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Research Article

Medical Anti-Aging Clinics and their Justification by Scientific Evidence

Ernst R von Schwarz[1,2,3]*, Aubriana D'Iwana Angel Schwarz[3], Julian Bruce[2] and Laurent Cleenewerck de Kiev[2]

[1]*Cedars Sinai Medical Center, Los Angeles, CA, USA*

[2]*Euclid University, Washington DC, USA*

[3]*Dr von Schwarz Stem Cell & Anti-Aging Institute, Beverly Hills, CA, USA*

Abstract

Anti-aging medicine is an evolving discipline that combines geriatric research with clinically applied therapies to prevent, treat and reverse age-related degeneration and diseases. Basic research has provided compelling work on cellular pathways and mechanisms associated with senescence, resulting in several agents and technologies being developed and touted to support geroprotection or reparative age-reversal. However, clinical studies supporting actual anti-senescent effects are promising but scarce. In spite of this, hundreds of anti-aging clinics are operating in the United States, marketing supplements without compelling scientific evidence, which tends to lead to non-acceptance of the validity of anti-aging medicine among scientific and medical communities. Still, it may be argued that medical or scientific anti-aging clinics are justified as long as they provide appropriate education and information about life-style modifications, risk factor reduction, as well as scientific, evidence-based medical gerotherapies and supplementation. By doing so, these establishments can provide a valuable opportunity to increase awareness, improve health consciousness and quality of life among the aging population.

Keywords: Anti-aging; Clinical studies; Evidence; Morbidity; Mortality; Regenerative therapy

Introduction

Anti-aging has evolved into a prominent discourse over the past few decades, largely shaped by the anti-aging movement of the 1990s [1], which formalized concepts long proposed by spiritual leaders and health gurus centuries earlier, now categorized as anti-aging medicine [2,3]. The well-covered case of anti-aging influencer Bryan Johnson and his quest for immortality has generated extensive news coverage and increased public awareness and interest in the myths vs reality of anti-aging medicine. As with many familiar ideas, anti-aging medicine fundamentally did not invent anything of novel applicability but instead, emphasized common sense knowledge of the benefits of the pillars of healthy lifestyle that predominantly focus on moderation in consumption [4], healthy diets [5], and exercise [6]. Simultaneously, aging itself has become a popular target for biomedical research and prospective interventions [7].

According to Gilbert's classic text on Developmental Biology, aging is defined as "…the time-related deterioration of the physiological functions necessary for survival and reproduction. The phenotypic changes of senescence (which affect all members of the species) are not to be confused with diseases of senescence, such as cancer and heart disease (which affect individuals)" [8]. The term senescence was introduced by Hayflick and Moorhead in 1961 and simply means old [9]. According to the National Cancer Institute, senescence is characterized as the "…process of growing old. In biology, senescence is a process by which a cell ages and permanently stops dividing but does not die. Over time, large numbers of old (or senescent) cells can build up in tissues throughout the body. These cells remain active and can release harmful substances that may cause inflammation and damage to nearby healthy cells. Senescence may play a role in the development of cancer and other diseases." It also means a non-proliferative but viable state, distinct from G0 quiescence and terminal differentiation…a response to numerous stressors, including exposure to genotoxic agents, nutrient deprivation, hypoxia, mitochondrial dysfunction, and oncogene activation, as defined by Gorgoulis et al. [10]. A few other terms need to be defined to avoid the risk of equivocation.

Geriatrics is defined as the healthcare specialty dedicated to supporting health, safety, and independence of the elderly by use of diagnostics, treatment, care and prevention, according to Healthcare Geriatric Professionals.

Gerontology is the science of physical aspects of aging in humans [11].

Geroscience an interdisciplinary field that combines genetics and molecular and cellular biology to study processes leading to aging and concomitant diseases [12].

Anti-aging means to lessen or prevent the effects of getting old. Anti-aging medicine applies advanced science and medical technology to early detection, prevention, treatment, and reversal of age-related dysfunctions, disorders, and diseases [13].

Geroprotection means to protect against aging or age-related conditions that impair quality and functionality of life and/or reduce life-span [14]. The term here is used synonymously with anti-aging.

Geropharmaceuticals and gerosuppressives refer to drugs that target aging pathways to reduce the burden of aging-related diseases and increase lifespan [15].

