

Age Regression Achieved by Objective Functional Age Lab Testing on 70-Plus Year Olds via Life Style, Behavior and Precision Scientific Nutritional Modification

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Abstract

Introduction:

Many studies demonstrate efficacy of individual or several concurrent anti-aging medical, complementary and alternative medicine (CAM) strategies, as well as lifestyle changes for improving health. Few studies evaluate the cumulative impact of comprehensive simultaneous nutritional scientific metabolic interventions, CAM and lifestyle modifications to improve disease progress, symptoms of aging and overall health.

Conclusions

This study demonstrates a remarkable achievement. We have not found other studies involving multiple health parameters in the middle old and oldest old population (70-100). All facets of the study are documented anti-aging medical and CAM therapies which were carefully assessed with recognized age-related markers, monitored by trained personnel and included physical, mental, emotional and social criteria. The study was independently funded by dedicated scientists involved in anti-aging, longevity, nutritional and physical medicine research. Healthy life span is improvable and measurable with practices already available even for those exceeding average life spans. The results were further confirmed with the DNA methylation clock with significant gains in 3 months. In an effort to disprove the long-held beliefs, that aging is inevitable...years of volunteer efforts by the authors have demonstrated that the traditional and long-standing paradigm of aging...essentially seniorhood beginning at age 47 and old age at 65 was incorrect. This paradigm busting study shows that aging is not immutable. Dramatic and significant functional objective improvements across the entire spectrum of measurable aging parameters can be achieved at any age. Old age senescence can and has been reversed in human subjects as validated by this study.

In the year 2000 the American Academy of Anti-Aging Medicine (A4M) prognosticated a future where practically immortality (common lifespans of 120 years or more) could soon be possible. The findings of the study appear to support this potential future.

Keywords: complementary and alternative medicine

Introduction

This study explored the intersection between complementary and alternative medicine (CAM) strategies, comprehensive lifestyle

interventions and anti-aging medicine. Many studies exist on the prevalence and efficacy of CAM techniques and lifestyle interventions in

treating specific illnesses. However, no studies found by the authors have examined whether a comprehensive lifestyle intervention using only CAM or holistic strategies could be applied to people in any state of health or illness to improve overall health, improve markers of biological aging, and extend life expectancy.

The authors of this study were interested in untangling the relationship between aging and disease. Their hypothesis was that illness and severe bodily degradation are not a requisite part of aging and that health and quality of life can be enjoyed by people at any age and gained or regained by anyone in any state of disease; and that a comprehensive holistic lifestyle modification program could result not only in improved health outcomes and reversal of diseases, but in healthy epigenetic changes and the potential for longer life expectancy. To explore these hypotheses, the researchers designed a comprehensive lifestyle program prescribing an organic, gluten-free, vegan diet, fruit and vegetable juicing, nutritional supplements, exercise, stress-reduction, environmental hygiene, intermittent fasting, counseling and examination of beliefs and attitudes.

The group study designed around this lifestyle program examined its effect on 14 senior subjects with comorbidities and pre-existing conditions. During the past three years, the same study was conducted on five other occasions (S1-5). Blood tests were conducted analyzing biomarkers of aging, including homocysteine (HCY), hemoglobin A1C (HgA1C), C-reactive protein (CRP), prostate-specific antigen (PSA), serum vitamin D, and diabetic and coronary heart disease risk markers. Improvements in strength and stamina were measured before and after exercise tests. The HRDS was administered prior to beginning the program. In the final study (S5), methylation DNA analysis was conducted to determine if the biological age of the participants was improved. Mean results of all measurements showed improvement in all biomarkers. These results demonstrated that a holistic program provides a means of improving overall health and ameliorating or reversing age-related chronic disease.

Background

CAM or holistic techniques include a wide range of therapies not used in Western conventional medicine, including nutritional approaches (special diets, supplements, botanicals and probiotics), psychological approaches such as mindfulness, physical approaches (e.g., massage and chiropractic or osteopathic manipulation), and combinations of these such as psychological and physical modalities (yoga, tai chi, acupuncture, dance or art therapies). CAM strategies have been widely investigated, and used to treat a range of illnesses such as colorectal cancer, breast cancer, and other cancers, diabetes, skin problems, cardiovascular disease, depression, autism, and chronic pain. CAM approaches are often used by individuals to self-treat, despite the fact that most are not regulated in the same way as pharmaceutical drugs by the U.S. Food and Drug Administration or licensed by boards of health or the American Medical Association. Although many CAM treatments have demonstrated efficacy compared to placebo, the range of therapies encompassed within the term is so broad that it is difficult to generalize them or categorically assert their efficacy or safety. Nevertheless, discrete therapies within the category have demonstrated safety and efficacy.

