JACOBS PUBLISHERS

OPEN ACCESS

Jacobs Journal of Gerontology

Review Article

Introduction to the Science of Anti-Aging Medicine: A State-of-The-Specialty Review

Ronald Klatz*[1]

[1]The American Academy of Anti-Aging Medicine, USA.

*Corresponding author: Dr. Ronald Klatz, M.D., D.O., President, The American Academy of Anti-Aging Medicine; 1510 West Montana St., Chicago IL 60614 USA, Tel: 773-528-6100; Email: drklatz@a4minfo.net

Received: 01-28-2015

Accepted: 02-13-2015

Published: 03-13-2015

Abstract

Anti-aging medicine is a clinical specialty is founded on the application of advanced scientific and medical technologies for the early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases. It is a healthcare model promoting innovative science and research to prolong the healthy lifespan in humans. As such, anti-aging medicine is based on principles of sound and responsible medical care that are consistent with those applied in other preventive health specialties. Today, thousands of physicians and practitioners in private medical offices, as well as at some of the most prestigious teaching hospitals around the world, now embrace the anti-aging medical model. Undeniably, anti-aging medicine is achieving demonstrable and objective results that beneficially impact the degenerative diseases of aging. Anti-aging medicine is transforming healthcare, one practice at a time. In this article, the authors establish the background, history, and accomplishments of the anti-aging medical model, and discuss future developments in this fast-growing clinical specialty.

Keywords: Aging Intervention; Anti-Aging; Advanced Preventative Medicine; Biomedical Technologies; Lifespan; Healthspan; Life Extension; Life Enhancement

Introduction

Today, thousands of physicians and practitioners in private medical offices, as well as at some of the most prestigious teaching hospitals around the world, now embrace the anti-aging medical model. Anti-aging medicine is achieving demonstrable and objective results that beneficially impact the degenerative diseases of aging. Herein, the physician co-founders of the anti-aging medical movement review the background, history, and accomplishments of the anti-aging medical model, and discuss future developments in this fast-growing clinical specialty.

Definition and Key Concepts in Anti-Aging Medicine

Anti-aging medicine is a clinical specialty is founded on the application of advanced scientific and medical technologies for the early detection, prevention, treatment, and reversal of age-related dysfunction, disorders, and diseases. It is a healthcare model promoting innovative science and research to prolong the healthy lifespan in humans. As such, anti-aging medicine is based on principles of sound and responsible medical care that are consistent with those applied in other preventive health specialties. The phrase «anti-aging,» as such, relates to the application of advanced biomedical technologies focused on the early detection, prevention, and treatment of aging-related disease.

Anti-aging medicine is the following:

- **It is scientific.** Anti-aging diagnostic and treatment practices are supported by scientific evidence and therefore cannot be branded as anecdotal.
- **It is evidence-based.** Anti-aging medicine is based on an orderly process for acquiring data in order to formulate a scientific and objective assessment upon which effective treatment is assigned.
- **Is well-documented by peer-reviewed journals.** As of this writing, the National Library of Medicine hosts more than 3,000 peer-reviewed articles on the subject of

anti-aging medicine. Scientific and academic journals that routinely publishing studies relating to life enhancement and/or life extension include:

Annals of Internal Medicine
BMJ (British Medical Journal)
Cancer Prevention Research
European Heart Journal
FASEB Journal (Federation of American Societies for Experimental Biology)
JAMA (Journal of the American Medical Association)
Lancet
Neurology
PLOS One

It is a seminal position of the anti-aging medical science, that aging is not inevitable, in that longevity is not finite. In a study conducted [1] by demographer J. R. Wilmoth and colleagues, the researchers found that in Sweden, the maximum age at death has risen from 100 years during the 1860s to about 108 years during the 1990s. They also make note that the increase in longevity has become expedited: before 1969, the increase in maximum age at death increased at 0.44 yr/decade; and since 1969, it has risen at the pace of 1.11 yr/decade. The team cites «an intensification of efforts … to prevent or even cure ailments such as coronary heart disease, stroke, and cancer» has profoundly contributed to «the more rapid rise in the maximum age since 1969".