***Corresponding author:** Ernst R von Schwarz, Dr von Schwarz Stem Cell & Anti-Aging Institute, 324 S. Beverly Drive, #711, Beverly Hills, CA 90212, USA, Tel: +1 9516984433; Fax: +1 9514618790; E-mail: info@drvonschwarz.com

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Senolytics are specialized drugs designed to target and eliminate senescent cells that accumulate with age and contribute to age-related illnesses. They induce apoptotic death of senescent cells, which has been shown in pre-clinical studies to possibly prevent or "…alleviate frailty, cancers and cardiovascular, neuropsychiatric, liver, kidney, musculoskeletal, lung, eye, haematological, metabolic and skin dis-orders as well as complications of organ transplantation, radiation and cancer treatments" [16,17].

Reverse aging refers to procedures or substances that reverse the body's natural aging processes, usually by repair of aged and or damaged tissues [18].

In contrast, de-aging is defined as the (non-medical) usage of cosmetic or visual and digital effects using computer generated imagery to make individuals appear younger, especially in film, television [19]. Nowadays, this is utilized by innumerable numbers of people on social media, at least in part to overcome aging or appearance insecurities using apps and programs with filters and other enhancement technologies to appear younger and more attractive [20].

Anti-aging clinics provide therapies directed towards age related deterioration of bodily and mental function by use of any preventative approach to reduce late-life pathology, based on the understanding that senescence is a disease syndrome, according to Gems [21].

In the context of this article, we define medical (or scientific) anti-aging (and the appropriate clinical settings accordingly as medical (or scientific) anti-aging clinics) as the professional implementation of several if not most geroprotective compounds, senolytic drugs, and technologies that have demonstrated scientific evidence from basic research laboratory studies and/or clinical trials into clinical practice to prevent, treat, delay, and reverse age-related degeneration and diseases with constant scholarly academic and clinical re-evaluation and reporting.

As a consequence of public demand and the fact that a large group of health care providers, namely physicians, now represent the baby boomer generation (i.e., those born between the 1950s and the mid 1960s), health consciousness [22] and life prolonging therapies are becoming extraordinarily fashionable. Compared to generations prior when doctors on televised debates were seen smoking in public [23], middle-aged doctors now are particularly more health-conscious and thus, concerned to improve or even prolong their own lives. Correspondingly, amplified medical practice revenues by adding income through the sale of anti-aging formulas, diet plans, and frequently re-labeled supplements substantiated additional commercial benefits for some practitioners [24]. Even though the numbers vary, according to ZipRecruiter, even work-from-home anti-aging physicians might earn between $129,000 and $288,000 annually.

Besides the plethora of research activities in the field of cellular aging and its possible exploitation efforts, anti-aging medicine is still not an adequately accepted academic discipline within the scientific community. In contrast, attempts to delay the processes of age-related deterioration of organ function oftentimes remain perceived as snake oil-trading endeavors [25], which does not appear to be justified in a world of precipitously evolving advances in anti-senescence research. In order to evaluate the scientific validity of anti-aging medicine and the clinics offering these services, we hereby discuss the following questions:

- Is there scientific evidence for anti-aging medical recommendations?
- Are there health and/or community benefits of anti-aging clinics?
- Is the sale of anti-aging products a hoax to lure patients into expensive memberships or sales or does it improve overall health?
- What is the future of anti-aging medicine?

To adequately address these questions systematically, an extensive literature search was conducted to evaluate the scientific merits and evidence surrounding anti-aging medicine in clinical practice at the current time.

Disapproval of Anti-Aging Medicine

A Pubmed search using the search term anti-aging reveals 9,876 results, anti-aging medicine reveals 13,814 hits, anti-aging clinics reveals 2417 results, whereas aging clinics reveals 167,071 publications. A Google search on the number of anti-aging clinics in the US provides no specific numbers but an estimate of approximately 800 anti-aging healthcare practices. An analysis uncovered a market of anti-aging products counting to 12.3 billion US $ in 2021 - with an estimated increase to more than 22 billion US $ by the year 2031 [26]. Other internet sources claim that the current anti-aging industry is valued at 47 billion US $ in 2023 - with an estimate of reaching over 80 billion US dollars over the next 10 years. Despite these rather astonishing numbers, we did not even find a single clinical study that has evaluated the clinical efficacy of designated anti-aging clinics in the US or elsewhere. Furthermore, the term anti-aging clinic is not clearly defined and encompasses a wide variety of different establishments-ranging from online stores selling products to medical practices that include self-described anti-aging programs to medical spas and infusion centers that sell anti-aging supplements and vitamin injections, among many other scenarios. Scientifically based medical institutions what we call medical (or scientific) anti-aging clinics (see above) that primarily focus on anti-aging medicine - though compulsory - appear to be extremely scarce.