Despite the fact that CAM is widely sought by patients, with some estimates of over 70% prevalence, the AMA and National Institutes of Health have maintained the linguistic distinction between CAM approaches and conventional medicine and see them as “alternative,” “complementary” or otherwise different from conventional standard of care. This distinction is also a regulatory one. CAM techniques are described as complementary and integrative (CIM) techniques, denoting their use as adjunct therapies, complementing or integrated into conventional standard of care. In 2016, the incoming editor of the Journal of Complementary and Alternative Medicine announced a growing collective preference for the word “integrative” over “alternative” to

emphasize multimodal approaches to medicine, combining conventional standard of care with those approaches considered complementary, alternative or traditional. In 2021, the Journal of Complementary and Alternative Medicine officially changed its title to the Journal of Complementary and Integrative Medicine.

Puzzlingly, although pharmaceutical interventions and conventional drug therapies are considered the standard of care after undergoing clinical trials and gaining FDA approval, when taken as a general category, they, too, have often demonstrated low safety and limited efficacy in prevention or cure of illness, with adverse drug reactions accounting for 4.2-30% of hospital admissions in the USA and Canada, 5.7-18.8% of admissions in Australia, and 2.5-10.6% of admissions in Europe in 2007. Indeed, many pharmaceutical interventions have been demonstrated to cause new harms to the patient, including death. The dangers and unreliability posed by many pharmaceutical interventions may be why there is growing interest in CAM techniques among patients and growing distrust of conventional approaches. Whatever the reasons, the demarcation between conventional and CAM strategies persists.

Daily habits and actions, generally referred to as lifestyle, are highly correlated with quality of life as well as short and long term health. Thousands of studies show evidence that exercise, body weight, smoking habits, and diet all impact risk for chronic metabolic diseases like coronary heart disease, diabetes, obesity and cancer. An individual's lifestyle can also encompass behaviors like coping-mechanisms and stress-management and environmental exposures to toxic pollutants. Because research has shown that non-native non-ionizing electromagnetic radiation (EMR) from modern wireless devices can negatively impact cellular function, mood and behavior, and this exposure can be modulated by habits, EMR exposure also falls into the category of lifestyle factors. Arguably related to lifestyle is mental outlook; in the present study, mental attitude and point of view were also addressed by the intervention, with a focus on transforming negative outlooks into positive ones.

In the domain of “lifestyle medicine,” comprehensive lifestyle interventions have been applied to deal with specific illnesses, such as obesity, cancer, diabetes, cardiovascular disease, and Alzheimer's disease and other mood and neurological disorders. In contrast to a single-drug approach to Alzheimer's disease, which may delay progression of certain symptoms like memory loss but have not prevented or reversed disease, the Bredesen protocol addresses diet, physical activity, sleep, stress, and environment, and how improvements in these parameters may positively modify Alzheimer's risk. Studies of the Bredesen protocol have demonstrated that this type of multi-factorial, comprehensive, and personalized therapeutic program can diminish risk for and stabilize or reverse the cognitive decline in Alzheimer's disease. Likewise, a comprehensive lifestyle modification program can produce a 7% to 10% reduction from initial weight, thus improving several CVD risk factors, including the prevention of type 2 diabetes.

Dean Ornish MD demonstrated that intensive lifestyle changes without the use of lipid-lowering drugs led to regression of severe coronary atherosclerosis and fewer cardiac events after 1 year and that these improvements increased after 5 years compared to a control group in which coronary atherosclerosis worsened and cardiac events increased. His well-known program prescribes a 10% fat whole foods vegetarian diet, smoking cessation, stress management training, aerobic exercise, and group psychosocial support. In 2006, Ventegodt et al. validated replications of his program and called for further allocation of resources and research into holistic lifestyle interventions as cures for disease. In 2000, Stampfer et al. found that a similar diet, exercise pattern, low alcoholic consumption, no smoking, and consumption of certain nutrients were associated with low cardiovascular disease risk, and that each separate element of a low-risk lifestyle predicted risk. More recently, in 2011 Gupta et al. investigated a similar intervention, called a happy healthy lifestyle (HLS) program, prescribing low-fat, high-fiber

vegetarian diet, moderate aerobic exercise and stress-management through yoga meditation. They found that 50%+ adherence to the program achieved significant healthy changes, 91% of patients showed a trend toward regression of coronary lesions, 51.4% of lesions regressed by more than 10 absolute percentage points, and that cardiac events were 11 among those most adherent and 38 among those least adherent over 6.48 years.