The goal of anti-aging medicine is not to merely prolong the total years of an individual›s life, but to ensure that those years are enjoyed in a productive and vital fashion. When we co-founded the American Academy of Anti-Aging Medicine (A4M; www.worldhealth.net) in 1991, we established the field of anti-aging medicine as a direct extension of sports medicine. Just as sports medicine aims to keep the athlete's body functioning at its optimum level, anti-aging medicine seeks to keep the body functioning at its peak. In other words, the similar principle, of extending and maximizing the healthy human lifespan, is at the core of both anti-aging medicine and sports medicine.

Around the world, people are seeking medical guidance for ways to stay healthy, active, and vital well into their older years. The exponential growth in the popularity of anti-aging medicine is largely a result of the global demographics shift towards a swelling aging population. The United Nations observes [2] that: "The world is in the midst of a unique and irreversible process of demographic transition that will result in older populations everywhere. As fertility rates decline, the proportion of persons aged 60 and over is expected to double between 2007 and 2050, and their actual number will more than triple, reaching 2 billion by 2050. In most countries, the number of those over 80 is likely to quadruple to nearly 400 million by then."

As a patient-centric, wellness-oriented model of advanced clinical preventive medicine, the principles of the anti-aging medical model. are gaining rapid and widespread acceptance as a framework for lifelong habits for healthy living . This innovative medical specialty is achieving demonstrable and objective results that beneficially impact the degenerative diseases of aging.

Fundamentals of Anti-Aging Medicine

As we age, changes take place in our body systems. Cellular processes slow down, and our organs and tissues become less robust in performing their tasks and functions. From head to toe, and beginning as early as the second decade of life, our body systems begin to demonstrate senescence – that is, signs of old age.

Table 1 presents the ten key systems in the body that age. While until now the declining performance in these biological processes has been accepted as a «natural» part of aging, in the anti-aging medical model we no longer consider the declines as inevitable. Anti-aging medicine addresses aging as a treatable medical condition, aiming to reduce or eliminate the disabilities, diseases, and dysfunctions we have grown used to assuming are a part of growing older.

Table 1. Key Body Systems that Age

1	**Endocrine system,** responsible for the hormonal response
2	**Immune system**, which mounts the body's response to infectious invaders
3	**Metabolic system,** involving age-related physiology changes
4	**Cardiovascular system**, involving the heart and arteries
5	**Gastrointestinal system,** affecting absorption of nutrients from food
6	**Reproductive system,** including menopause (in women) and andropause (in men)
7	**Nervous system,** responsible for the body's muscular response to stimuli
8	**Brain function,** including memory and cognition
9	**Muscular system,** involving strength and function
10	**Sensory system,** including the senses of touch, taste, smell, sight, and hearing

The clinical specialty of anti-aging medicine is concerned with extending lifespan – the maximum number of years a person lives, as well as healthspan – how well, absent of infirmity and disability, a person lives. Currently, clinical approaches to enhance the healthspan while extending the lifespan are conducted in twelve major focus areas, as listed in Table 2.

Table 2. Major Focuses of Clinical Anti-Aging Medicine

Anti-Aging Endocrinology & Hormone Replacement Therapy	Metabolic & DNA Repair
Antioxidant Analysis & Optimized Supplementation	Skin De-Aging & Repair
Maximized Immune Function	Lifestyle Modification
Detoxification	Musculoskeletal Rehabilitation-Sports Medicine-Conditioning
Cardiovascular Protection	Biomarkers of Aging Assessment & Prospective Advanced Diagnostics
Cognitive Function Assessment & Repair	Human Augmentative Biomedical Technologies

The anti-aging lifestyle can add 25.3 more years of productive lifespan. Researchers from the Harvard School of Public Health found [3] that the longest-living Americans are Asian-American women residing in Bergen County, New Jersey USA. They live longer than any other ethnic group in the United States – to an average lifespan of 91.8 years. In contrast, the Harvard team found that the shortest-living Americans are Native American populations in South Dakota, despite receiving free or low-cost government provided medical care - living an average lifespan of 66.5 years. As a group, the Bergen County women have ready

access to preventative health services, consume a healthy diet, received higher education, are/were professionally employed, and enjoy a network of family and friends. These are proven life-extending factors that – when combined, exert a synergistic effect on longevity. These factors are also the cornerstones of the anti-aging medical model.

A ten-year long study [4] of 2,432 elder Canadians demonstrated that the most important predictors of excellent health were:

- Absence of chronic illness
- Annual income over US 30,000$
- Having never smoked
- Drinking alcohol in moderation
- Maintaining a positive outlook, managing stress levels

The study authors conclude that: "Many of these factors can be modified when you are young or middle-aged. While these findings may seem like common sense, now we have evidence of which factors contribute to exceptional health [as we age]."