The term anti-aging, in general, is still not well accepted within the established medical community. One reason might be the fact that there is an enormous amount of products for sale that allege anti-aging effects but lack any reputative clinical data to support these claims. This includes agents that supposedly prevent chromosome length reduction to multi-vitamins as well as so-called senolytic activators, antiaging pills, rejuvenation capsules, longevity supplements, among innumerable others. There is no real objective institutional evaluation of supplements, i.e., the US FDA has no authority valuing supplements that are sold over the counter with anti-aging labels. Even though the criticism regarding the paucity of data supporting efficacy of certain products in contrast to the enormous marketing efforts of industry and practitioners to sell these miracle compounds is justified, this should not translate in dismissal of scientifically based anti-aging efforts in general. The non-acceptance of the anti-aging concept, however, represents intolerable and immutable ignorance in view of the enormous amount of research activities on aging and anti-aging over the last few decades. At the latest since the establishment of the National Institute of Health's (NIH) own Institute for Aging Research (IAR) in the 1970s, the subject matter evolved to an academic discipline and as such, should be taken more seriously among established scientific and community minds. As early as 1971, a White House Conference on aging has proposed to create a separate dedicated aging institute within the National Institute of Health (NIH) in the US. In October 1974, the National Institute of Aging (NIA) was formally established. Since the US government has dedicated

financial resources for aging research, one could have expected that anti-aging medicine would have much more advanced over the last 50 years than it actually did. It was not until 2018 when the World Health Organization (WHO) added aging into the 11th edition of the International Classification of Diseases as an entity [27]. Nowadays, aging is more than just an inevitable biologic course of life but is considered a pathologic condition associated with a multitude of degeneration and diseases, especially cardiovascular issues, neurodegenerative and musculoskeletal illnesses, frailty, immobility and cancer. Aging itself is a disease, and ought to be treated as such [28]. While some scholars like Blagosklonny state that "aging can be easily treated" [29], fact is, however, that not much has happened in the scientific field that can be applied to translational medicine to be implemented into clinical practice. On the other hand, basic researchers such as David Sinclair as an example, have become popular faces through books and presentations on anti-aging. In particular, Sinclair, who is a Professor of Genetics at Harvard Medical School and co-editor of the journal Aging, states that aging primarily is caused by loss of intracellular information rather than by accumulation of metabolic garbage [30]. Despite utterly useful information from basic research labs on aging, the number of clinical trials assessing anti-aging effects of specific interventions or agents in humans remain rather sparse.

In 2003, Binstock even claimed that some kind of "war" was initiated by some gerontologists against anti-aging medicine, possibly arising from the fear to lose funding for gerontology research while popular anti-aging clinics are selling unverified and unapproved therapies to the public [31]. Indeed, anti-aging science is not straightforward. Evaluating the scientific validity of studies that have investigated the processes of cellular aging, one might come across early occurring markers of senescence that accumulate prior to signs of aging emerge but can be targets for anti-aging therapies [32]. Vascular changes such as endothelial dysfunction can be seen as an indicator for aging [33]. Senescence leads to vascular dysfunction and atherosclerosis, and atherosclerosis is affiliated with aging [34]. Other mechanisms connected with cellular degeneration, organ dysfunction and aging related diseases are a reduction of telomere length, DNA damage, reduced cell proliferation, growth arrest, accumulation of metabolic garbage, and a reduction of both the quantity and quality of repair mechanisms such as stem cells [35]. These and others are targets for anti-aging technologies, for both the basic research arena [36] and the clinical scenario.

A Few Anti-Aging Drugs and Compounds

Nicotinamide Adenine Dinucleotide (NAD+) is a widely discussed compound, especially since levels in the body deplete with aging. It is associated with downregulation of energy production in mitochondria, oxidative stress, DNA damage, cognitive impairment, and inflammation. Nicotinamide mononucleotide (NMN), the precursor of NAD+, can slow down these processes by elevating NAD+ levels in the body in vitro and in vivo experiments [37]. In addition to the advances of anti-aging properties by certain substances in the experimental settings such as NAD, its metabolite NMN has prevented age-associated gene expression changes in metabolic organs and enhanced mitochondrial oxidative metabolism and nuclear protein imbalance in skeletal muscle in mice [38]. NAD supplementation in animal studies also significantly improved wheel-running activity and extended lifespan in older mice [39]. These basic research laboratory data coerced several researchers to market and sell NAD supplements for protective anti-aging usage despite lack of clinical data in humans, as Taylor proposed: "it works well - if you are a mouse" [40].