The United States is plagued by worsening general health and growth in persistent chronic health conditions. A chronic health condition is “a physical or mental health condition that lasts more than one year and causes functional restrictions or requires ongoing monitoring or treatment.” Chronic diseases are prevalent in the United States, causing suffering to those who have them, as well as great expense to the healthcare system. They are the leading cause of death and disability in the U.S. Nearly half of all people in the United States have at least one chronic disease, which include cancer, diabetes, hypertension, stroke, heart disease, respiratory diseases, arthritis, obesity, and oral diseases. Three in five adult Americans had at least one chronic condition in 2014, and two in five had more than one. More than 70 million Americans over the age of fifty, or 80% of older adults, suffer from at least one chronic condition.

Aging is thought to be an irreversible, complex, time-dependent process manifesting as progressive physiological and functional deterioration on the molecular level leading to increased risk of chronic disease, including dementia, cardiovascular disease and cancer. As life spans have lengthened over the recent centuries, health spans have not, and there is a need to reduce the risk of developing disease in aging populations.

Anti-aging medicine refers to treatments that slow or reverse the aging process. Natural approaches include therapies such as acupuncture, chiropractic, calorie restriction and the consumption of antioxidants. Conventional approaches include pharmaceuticals, use of stem cells and hormone therapy.

Correlated to anti-aging medicine is the study of epigenetics, the branch of genetics which studies how preexisting genes can be made active or silent through choices and environmental factors, resulting in changes to chemical components of the DNA. Epigenetic changes are directly involved in the aging process and the development of age-related disease. DNA methylation is one of these epigenetic changes that is characteristic of aging, which affects cellular processes and impacts disease development. Sampling the blood is a tool used to analyze the epigenetic markers of one's genome and the presence and prevalence of proteins related to DNA methylation. Epigenetic scores based on protein levels in the blood could predict a person's risk of contracting these chronic diseases.

Most diseases related to aging coincide with the presence of chronic inflammation, which can be seen in blood samples by the presence of inflammatory cells and increased prevalence of pro-inflammatory cytokines. In this inflammatory state, epigenetic changes and DNA methylation occur, which cause systemic disruption and results in illness, including neurodegenerative disorders, cardiovascular disease, cancer and diabetes.

DNA methylation biomarkers can be used to ascertain the biological age of any tissue at any age in the human life. New evidence is emerging to support the relationship between epigenetic age acceleration and environmental factors or disease. The term DNA methylation-based clocks has been coined to describe biomarkers of disease risk and predictors of life expectancy and mortality.

Biomarkers related to aging examined in the present study include homocysteine (HCY), a cardiovascular biomarker and amino acid that plays a role in lipid metabolism folic acid and vitamin B break down; C-reactive protein (CRP), a protein that indicates blood levels of

inflammation; serum vitamin D levels, a biomarker in neurological, psychiatric and autoimmune disease, production of which is reduced by 50% as a result of age-related decline in renal function, causing a decrease in calcium absorption; hemoglobin A1C (HgA1C), a metabolic biomarker that measures the amount of sugar bound to hemoglobin in red blood cells; prostate-specific antigen (PSA), a widely used biomarker for tumors, highly correlated to prostate cancer; and estimated coronary heart disease (CHD) risk.

Methods

Over a three-year period, five successive discrete small groups of averaging forty individuals were recruited from the audience of a health radio program on the Progressive Radio Network, The Gary Null Show, to attend a health retreat at an idyllic rural retreat center in Mineola, Texas. Recruitment periods for each replication of the retreat were six months prior to the beginning of each study. All volunteers were questioned over the phone by one of the authors of the study to determine whether they would be willing to commit to a comprehensive lifestyle program and participate in a clinical study lasting three months, the first two weeks of which (1 month in S1) would be held at the retreat center, and the remaining 2.5 months of which (2 months in S1) would be individually completed at home with remote support from two of the study leaders. The study dates were from September to November 2020 (S1); April to June 2021 (S2); September to November 2021 (S3); April to June 2022 (S4) and September to November 2022 (S5). All volunteers who were accepted based on this criteria for eligibility happened to be over age 70. Among the totality of participants, the oldest was 95, and the youngest was 70.

All of the participants were required to have a negative PCR test for the SARS-CoV-2 virus prior to entering the campus. An enrollment criterion was that no participant was taking any prescription medication. Participants of each observational group arrived at the retreat location at the start of their respective observational period and remained there for the first 2 weeks (1 month in S1). On campus, participants were instructed and guided to follow a strict lifestyle and behavior modification program. Because each group spent the first two weeks of the study in a retreat setting with other participants and the study facilitators, there was a group dynamic which supported individual progress. All participants followed the identical program. The therapeutic elements stipulated by the program were chosen based on the criteria for inclusion that each element must be supported by a minimum of five distinct peer-reviewed studies from the National Library of Medicine. These references are included in the supplementary material.

Blood samples were taken at the beginning of the study and at the end of three months. Every morning, a nurse took everyone's pulse, temperature, and, when necessary, the blood sugar measurements of diabetics. All participants were required to have regular impedance tests to measure BMI, muscle mass, bone mass, and hydration levels.

