Southwestern Medical Center and 2M Companies to research drug development for neurodegenerative disorders caused by the aging and death of nerve cells. UT Southwestern researchers

had recently published a paper showing that P7C3 compounds were effective in animal models of neurodegeneration and licensed them to Dallas-based 2M companies. Calico has now entered into new agreement in which they will fund 2M research and be responsible for commercializing any new products that have been developed.

March 17 2015 - Calico and the heavily endowed and renowned Broad Institute of MIT and Harvard announced a partnership "to advance research on age-related diseases and therapeutics" that will focus on the biology and genetics of aging and early-stage drug discovery. Much of the Institute's work focuses on uncovering the genetic basis of major diseases and brings together researchers from Harvard, MIT, Harvard-affiliated hospitals, and other partner institutions. Broad Institute contains one of the largest genome sequencing centers in the world and was the largest contributor of sequence information to the Human Genome Project. The Institute has a wide range of collaborations, including more than 100 projects across more than 40 countries. The collaboration will foster progress on the understanding and treatment of age-related disease by combining the Institute's scientific knowledge with Calico's expertise in therapeutics.

March 24, 2015 - Calico launched a four-year partnership with QB3, a University of California institute, famous for its biotechnology innovation. to conduct research into longevity and age-related diseases. With committed funding from Calico, the partnership will identify and support QB3 research projects focused on aging and innovative approaches to extend healthy longevity. Calico has the option to obtain exclusive rights to discoveries made

under the sponsored research agreement. As Hal Barron, President of Research & Development at Calico stated, "*QB3's focus on leading-edge life science and interdisciplinary projects makes it an ideal partner for the difficult challenges posed by aging and age-related diseases.*" The partnership builds on momentum gained from a 2013 QB3 symposium "The Science of Staying Younger Longer," which featured leaders in the field such as National Academy of Sciences member Cynthia Kenyon, then a professor at UC San Francisco, who is now Vice President of Aging Research at Calico.

March 31, 2015- It was announced that Calico, whose mission is to harness advanced technologies to increase understanding of the biology that controls human lifespan, and UC San Francisco (UCSF), a University of California health sciences campus, have partnered on an innovative project to develop potential therapies for cognitive decline. Under the agreement, Calico will receive an exclusive license to technology discovered in the laboratory of Peter Walter, Professor of Biochemistry and Biophysics at UCSF. Dr. Walter is a Howard Hughes Medical Institute investigator at UCSF, a member of the U.S. National Academy of Sciences, and the 2014 recipient of the prestigious Albert Lasker Basic Medical Research Award, often referred to as the "American Nobel." The technology developed in his laboratory modulates the Integrated Stress Response, a set of biochemical pathways activated in response to stress, that plays an important role in age-related cognitive decline. Much of this research was led by Carmela Sidrauski, a former UCSF researcher, and now a scientist at Calico. Under the terms of the agreement, UCSF will receive an undisclosed up-front fee,



and potential milestone and royalty payments. Calico will take responsibility for further research, development and commercialization of resulting therapeutics.

April 2015 – Calico announced it would partner with the Buck Institute for Research on Aging to support research into longevity and age-related diseases. This is not surprising since the Buck is the first private, independent research facility dedicated to extending the human life span and is also in the San Francisco area. Since 1999, their scientists have studied ways to make organisms live much longer, and with better health, than they naturally would. They have already quintupled the life span of laboratory worms and using Lilliputian electrocardiogram machines and toy-size CT scanners to examine the internal organs of mice, they have been able to make them live 25 percent longer and healthier by reducing the incidence of cancer and heart disease. They have also been able to reverse age-related heart dysfunction. The details of the collaboration were not revealed but Calico will establish and maintain unspecified science operations at the Buck Institute that will give Calico the opportunity to identify, fund, and support research ranging from basic biology to potential therapies for age-related diseases. The agreement also gives Calico the option to obtain exclusive rights to discoveries made under research it supports.