In addition, several studies showed that certain supplements such as resveratrol, as an example, might exert anti-autophagic effects, thus reducing cell death in the lab, as shown by Sinclair's group [41]. These basic research results of potential anti-aging remedies such as NAD or the immunosuppressive drug rapamycin are clinically quite promising [42,43]. However, as stated by others before, robust large-scale placebo-controlled clinical trials in humans are indispensable before implementing these substances into any anti-aging clinical practice is justified [44].

More recently, more studies, however, have tested the safety and efficacy of NMN supplementation for its possible anti-aging effects. In 2022, Huang reported a multi-center trial using NMN in 66 healthy individuals resulting in increased intracellular NAD levels indicating plausible anti-aging effects [45]. Yi et al., reported NMN supplementation in 80 healthy individuals over 2 months with enhanced functional capacity, improved overall health as measured by the SF 36 quality of life questionnaire, and elevated NAD blood levels without any major side effects [46]. Moreover, Liao showed augmented aerobic capacity among 48 healthy individuals [47], and Katayoshi et al., demonstrated reduced arterial stiffness using NMN supplementation in 36 healthy middle-aged individuals versus placebo as measured by pulse wave velocity assessment [48].

As reviewed recently by Yu et al., NAD/NMN provides a unique opportunity for metabolic and anti-aging research and its clinical applications in the near future [49]. The studies conducted predominantly show beneficial effects, therefore NAD/NMN supplementation seems to gain a role as part of an anti-aging regimen in the appropriate setting, but several questions remain unanswered including dose, application, formulation, duration and long term effects that need to be further investigated.

Similarly, several experimental data revealed potential anti-senescence effects of potential gerotherapeutics such as metformin [50], a well-known and relatively cheap medication commonly used for patients with type 2 diabetes mellitus. It is well established that both hyperglycemia and hyperinsulinemia are related to advanced aging processes [51,52]. Animal studies showed increased lifespan in rodents using metformin [53]. Clinical trials in humans are underway but are rare. A recent human trial demonstrated that metformin therapy significantly improved metabolic parameters and insulin sensitivity, increased SIRT1 gene/protein expression and SIRT1 promoter chromatin accessibility as well as elevated mTOR gene expression, all which are all so-called longevity effectors [54]. Other multi-center trials testing metformin's potential anti-aging effects such as the TAME (Targeting Aging by Metformin) and the MILES (Metformin in Longevity Study) trials are underway but have not been reported, yet [55,56].

Rapamycin, a TOR inhibitor and immunosuppressive agent used in patients after organ transplantation, has also potential anti-aging effects as demonstrated in several basic experimental studies [57]. It also showed life prolongation in rodents [58]. In 2023, Kaeberlein and colleagues reported 333 adult patients on off-label therapy with rapamycin [59], but clinical outcomes are pending. Blagoskonny even states that not taking proven geroprotective drugs like rapamycin would inevitably lead to age-related illnesses, weaknesses, frailty and death [60]. Altogether, it seems to be fair to state that there are life-style modifications, interventions and potential therapies with ample scientific evidence to support a healthy lifestyleand atleast to some degree, might generate anti-aging effects via

reduced inflammation and cellular degradation by altering pathways of senescence and stabilizing cellular membrane integrity. Anti-aging drugs are still under investigation and presume additional clinical evidence of efficacy and safety.

Anti-Aging Intervention Clusters

To categorize the large variety of agents and techniques that have potential geroprotective or anti-senescent effects, we here propose to distinguish between seven different clusters of Anti-Aging Interventions (AAI 1 to 7). This categorization might assist medical anti-aging programs and clinics to objectively evaluate the large armamentarium of antiaging supplements, medications and technologies and then utilize published data to personalize anti-aging treatment plans using those backed-up by science. Since there is no single miracle pill to delay or reverse aging, any integrated anti-aging program or clinic should be able to discuss, educate and provide at least part of the more or less established anti-aging interventions.