The precepts of the anti-aging lifestyle are validated as key approaches that help people to maintain physical and cognitive capacities as they age. Researchers from University College London (United Kingdom) studied [5] a group of 5100 men and women, ages 42 to 63 years, who were enrolled in the Whitehall II study. The team defined a set of four healthy behaviors: namely, never smoking, moderate alcohol consumption, physical activity (2.5 h/wk or more of moderate physical activity or1 h/wk or more of vigorous physical activity), and eating fruits and vegetables daily. We defined successful aging, measured over a median -16.3year follow-up, as good cognitive, physical, respiratory and cardiovascular functioning, in addition to the absence of disability, mental health problems and chronic disease (coronary artery disease, stroke, cancer and diabetes). The researchers revealed that people in the successfully aging group were younger than the normally aging group (mean age 49.7 versus 51.3 yr), and %81 were married compared with %78 in the second group and %71 in the deceased group. Successful agers were more likely to have higher education than the normally aging group (%32 v. %24) and %18 in the deceased group. In the study population, Observing that: "participants engaging in all 4 healthy behaviours had 3.3 times greater odds of successful aging," the study authors conclude that: "Although individual healthy behaviours are moderately associated with successful aging, their combined impact is substantial."

Research and Evidence in Anti-Aging Medicine

Lab Models of Aging Intervention

A drug originally designed to suppress the immune system in organ transplant recipients, rapamycin is shown in lab models to exert life-extending properties. The University of Texas Health Science Center at San Antonio (Texas, USA) team observed [6] that rapamycin increased the lifespan of male and female C57BL/6J mice by 11 to %16, by exerting changes on the liver transcriptome.

Researchers from the Buck Institute of Aging (California, USA) successfully and markedly amplified [7] the lifespan of Caenorhabditis elegans (earthworm). The team altered two genetic pathways via a "combination of mutations in daf2- and rsks1- [to produce] a nearly -5fold increase in longevity that is much greater than the sum of single mutations." The worms lived to the human equivalent of 500 years.

Scientists from the University of California/Los Angeles (UCLA; California, USA) activated [8] a gene called AMPK in the nervous system, thereby inducing the anti-aging cellular recycling process of autophagy in both the brain and intestine. The team observed that this ‹inter-organ› communication during aging can substantially prolong the healthy lifespan of Drosophila (fruit flies), writing that "we see the aging process is slowed beyond the organ system in which the gene is activated."

Delayed aging could increase life expectancy by an additional 2.2 years, most of which would be spent in good health. Observing that: "Recent scientific advances suggest that slowing the aging process (senescence) is now a realistic goal … Yet most medical research remains focused on combating individual diseases," Dana Goldman, from the University of Southern California (USC; California, USA), and colleagues submit [9] that research to delay aging and the infirmities of old age would have better population health and economic returns, as compared to advances in individual fatal diseases such as cancer and heart disease. Using the Future Elderly Model – a microsimulation of the future health and spending of older Americans – the researchers compared optimistic «disease specific» scenarios with a hypothetical «delayed aging» scenario in terms of the scenarios› impact on longevity, disability, and major entitlement program costs. The team found that delayed aging could increase life expectancy by an additional 2.2 years, most of which would be spent in good health, with the economic value of delayed aging estimated to be 7.1$ trillion over fifty years. The study authors that: "Overall, greater investment in research to delay aging appears to be a highly efficient way to forestall disease, extend healthy life, and improve public health."

Evidence in Human Aging Intervention

A number of scientifically validated interventions that aim to promote the healthy human llfespan presently exist.

As mentioned above, the power of lifestyle is not to be underestimated, To quantify the health benefits of positive lifestyle choices, a Harvard School of Public Health study analyzed [10] data collected from 80,000 women nurses, followed for two decades. The researchers found that %55 of the deaths could have been avoided if the women followed four key decisions – namely: (1) Had never smoked.

Smoking was the factor with the biggest role in premature deaths, responsible for an estimated %28 of the deaths; (2) Exercised regularly; (3) Eaten a healthy diet (low in red meat and trans fats); and (4) Maintained a healthy weight.