July 2015 – Calico announced it had arranged for access to genetic information from AncestryDNA, which has 16 billion genealogic records, the largest online collection of Wills and probate records, millions of family trees, and more than 170 million pages plus searchable records. It also offers a simple DNA test for \$99.00

that will provide information on your ethnic mix, and possibly discover distant relatives. AncestryDNA and Calico will work together to analyze and investigate the role of genetics and its influences in families experiencing unusual longevity using Ancestry's proprietary databases, tools and algorithms. Calico will then focus its efforts to develop and commercialize any potential therapeutics that emerge from the analysis. As Dr. David Botstein, a leading geneticist who is Calico's Chief Scientific Officer and a member of the US National Academy of Sciences explained,

*"Our common experience suggests that there may be hereditary factors underlying longevity, but finding the genes responsible using standard techniques has proven elusive. This is an extraordinary opportunity to address a fundamental unanswered question in longevity research using high quality human pedigrees."* Financial terms were not disclosed.

August 2015 - Google announced plans to restructure into Alphabet Inc., wherein Google and Calico would become two of the subsidiaries of the new company along with Fiber, Google Ventures, Google Capital, Google X, and Nest Labs. However, the emphasis will be on Calico, whose budget is likely to exceed the NIH National Institute on Aging's \$1.2 billion/year. Some of this goes to other anti-aging research being conducted at The University of Michigan, the University of Texas, the University of California at San Francisco and the Mayo Clinic.

In addition, six months after Calico's charter was announced, Craig Venter, the biotech entrepreneur who spent \$100 million 15 years ago in racing the U.S. government to map the human genome and

created synthetic life in 2010, also founded a start-up to seek ways to slow aging. In March 2014, Venter teamed up with stem cell pioneer Dr. Robert Hariri and X Prize Foundation founder Dr. Peter Diamandis to form Human Longevity Inc. (HLI), a company that will use both genomics and stem cell therapies to find treatments that allow aging adults to stay healthy and functional for as long as possible. He now operates what is promoted as the world's largest DNA-sequencing lab. Its goal is to tackle one million genomes inside of four years, in order to create a giant private database of DNA and medical records. HLI has assembled a team of machine-learning experts in Silicon Valley, led by the creator of Google Translate, to build models that can predict health risks and traits from a person's genes. In an initial project, volunteers have had their facial features mapped in great detail and the company is trying to show it can predict from genes exactly what people look like. Venter says the project is unfinished but that just from the genetic code, HLI *"can already describe the color of your eyes better than you can."*

Venter also said that during October, 2015 the company will open a "health nucleus" at its La Jolla headquarters, with expanded genetic and health services aimed at self-insured executives and athletes. The center, the first of several he hopes to open, will carry out a full analysis of patients' genomes, sequence their gut bacteria or microbiome, analyze more than two thousand other body chemicals, and put them through a full-body MRI scan. He described it as being *"Like an executive physical on steroids."* The health nucleus service will be priced at \$25,000. These individuals would also become part of the

database, and would receive constant updates as discoveries are made.

However, to bring genome testing to the public, last month he announced an arrangement with Discovery Health, which insures four million people in South Africa and the United Kingdom, to make the genome service available as part of a wellness program. Discovery will pay half the \$250 fee, with individual clients covering the rest. Gene data would be returned to doctors or genetic counselors, not directly to individuals, who will receive a comprehensive report detailing their risks for specific diseases and potential strategies to modify those risks. The data collected, called an "exome," is about 2 percent of the genome, but includes nearly all genes, including major cancer risk factors like the BRCA genes, as well as susceptibility factors for conditions such as colon cancer and heart disease. Typically, the BRCA test on its own costs anywhere from \$400 to \$4,000. Last January, Human Longevity signed a multiyear deal to sequence and analyze tens of thousands of genomes for Roche Holding's Genentech unit in an effort aimed at identifying new drug targets and biomarkers.

It would not be surprising if Human Longevity was Calico's next acquisition or partner. Space constraints preclude a discussion of the numerous exciting advances that have already been made with rapamycin, the Integrated Stress Response and stem cell therapy, but these and others will be discussed in the next Newsletter — so stay tuned!!

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Editor-in-Chief

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