AAI-1 represents the control of risk factors that are known to hasten cardiovascular and overall degeneration leading to age related degeneration and disease. These include

- Avoidance of toxic substances known to cause physical damage including smoking, drugs, excessive alcohol
- Reduction of conditions that lead to immobility, bodily degeneration and advanced aging such as obesity, sedentary lifestyle, and lack of physical activity
- Reduction of risk factors affecting the cardiovascular and metabolic system such as hypertension, diabetes, and hyperlipidemia
- Usage of medications that reduce arthrosclerosis or slow down the progression of underlying conditions such as statins or PCSK-9 inhibitors (Repatha) for high cholesterol or GLP-1 agonists such as semaglutide (Ozempic, Wegovy) or tirzepatide (Mounjaro) for diabetes and weight loss.

AAI-2 represents active patient directed life-style modifications such as implementation of a heathy Mediterranean style diet and a regular activity and exercise program. It also includes the involvement of interventions that provide the basis for a spiritual equilibrium for mental health such as religious faith, prayers, meditation and yoga.

AAI-3 represents the substitution of deficiencies using dietary changes and supplements such as Vitamin D, Vitamin B12, among others, and possibly hormone replacement therapy even in case of a mild reduction in thyroid or sexual hormones such as testosterone and estrogen, if clinically indicated.

AAI-4 summarizes those agents that if supplemented, may have direct anti-senescent and anti-aging effects such as Vitamin or trace element supplementation (even without measurable deficiencies), NAD/NMN supplementation, nitric oxide, resveratrol, curcumin augmentation, infrared light therapy among other interventions.

AAI-5 represent means to surgical repair aging or damaged tissues including joint replacement for advanced arthritis, but also skin tightening procedures and injections that might lead to improved functionality and mobility and also techniques that might improve overall wellness including cosmetic procedures (such as fat removal, face lifts, injections) and the use of skin cosmeceuticals [61].

AAI- 6 represent active anti-aging drugs like metformin and rapamune that are approved and used for different medical conditions but are oftentimes used off-label since they have shown to provide some degree of anti-aging or even rejuvenating effects.

AAI-7 finally includes everything under the umbrella of regenerative therapy including the exogenous administration of growth factors, stem cells and derived products such as exosomes among others.

AAI - Credentials

Some of the above interventions have undoubtfully gained acceptance not only among the public but also among the scientific community. There is hardly any doubt on the beneficial effects and anti-aging effects of a low-calorie diet [62], a low carb diet, a reduction in the consummation of ultra-processed foods, reduced salt intake or the consequences of a regular cardio-exercise regimen on overall health and risk reduction [63]. Several other interventions, however, remain controversially discussed and not well acknowledged.

AAI-1 (risk factor reduction) and AAI-2 (life-style modification) are generally accepted as antiaging tools. AAI-3 (substitution of deficiencies) are tolerated but not widely enough utilized in clinical practice, while AAI-4 (supplements) is predominantly overlooked and neglected outside a specific anti-aging environment. AAI-5 (surgeries to repair damage) are widely accepted methods that are financially reimbursed by health insurance providers. AAI-6 (antiaging medications) are completely snubbed by the ignorance of many within the scientific and medical communities and remain still largely unknown among a broader public. AAI-7 (regenerative medicine using stem cells), despite its enormous success rates in few published clinical trials for a multitude of various conditions including cardiovascular, neurodegenerative and musculoskeletal conditions and a considerable public interest, is not only ignored but in contrast, disregarded, aggressively alienated, and mostly disallowed by regulatory agencies like the FDA [64]. The reasons are multifaceted but in large caused by 1) a paucity of large systematically conducted clinical trials, and 2) manipulative marketing using false claims oftentimes by non-scientific providers who charge patients large monetary amounts for unapproved therapies that may exert benefits but are neither standardized nor subject to any independent quality control at the current time. Stem cell therapy, however, for many represent the future of repair and regeneration in modern medicine that potentially might provide reversal of age-related degeneration and diseases.

Effects of AAI

Even if there would be no truth to potential anti-aging effects of any of the above AAI clusters, then alone the public promotion of health and wellness through anti-aging practitioners and clinics itself would be beneficial for the society as a whole, and for individuals similarly. Based on scientific evidence, however, several of the AAI efforts have demonstrated health benefits and some even prolong life:

- AAI-1 (risk factor reduction): Smoking cessation using behavioral counseling, medication and nicotine replacements are successful and might lead a prolongation of life of approximately 10 years [65]. As a recent example, even among HIV patients, smoking cessation has shown to prolong life [66].