Conversely, a University of Oslo (Norway) -20year long study of 4,886 United Kingdom adults clearly elucidates [11] the consequences of poor lifestyle choices. These researchers found that all-cause mortality risk rose %85 for individuals with any one of the risky health behaviors – namely, physical inactivity, poor diet, smoking, and excess alcohol consumption.. Moreover, those who engaged in all four activities raised their mortality risk by nearly 3.5 times, equating to prematurely ageing a person 12 years in terms of death risk. The team urges that: "The combined effect of poor health behaviors on mortality was substantial, indicating that modest, but sustained, improvements to diet and lifestyle could have significant public health benefits."

Maintaining a routine of physical activity is another well-studied anti-aging intervention. Karolinska University Hospital (Sweden) team analyzed [12] data collected on 4,332 men and women, average age 60 years, residing in Stockholm, followed for an average of 12.5 years At the study›s start, subjects with a high level of non-exercise physical activity of daily life, regardless of regular exercise, achieved more preferable metabolic risk factors, as compared to those with low levels of physical activity. Interestingly, a high non-exercise physical activity of daily life level, regardless of exercising regularly or not, also associated with a lower risk of a first cardiovascular disease event and lower all-cause mortality. The study authors conclude that: «A generally active daily life was, regardless of exercising regularly or not, associated with cardiovascular health and longevity in older adults.»

As a corollary to routine physical activity, it is essential to avoid being sedentary. Extended periods of sitting are associated with a higher risk of heart disease, diabetes, cancer, and death, regardless of regular exercise. Researchers from the University of Toronto (Canada) report [13] findings of their meta-analysis, involving studies assessing sedentary behavior in adults on cardiovascular disease and diabetes (14 studies), cancer (14 studies), and all-cause mortality (13 studies). Sitting for prolonged periods raised the risk of cardiovascular disease by %14, cancer by %13, and diabetes by %91. Those who sat for long stretches and got no regular exercise had a %40 higher risk of early death. With regular exercise, the risk was smaller but still significant: about %10. The study authors warn that: "Prolonged sedentary time was independently associated with deleterious health outcomes regardless of physical activity."

The Biotech Factor

Today, we can detect, forestall, and prevent most forms of cardiovascular incidents, cancer, diabetes, and Alzheimer's Disease. Therapies to reverse such life-robbing conditions are on the horizon, thanks to biomedical and biotech R&D. Medical knowledge doubles every three years. By 2017, we will know twice as much as we do today, by 2020 four-times, and so on. We submit that 2029 signals the arrival of the Biotech Singularity, when advancements in anti-aging and regenerative medicine reach maturity:

- Stem cell therapeutics, technologies aiming to beneficially alter the very basic cellular sources of dysfunctions, disorders, disabilities, and diseases

- Therapeutic cloning, technologies to develop ample sources of human cells, tissues, and organs for use in acute emergency care as well as the treatment of chronic, debilitating diseases

- Genetic engineering and genomics, advancements that permit the identification and alteration of genetics to ameliorate dysfunctions, disorders, disabilities, and diseases

- Nanotechnology, deploying micro- and molecular-sized tools to manipulate human tissue biology for microsurgical repair on a gross level, as well as microscopic nano-biology for repair at the most basic cellular level

Today, thanks to the Pharma pipeline [14] of 465 drugs "targeted on 10 chronic conditions in seniors," most adults in developed nations enjoy lifespans of around 80 years. With progress in stem cells, DNA repair, and telomerase, by 2029 lifespans of 120 years are realistically foreseeable. As genomic medicine and artificial organ technologies advance, by 2050 to 2095 we may achieve the 150 year lifespan. Past that, machine-based human enhancements may herald living -200plus, disease-free years.

Taken collectively, the advancements offered by anti-aging and regenerative medicine to improve the quality of, and/or extend the length of, the human lifespan, are the singlemost potent emerging biomedical technologies today.