The protocol to which participants adhered for the duration of the study prescribed regimens of diet, supplementation, exercise, intermittent fasting, stress-reduction, environmental hygiene, and examination of emotions and beliefs.

Diet

The prescribed diet was organic, vegan and gluten-free. A plant-based diet has been associated with lower risk of cardiovascular disease, heart attack, stroke, hypertension, diabetes and cancer. A gluten-free diet has been recognized as useful in treatment of Celiac disease, gluten ataxia, dermatitis herpetiformis, cognitive impairment, inflammatory bowel disease and irritable bowel syndrome, non-celiac gluten sensitivity, fibromyalgia, endometriosis and chronic pelvic pain, although careful planning of a gluten-free diet is advisable to avoid nutritional deficiencies. Consumption of organic foods versus conventional foods has certain

nutritional advantages, reduces exposure to pesticide residues and antibiotic-resistant bacteria, and is associated with lower incidence of infertility, birth defects, allergic sensitization, otitis media, pre-clampsia, metabolic syndrome, high BMI, and non-Hodgkin lymphoma.

The studies' diet was focused on phytonutrient rich fruits, vegetables and 'superfoods,' whole grains and legumes. The major daily meal was lunch followed by a light vegan meal for dinner, which comprised soups and salads. The foods served at the retreat and which the participants were asked to eat on their return home were all shown to be health-promoting by peer-reviewed studies from the National Library of Medicine and included in the references. They included acai, acerola, almonds, aloe vera, apples, banana, barley grass, beets, blueberries, broccoli, brown

rice, Brussel sprouts, cabbage, carrots, cauliflower, cayenne, celery, chlorella, cocoa, collard greens, cranberry, flaxseed, garlic, ginger, goji, grapes, green tea, kale and spinach, kelp and seaweed, lemons, legumes, millet, moringa, mushrooms, onion, oranges, parsley, peaches, peanuts, peppers (capsaicin), pineapple, pomegranate, pumpkin seeds, quinoa, sesame seed, spirulina, strawberries, sunflower seeds, walnuts, watercress, watermelon, and wheatgrass.

Nutritional Supplementation

The participants took the following nutritional supplements and vitamins daily as listed in the chart below with daily doses.

Daily Supplement Regimen					
Vitamin B Complex		Vitamin K2	250 mcg	L-Carnosine	1000 mg
- Vitamin B1	100 mg ^{ccix}	Omega-3 ^{cc}		L-Ergothionine	5 mg
- Vitamin B2	75 mg ^{cci}	- DHA	500 mg	L-Taurine	800 mg
- Niacin	100 mg ^{ccii}	- EPA	700 mg	Curcumin	500 mg ^{cciii}
- Vitamin B6	200 mg ^{cciv}	CoQ10	100 mg ^{ccv}	Green Tea Extract	725 mg
- Folate	680 mg ^{ccvi}	Magnesium	250 mg ^{ccvii}	Livitol (kokum)	500 mg
- Vitamin B12	300 mcg ^{ccviii}	Quercetin	260 mg	Pycnogenol	100 mg ^{ccix}
- Biotin	1000 mcg ^{ccx}	NAD+	100 mg ^{ccxi}	Actiponin	450 mg
- Pantothenic acid	500 mg ^{ccxii}	DHEA	25 mg	Hesperidine	500 mg
- Inositol	100 mg	R Lipoic Acid	150 mg ^{ccxiii}		
- PABA	50 mg	Resveratrol	220 mg ^{ccxiv}		
Vitamin D3	5000 IU ^{ccxv}	PQQ	40 mg ^{ccxvi}		

Juicing

Juicing fruits and vegetables removes the fibrous part of the plant and leaves the polyphenol rich juice which has been shown to improve the cardiovascular system, inhibit platelet aggregation, prevent hyperhomocysteinemia and possess anti-inflammatory, antioxidative, immune-modulatory and antimicrobial benefits to the gut microbiome and the body as a whole. To flood the body with these nutrients, the participants were required to drink twelve 8-oz vegetable and fruit juices per day, though juice was available for them at all times in case they wanted more. The ingredients in the juices included: ginger, aloe vera, lemon, cocoa, acerola, agaricus (mushroom), and moringa. Juices were prepared according to a sequence of fruit juices in the morning and vegetable juices in the afternoon; this regimen was continued at home. All the participants were provided with juice recipes and received class instruction about the health benefits of juicing and how to prepare during their stay on-campus.

Exercise

Exercise is a quintessential component of lifestyle interventions and is associated with low all-cause mortality. The exercises included power walking in the morning; and later in the day, a series of exercises practiced in the gym, including water aerobics, biking, lateral pulls, sit-ups, push-ups, arm curls, squats, battling ropes, versa climbing and endurance exercises.

Intermittent Fasting

Intermittent fasting has been shown to improve metabolic health. The participants were instructed to fast for a period of about fifteen hours, from evening (7 pm) until late morning (10 am) of the following day. Participants were permitted to have lemon water at 8 am prior to a morning power walking and exercise. The same fasting regimen was repeated during throughout the remainder of the study at home. On

weekends (Saturday and Sunday), only juicing was consumed and no solid foods.

Stress Reduction

Stress is an important factor implicated in the development of disease. Stress reduction techniques have shown significant benefits for health. The techniques for stress reduction followed by the participants included yoga, mindfulness meditation, tai chi and qi gong, making art and time in nature.

Environmental Hygiene

Environmental factors are strongly correlated with good health, quality of life and longevity. The first part of the study conducted on campus was in a bucolic rural environment with clean air, filtered water, no noise or sound pollution, and extremely limited non-native non-ionizing electromagnetic radiation. The participants had no access to a computer and were asked not to bring their cell phones but to leave them at home. The participants were instructed about environmental hygiene as a part of a lecture series delivered by one of the study leaders. They were asked upon their return home to remove environmental toxins and chemicals from their lives and routines and replace chemical-laden products with non-toxic alternatives.

Counseling

Part of the program was dealing with negative emotions and examining inhibitory and harmful belief systems. There were professional counselors present on campus to provide counseling to people to help them overcome these psychological barriers to mental well-being. The participants also engaged in keeping a daily journal. Also, the lecture series delivered by Gary Null, PhD provided techniques for improving state of mind and a sense of well-being. Lecture topics included: happiness, anger, discovering purpose in life, love, life energies, forgiveness and honoring one's self.

Overseeing the administration of and adherence to the program were at least 2 registered nurses and a separate supervisor for each part of the protocols: one overseeing exercise, another overseeing meal planning and juicing, another overseeing supplementation. Additional experts remained on campus to present classes on fermentation and the importance of probiotics in the diet. A separate supervisor oversaw the

stress management program, and another made sure that all of the health measurements were taken on a daily basis. All workshops were held in silence (excluding the instructors), unless participants had questions to be answered.

A typical weekday is represented in the following chart.

	Weekday schedule
7:00 AM	Stretching classes, followed by power walking 10,000 feet, increased by 1,000 feet per day
8:00 AM	Round 1 of fresh organic fruit and/or vegetable juice and protein shakes; consumption of one or two 8-oz juices (fresh juice was accessible for participants to consume all day in addition to pre-determined times)
8:15 AM	1 hour workout in gym (e.g. biking, lateral pulls, sit-ups, push-ups, arm curls, squats, battling ropes, versa climbing and/or endurance exercises)
9:15 AM	Round 2 of juice
9:20 AM	30 minutes water aerobics
9:50 AM	Round 3 of juice
9:55 AM	1 hour yoga
10:55 AM	Round 4 of juice
11:00 AM	2 hours of mindfulness meditation, stress reduction, tai chi, chi gong, art and/or time in nature
1:00 PM	Round 5 of juice and 1 hour vegan lunch
2:00 PM	Quiet journaling time conducted in silence
3:00 PM	Round 6 of juice
3:05 PM	1-hour self-empowerment class, e.g. on the impact of negative emotions on daily choices (anger, guilt, fear, insecurity, shame, uncertainty), how to consciously make healthy choices when faced with negative emotions for improved health outcomes.
4:05 PM	Round 7 juice
4:15 PM	Exercise class
5:00 PM	Light vegan meal
6:00 PM	Lecture on issues impacting aging, e.g., telomeres, stem cells, inflammation, stress, exercise, caloric intake, fasting, genetics, environmental toxins, electromagnetic radiation, and social conditioning.
7:00 PM	Round 8 juice
7:15 PM	Instruction in fifteen hour intermittent fasting regimen
10:00 PM	Bedtime, lights out

On Saturdays and Sundays, the participants followed a juice fast and observed silence for the entire day, engaging in limited exercise once per day, and meditation. There were no workshops or lectures on Saturday or Sunday, but various self-empowerment video presentations were made available, such as Wayne Dyer and Deepak Chopra. The idyllic, landscaped grounds and gardens of the retreat center were available for participants to spend time in nature. At the end of their two-week stay on campus, participants returned home and continued the same program. Weekly conference calls were held with Dr. Gary Null and Luanne Pennesi RN to maintain the motivation and discipline of the attendees as well as to address any changes in their health status. At the end of 90 days, everyone completed exit blood tests, which were conducted under the supervision of the Life Extension group who also collated the results. A

second set of physical examinations, identical to those made on the first day of the study, were again made at the end of the study: impedance tests, body measurements and tests of endurance and strength. The HRSD was again administered. The self-report survey of QOL measurements was taken again at the end of the three months.