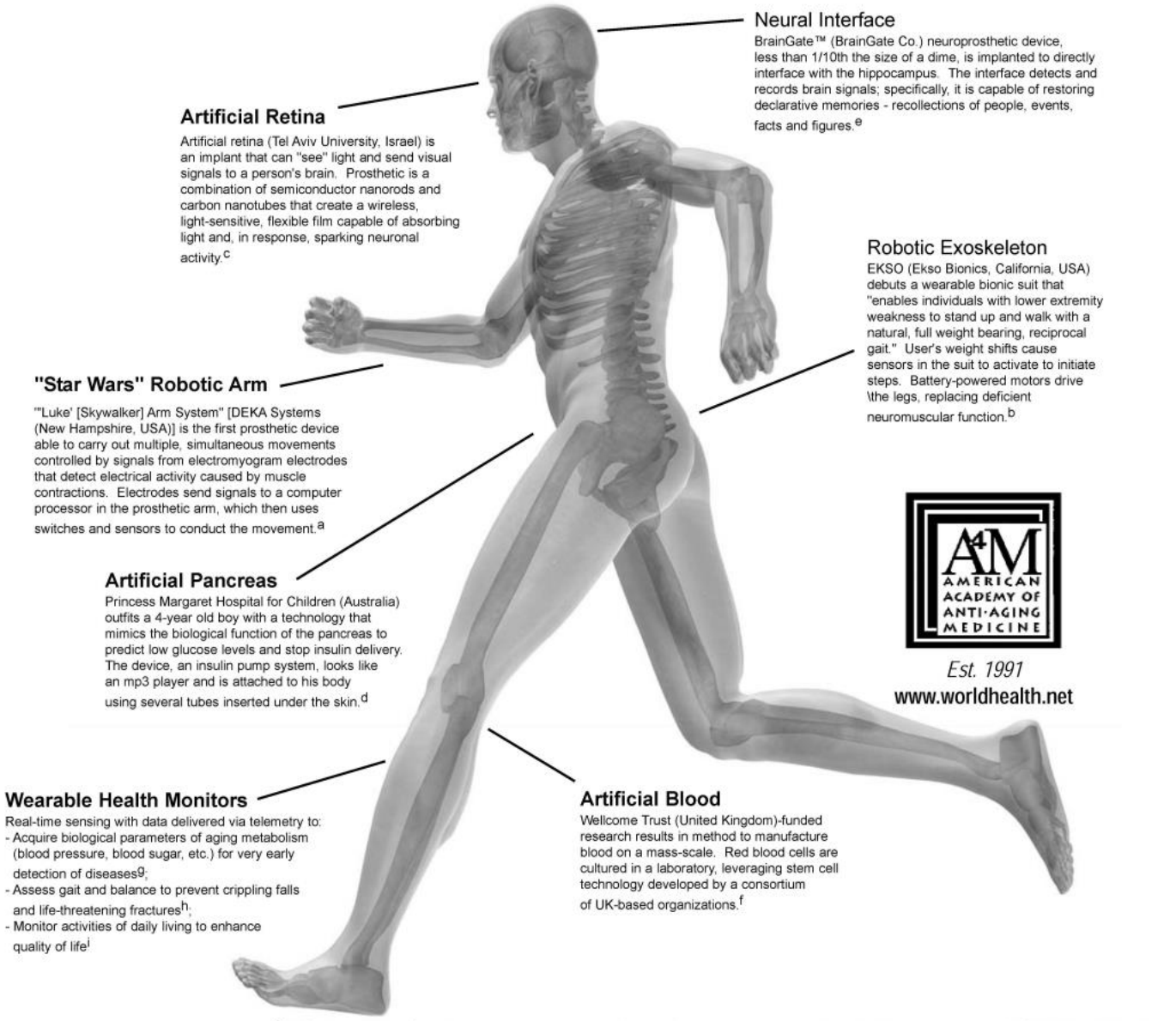
Across the globe, research teams are designing and perfecting technological advancements to boost peak mental and physical performance [15], such as those presented in Figure 1.

The notion of humans displaying better, stronger, and faster parameters of physical and mental performance – is not far away.

Concluding Remarks

Researchers from the Max Planck Institute for Demographic Research (Germany) report [16] that: "Life expectancy is increasing in most countries and has exceeded 80 in several, as low-mortality nations continue to make progress in averting deaths." Observing a sharp decline in early mortality in the past four generations that points to "the bulk of this mortality reduction has occurred since 1900," the study authors cite improvements in clean water, shelter, food, and medicine as primary factors in the life expectancy

Figure 1. Advancements in Human Augmentation



[a] "U.S. FDA approves 'Star Wars' robotic arm for amputees"; at http://www.reuters.com/article/2014/05/09/us-usa-health-arm-idUSKBN0DP1ID20140509.