In S5, each participant had a before and after methylation DNA analysis test performed to determine whether the intervention had extended their potential life expectancy.

Results

Comparing the health criteria on entry with final results, among the improvements of greatest import are that there was a 15% decrease in

group risk of coronary heart disease, appreciable decreases in inflammatory markers such as CRP and substantial decreases in diabetes markers such as HgA1C. Hormone levels increased, vitamin D levels stabilized across all participants and there was a noticeable increase in insulin-like growth factor 1. There were improvements in energy, stamina and strength, and self-reported emotional improvements.

The implications of the present findings bear significance: multiple pre-existing health conditions borne by the participants, substantially improved within 90 days. Several attendees began the study overweight and lost significant weight during the observational period. The majority of participants came in with chronic stress, clinical depression and anxiety disorders; some had high blood pressure or type II Diabetes; all showed improvements.

Below is a brief sampling of improvements.

Member 1: Homocysteine decreased from 22 to 12 umol/L, increased insulin growth factor from 38 to 98 ng/mL, muscle mass went up from 43 to 49%, lost 2" in the hips (39" to 37").

Member 2: C-Reactive Protein decreased from 14 to 3 mg/L; triglycerides went from 159 (high) to 101 mg/dL (normal).

Member 3: increased physical stamina: squats from 41 to 90, arm curls from 24 to 45, decreased homocysteine from 9.3 to 6.6 umol/L, dropped elevated Hemoglobin A1C from 5.8% to 5.5 % (normal), increased free testosterone from 0 to 37 ng/dL.

Member 4: lost 23 pounds (199 lb to 176 lb) after being overweight for years; blood pressure dropped from 132/80 to 120/70, increased energy and stamina (squats 30 to 46, ab curls 47 to 75), resting pulse went down from 90 to 75 bpm, dropped cholesterol from 206 (high) to 180 mg/dL (normal).

Member 5: elevated triglycerides (pre-diabetes) decreased from 182 (high) to 97 mg/dL (normal), insulin resistance LP-IR Score went from 63 (elevated) to 34 (normal).

Member 6: Hemoglobin A1C went from 5.7% (elevated) to 5.1% (normal), dropped 6 pounds (112 lb to 106 lb), almost quadrupled capacity for push ups (from 10 to 37), capacity for sit ups almost tripled (from 30 to 75).

Member 7: lost 2" in waist (37" to 35"), 1.5" from hips (42" to 40.5") and 3.5" from thighs (23.5" to 20"); resting heart rate down from 75 to 62 bpm; increased strength and stamina: capacity for pushups increased from 25 to 40 (almost doubled), capacity for sit ups increased from 20 to 40 (doubled).

Member 8: overweight woman lost 29 pounds (168 to 139 lb), liver enzymes went from 47 (elevated) to 21 IU/L (normal), cholesterol went down from 212 to 190 mg/dL; lost 4 inches in chest (38 to 34"), lost 17 inches around her waist (39 to 22"), lost 8 inches around her hips (44 to 36") and 5 inches around her thighs (26 to 21").

Member 9: Estimated CHD risk decreased from 1.3 (high) to 0.7 (normal); BP systolic dropped 10 points (124/70 to 114/70), strength and stamina doubled in pushups (15 to 30), squats (100 to 200), ab curls (15 to 30).

Member 10: decreased elevated liver enzyme LDH from 234 to 196 IU/L (normal), decreased homocysteine from 17.5 (elevated) to 15.9 umol/L (normal), decreased insulin resistance LP-IR Score from 59 (high) to 32 (normal).

In addition, the S5 group also had before and after DNA demethylation test performed. This segment of the study will be the subject of a separate article. However, during a conference call with Robert Brooke, Director of the Epigenetic Clock Development Foundation (ECDF) at UCLA, the analysis concluded that the intervention had improved the participants'

life expectancy on the GrimAge baseline by an average 2.15 years ($p = 0.02$). The outliers were one participant who gained 7.5 years and another patient who lost approximately 4 years.

Discussion

Two of this study's limitations are the small number of participants enrolled and the controls to assure the participants' compliance to follow the protocol throughout the entire length of the three-month study. All participants adhered to the identical protocol of diet, juicing, supplementation, exercise, intermittent fasting and stress reduction exercises daily during the first two weeks while they were in residence together. The first two weeks were conducted under strict professional supervision and regular medical evaluation. During the second 2.5 months, participants were expected to follow the full protocol individually at home. Despite regular weekly online check-ups with each participant after the in-residence period, two of the fourteen participants failed to comply with the protocol adequately. The blood tests indicate that these two participants' results are negative outliers to the remainder of the group and were not included in the study results. This was also the case for the prior studies where initial recruitment averaged at approximately 20 persons with a 30 percent dropout rate during the on-campus section of the study and several additional participants unable to complete the entire 3 months.

Subjective factors that contribute to objective outcomes

In the field of anti-aging medicine much attention is given to objective measurements of blood pressure, heart rate, blood flow, acuity of cognition, muscle tone, co-morbidities, body mass index and other measurable variables. These confer useful data necessary to infer the effects of certain lifestyle choices such as diet, hydration, exercise and sleep patterns. To benefit from these lifestyle choices, subjective factors, such as mood, motivation to change habits, and the experience of negative emotions, play a role. Such subjective factors contributed to whether the participants completed the present study and were willing to make the changes in lifestyle and behavior that offered benefits.

It took a period of the first two weeks in each replication of the study to ameliorate the diseases suffered by the participants enough to establish a base-line of health for engagement in the protocols. Because the study design did not account for the obstacle of inadequate participant motivation to complete the study, the study authors formulated several techniques to increase motivation, such as the delivery of twenty-six motivational lectures in the first week, on topics such as what does one have to live for. These lectures improved the motivation needed to make such comprehensive changes in lifestyle and habits as were required by the protocols. A key factor differentiating those participants who successfully completed the study, following the protocols until the end, from those who dropped out was motivation.

In study 5, 20 individuals began the study and 12 adequately completed it. Six dropped out in the first two weeks. Those who dropped out reported that the regimen was too difficult. Specific reasons given included that they were not used to taking supplements, that the protocol was too rigorous, that they weren't used to certain foods like seaweed, they weren't used to juicing, they were not used to spending time in silence, and they were not used to rigorous exercise (most did no habitual exercise prior to joining the study).

When on their own back in their home environments, 2 participants dropped out, citing difficulty following the protocols on their own. The adherent participants experienced ongoing improvements, with continued remote support from Dr. Gary Null and Luanne Pennesi.

The study leaders found, in each of the five studies, that intellectually-oriented explanations alone were not motivating enough for participants to want to take up a new set of habits. The group dynamic was observed

to support adherence to the new habits. However, why some participants could continue to adhere to the new habits at home on their own and some could not require further investigation.

Difficulties pertaining to senior cohorts.

This study's primary participants were exclusively senior citizens. This population tends to suffer from and experience a higher degree of loneliness, depression, and anxiety, as well as poorer health and immune function. Seniors are more subject to comorbidities, have less neuroplasticity and greater loss of both memory and cognitive function. According to the National Council on Aging, approximately 30% of seniors suffer from some degree of depression. Daniel Murman's study in the National Library of Medicine of cognitive decline in older adults shows this trend is significant and increasing.

Clinical trials and research that attempt to include older adults suffer from exclusion criteria, and therefore the enrollment of older people in clinical research has suffered from underrepresentation. For example, although cancer primarily affects older adults, most clinical cancer trials enroll younger participants. Exclusion of older participants is common, especially in small group studies. Maintaining the recruitment numbers of older adults is also problematic with upwards of 49% being excluded; average drop-out rates can be as high as 37%. A fundamental reason for the high exclusion rate among the elderly is pre-existing comorbidities. There is also the difficulty in assessing probable undiagnosed comorbidities. Drop-out rates are largely due to older people struggling more to follow a clinical trial regimen for the trial's entire length. In addition, unexpected complications are more likely to occur.

Clinical trials evaluating new pharmaceutical interventions frequently exclude anyone with a pre-existing health condition that would adversely affect the outcomes of the trial. Conversely, the present study did not exclude anyone who volunteered to participate, unless he or she was not ambulatory and/or otherwise could not participate in all the activities. Multiple participants had pre-existing diagnoses of clinical depression, anxiety, obesity, Alzheimer's disease, as well as other medical conditions. Many with pre-existing illnesses showed remarkable improvement, or complete reversal of their conditions. The mean self-reported improvement in all 16 markers of mental health of the participants in Study 5 was between 11.5% and 34.7%.

Difficulties in home access to requisite equipment

At the end of the two weeks on campus, all of the participants had completed 12 separate exercise protocols. They made improvements in performance, indicating improved overall health. These exercises included lateral pulls, sit-ups, push-ups, arm curls, squats, battling ropes, power walking, versa climbing and endurance exercises. However, the authors of the study did not anticipate that upon returning home, the participants would not all have access to exercise equipment and gyms to continue progress in these exercises. Therefore, included in the chart of those improvements are only those participants who continued these exercises at home.

Conclusion

This study series demonstrated that comprehensive CAM lifestyle modifications can positively alter both objective and subjective markers of disease progression, symptoms of aging/overall health and longevity potential. Though these improvements were gained initially in a controlled environment, through the distance-support system, they were continued and advanced once the participants left the campus and returned to their homes and lives.