[b] Ekso Bionics; at http://eksobionics.com/ekso

[c] Lilach Bareket, Nir Waiskopf, David Rand, Gur Lubin, et al. "Semiconductor Nanorod-Carbon Nanotube Biomimetic Films for Wire-Free Photostimulation of Blind Retinas." Nano Letters 2014 14 (11), 6685-6692.

[d] Reported by http://medicalxpress.com/news/2015-01-australian-boy-world-artificial-pancreas.html

e Reported by http://medicalxpress.com/news/2014-05-brain-implant-memory.html

[f] Ivanovs A, Rybtsov S, Anderson RA, Turner ML, Medvinsky A. "Identification of the niche and phenotype of the first human hematopoietic stem cells." Stem Cell Reports. 2014 Mar 27;2(4):449-56.

[g] Arsand E, Muzny M, Bradway M, Muzik J, Hartvigsen G. "Performance of the First Combined Smartwatch and Smartphone Diabetes Diary Application Study." J Diabetes Sci Technol. 2015 Jan 14. pii: 1932296814567708.

[h] Schwenk M1, Mohler J, Wendel C, D'Huyvetter K, Fain M, Taylor-Piliae R, Najafi B. "Wearable Sensor-Based In-Home Assessment of Gait, Balance, and Physical Activity for Discrimination of Frailty Status: Baseline Results of the Arizona Frailty Cohort Study." Gerontology. 2014 Dec 24.

[i] Kantoch E, Augustyniak P, Markiewicz M, Prusak D. "Monitoring activities of daily living based on wearable wireless body sensor network." Conf Proc IEEE Eng Med Biol Soc. 2014 Aug;2014:586-9.

gains. The study authors note that: "This observed plasticity in age-specific risk of death is at odds with conventional theories of aging."

Anti-aging medicine is now practiced by thousands of physicians in private medical offices, as well as at some of the most prestigious teaching hospitals around the world. Universally, those involved in healthcare, or those whose fields of expertise intersect with healthcare issues, support anti-aging medicine as a healthcare model promoting innovative science and research to prolong the healthy human lifespan. Public policy organizations and government agencies are now embracing anti-aging medicine as a viable solution to alleviate the mounting social, economic, and

medical woes otherwise anticipated to arrive with the aging of nearly every nation on the planet.

Attempting to rebrand what it cannot deny, those in positions of power in academic, political, and regulatory arenas are inventing new catch phrases including «longevity medicine,» «successful aging,» «healthy aging,» and the like, in an effort to dilute and absorb the A4M›s original definition of anti-aging medicine. Regardless of what name you use to describe "anti-aging medicine," the clinical field was established in 1991 by the physicians of the American Academy of Anti-Aging Medicine, A4M.

Attributable to James Fries of Stanford University (California, USA), "successful aging" advances the concept of "morbidity compression," that is, shortening the period of infirmity into a shorter period closer to death. In a recent interview, Dr. Fries admits [17] that: "studies show that common sense moves like exercising and eating well really can help us stay healthier for longer."

Similarly, Buck Institute of Aging (California, USA) researchers herald [18] the merits of preventing the diseases of aging. The team submits that a "healthy diet and regular exercise … slow the metabolic and molecular causes of human aging." They also warn that "our current health care approach is not sustainable. Targeting diseases has helped people live longer, [but] they are spending more years being sick with multiple disorders relating to aging, and that's expensive."

Representing over 26,000 physicians, health practitioners and scientists hailing from 120 nations, The American Academy of Anti-Aging Medicine (A4M; www.worldhealth.net) is a leading professional medical organization spearheading the acceptance and accessibility of anti-aging medicine worldwide. Founded in 1991, the A4M serves as an advocate for the new clinical specialty of anti-aging medical science and acts as a conduit to physicians, scientists, and the educated public who wish to benefit from the almost daily breakthroughs in biotechnology which promise both a greater quality as well as quantity of life. As far as the global culture of adoption of anti-aging medicine, the A4M has been a major force in advancing the medical specialty worldwide. The A4M has been responsible for positioning the anti-aging clinical medical specialty as a leading innovative paradigm for healthcare in the aging nations around the world. A US-federally registered non-profit organization, the A4M does not promote or endorse any specific treatment nor does it sell or endorse any commercial product.