We performed five clinical studies using the same protocol during a 3-year period. The results produced by the protocol in each succeeding study confirmed the findings of the one prior to it. The improvements generated by adherence to the protocol were consistent through all five studies. The study's results establish a basis that it is possible, under the right circumstances, to prevent illnesses, reverse illnesses, and extend the lifespans of human beings through interventions.

The present findings suggest that the aging process is not a static, unrelenting, and inevitable descent into disease, or the inexorable decline of one's cognition and physical capacities. This data provides a basis for understanding aging as the manifestation of a dynamic and sensitive set of responses of a person to the physical, mental and emotional stimuli to which he or she is exposed. Aging can be steered towards health or illness depending on individual choices related to quality of nutrition, regular exercise and stress reduction. A comprehensive program prescribing healthy nutritional choices, regular exercise and stress reduction can improve markers of aging and disease and restore normal health to unhealthy seniors.

Anti-Aging Markers – Blood Tests (3 months)

n=12 participants (male = 4; female = 8)

Marker	Start Value	End Value	Change	% Change
Est. CHD Risk				
Sum	10.0	8.5	-1.5	-15.0%
Mean	0.8	0.7	-0.1	-15.0%
Homocysteine				
Sum	152.2	144.2	-8.0	-5.3%
Mean	12.7	12.0	-0.7	-5.3%
C-Reactive Protein				
Sum	32.22	18.17	-14.05	-43.6%
Mean	2.7	1.5	-1.2	-43.6%
Hemoglobin A1C				
Sum	66.3	64.0	-2.3	-3.5%
Mean	5.53	5.33	-0.19	-3.5%
Vit D, 25-Hydroxy				
Sum	675.8	711.0	35.2	5.1%
Mean	56.30	59.25	2.95	5.1%
Prostate Spec Ag	(men only)			
Sum	70.0	66.3	-3.7	-5.3%

Mean	17.50	16.58	-0.93	-5.3%
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Exercise Performance & Hamilton Depression Scale

	3 min step test – heart rate before	3 min step test – heart rate after	Push Up to Failure	Squat to Failure	Arm Curl Test – R Arm	Arm Curl Test – L Arm	Hamilton depression survey
AGGREGATE RESULTS	5.06%	-4.99%	171.10%	117.62%	66.30%	60.22%	-41.19%

Self-Report Subjective Improvement Survey (5 months)

(individual participant Scale, 1=worst through 10=best) n=12 participants

Marker	Start Value (mean)	End Value (mean)	Change (mean)	% Change
Sleep	6.25	8.42	2.17	34.7%
Pain	7.00	8.92	1.92	27.4%
Energy	6.67	8.75	2.08	31.3%
Fatigue	6.33	8.33	2.00	31.6%
Clarity	7.50	9.08	1.58	21.1%
Outlook	7.25	9.00	1.75	24.1%
Breath	7.75	9.08	1.33	17.2%
Loneliness	7.25	8.08	0.83	11.5%
Motivation	7.58	8.92	1.33	17.6%
Discipline	7.42	8.92	1.50	20.2%
Challenges	6.75	8.08	1.33	19.8%
Relevance	7.50	8.83	1.33	17.8%
Emotional Control	7.25	8.58	1.33	18.4%
Depression	7.42	9.00	1.58	21.3%
Anxiety	6.00	7.75	1.75	29.2%
Relationships	7.08	8.50	1.42	20.0%

Ethical Approval

The study did not require ethical approval as it did not involve the introduction or use of any drug or medical device and the participants in the study were not treated as patients. It was strictly a lifestyle and behavioral modification program and there was no medical intervention involved. Participants signed a release form prior to joining the study.

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collectively donated more than 2000 hours over a period of one year in preparing the study, as well as over 1000 hours after completion. The study participants covered the costs of their lodging and transportation to and from the venue.

Author contributions

William Faloon formulated criteria for assessment of improved health; Life Extension group provided blood chemistry analysis and the intermittent fasting regimen. Robert Goldman formulated the exercise protocols and criteria for blood analysis. Ronald Klatz formulated criteria for assessing behavioral changes, anxiety, and depression. Scott Fogle formulated the protocol for nutritional supplementation. Luanne Pennesi oversaw the entire study, assembled an observational team for venipuncture, administered impedance tests, provided individual health counseling, organized lectures, took daily participant and staff

temperatures, resting pulse rates, and blood pressure, and supervised the daily stress management regimen. Gary Null formulated the dietary protocol, including daily menus and juicing. Richard Gale researched the protocols and verified all elements were supported by five peer-reviewed articles. Philip DeRossi compiled the data and drew the tables.

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