The future for human longevity is promising. The professional members of the A4M lead the cutting-edge R&D efforts in human aging intervention. The A4M brings lab-to-market by applying such discoveries in the clinical setting. We have the here-and-now answers in our hands today, and the -26,000 plus physician, scientist, and health practitioner members of the A4M engage them to help hundreds of thousands of patients to enjoy prolonged quality – and quantity, of life.
The A4M is the leading resource for physicians and health practitioners pursuing education and training in the fast-growing medical specialty, as well as the trusted informational reference for consumers seeking to learn ways to promote an extended, healthy, productive, fit, and vital lifespan. Visit the Internet's 1# Ranked Anti-Aging educational website and sign up for the FREE Longevity Magazine™ e-Journal, at www.worldhealth.net.

References

1. Wilmoth JR, Deegan LJ, Lundstrom H, Horiuchi S, «Increase in Maximum Life-Span in Sweden, 1861-1999,» Science Sep 29 2000; 2366-2368.

2. http://www.un.org/en/globalissues/ageing/index.shtml

3. "Bergen County, NJ is long in longevity," New York Times, September 12, 2006; "Asian women in Bergen have nation's top life expectancy," Free Republic, September 12, 2006; "Asian-Americans live well in Garden State," Wall Street Journal, Nov. 15, 2010. 4.

4. Kaplan MS, Huguet N, Orpana H, Feeny D, McFarland BH, Ross N. "Prevalence and factors associated with thriving in older adulthood: a 10-year population-based study." J Gerontology Series A, October 2008.

5. Severine Sabia, Archana Singh-Manoux, Gareth Hagger-Johnson, Emmanuelle Cambois, Eric J. Brunner, Mika Kivimaki. "Influence of individual and combined healthy behaviours on successful aging." CMAJ, October 22, 2012.

6. Fok WC, Chen Y, Bokov A, Zhang Y, Salmon AB. Mice fed rapamycin have an increase in lifespan associated with major changes in the liver transcriptome. PLoS One. 2014 Jan 7;9(1): e83988.

7. Chen D, Li PW, Goldstein BA, Cai W, Thomas EL, Chen F, Hubbard AE, Melov S, Kapahi P. Germline signaling mediates the synergistically prolonged longevity produced by double mutations in daf-2 and rsks-1 in C. elegans. Cell Rep. 2013 Dec 26; 5(6): 1600-10.

8. Ulgherait M, Rana A, Rera M, Graniel J, Walker DW. AMPK Modulates Tissue and Organismal Aging in a Non-Cell-Autonomous Manner. Cell Rep. 2014 Sep 25; 8(6): 1767-8.

9. Goldman DP, Cutler D, Rowe JW, Michaud PC, Sullivan J, et al. "Substantial Health And Economic Returns From Delayed Aging May Warrant A New Focus For Medical Research." Health Aff (Millwood). 2013 Oct; 32(10): 1698-1705.

10. Rob M van Dam, Tricia Li, Donna Spiegelman, Oscar H Franco, Frank B Hu. "Combined impact of lifestyle factors on mortality: prospective cohort study in US women." BMJ 2008; 337: a1440; published 16 September 2008.

11. T Elisabeth Kvaavik; G. David Batty; Giske Ursin; Rachel Huxley; Catharine R. Gale. "Influence of Individual and Com-

bined Health Behaviors on Total and Cause-Specific Mortality in Men and Women: The United Kingdom Health and Lifestyle Survey." Arch Intern Med, Apr 2010; 170: 711 - 718.

12. Ekblom-Bak E, Ekblom B, Vikström M, de Faire U, Hellénius ML. «The importance of non-exercise physical activity for cardiovascular health and longevity.» Br J Sports Med. 2014 Oct 28.

13. Biswas A, Oh PI, Faulkner GE, Bajaj RR, Silver MA, Mitchell MS, Alter DA. "Sedentary Time and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults: A Systematic Review and Meta-analysis." Ann Intern Med. 2015 Jan 20; 162(2): 123-132.

14. "Medicines in Development: Older Americans," Pharmaceuticals Research and Manufacturers of America, 2013.

15. http://www.nsf.gov/od/lpa/news/02/pr0257.htm

16. Burger O, Baudisch A, Vaupel JW. Human mortality improvement in evolutionary context. Proc Natl Acad Sci U S A. 2012 Oct 4-18210:(44)109;30.

17. "'Successful aging' protects health and wealth," Marketwastch.com, 9 June 2013.

18. Strategy proposed for preventing diseases of aging," Medical Xpress.com, 24 July 2014.