- Obesity and weight gain is associated with increased mortality among adults [67]. Weight loss therapies using behavior-based interventions and related pharmacotherapy has reduced hypertension [68] and overall morbidity [69]. Combining more than one weight loss strategy also has been shown to reduce all-cause mortality [70]. Further, overall calorie reduction has been demonstrated to yield anti-aging effects [71].
- AAI-2 (life-style modification): Implementing exercise regimen even among older adults reduces age-related morbidity [72], and in combination with other life-style modification factors, prolongs life [73].
- AAI-3 (substitution of deficiencies): Several studies have reported a reduction in mortality using Vitamin D supplementation. The NHANES (National Health and Nutrition Examination Survey) studies showed lower cardiovascular mortality in patients with osteoarthritis [74], while others showed reduced all-cause mortality in patients with depression [75] or diabetes [76] as a result of taking Vitamin D.
- AAI-4 (supplements): NMN or NAD supplementation seem to have significant anti-aging effects [44] but has not shown to prolong life in human clinical studies, so far.
- AAI-5 (reparative surgeries): Hip and joint replacement surgeres in combination with an age adjusted geriatric co-management program has shown to reduce morbidity and mortality, according to a recently published study from Germany [77]. Data from a Swedish arthroplasty register for the first time demonstrated prolongation of life after total hip replacement [78].
- AAI-6 (anti-aging medications): There is ample evidence that metformin reduces mortality [50,79], in experimental animals and in humans, whether it prolongs life in humans remains to be ascertained. Rapamycin has been shown to improve survival in experimental animal models but not yet in humans [80].
- AAI-7 (regenerative medicine): Regenerative therapy using stem cells may have significant anti-aging effects caused by repair of damaged tissues and improved circulation [81] but clinical studies demonstrating prolongation of life are lacking, to date.

Altogether, the above classified anti-aging interventions AAI 1 to AAI-7 have convincing data supporting anti-aging efficacy, some even have evidence for life prolongation, but more large-scale controlled clinical trials are required to verify these initial promising results.

Medical Anti-Aging Clinics

Medical (scientific) anti-aging medicine should not be confused with biohacking. Biohacking represents a do-it-yourself non-professional specialty attempting to adapt technologies to achieve bodily modification and longevity, that usually lacks any scientific evidence [82]. Age-biohacking has become very popular in the lay press, predominantly through wealthy individuals who spend unbelievable financial means to try to rejuvenate themselves [83]. There are, however, atrocious risks involved to attempt genetic manipulations, self-made plasma injections and/or self-administration of unregulated drugs, which can present serious personal and public health dangers [84].

In contrast to individual biohacking, medical (scientific) anti-aging should be based on scientifically proven methods to improve quality of life, increase functionality, delay age-related degeneration, avoid frailty and immobility and by thus, provide comprehensive anti-aging methodologies. Dedicated medical (scientific) anti-aging clinics, therefore, should be able to grant the following to their patients:

- Appropriate education of processes and consequences of aging.
- A guidance for life-style modification implementation using assistance of nutritionists and/or qualified dietitians and exercise physiologists, physical therapists or certified trainers who help to craft a personalized life-style modification program to the individual needs of the patient under the supervision of a physician expert familiar with all aspects of anti-aging.
- Evaluate risk factors and deficiencies by conducting a complete history, physical examination and perform laboratory testing and imaging tests if clinically indicated.
- Provide objectifiable information based on published studies rather than based on manufactures' marketing materials on an array of supplements with some degree of scientific evidence for possibly beneficial effects in order to make a joint decision for or against supplementation.
- Provide proper education on anti-aging medications (such as metormin, rapamycin) including effects, side effects, medication interactions and risks prior to obtaining informed consent for possible treatment regimen with appropriate follow-up evaluation and testing.
- Provide objective information on regenerative medicine including stem cell therapy that include the fact it is not FDA approved and not covered by any health insurance. Stem cell therapies, though of enormous anti-senescent potential, should be conducted within the scope and frame of clinical trials at the current time.

Reality is, however, that most currently operating anti-aging clinics do not provide the expertise or knowledge for all of the above anti-aging interventions. Most anti-aging clinics are of relatively small caliber and might recommend some branded oral supplements or weight loss drugs, but frequently lack scientific reputation, which renders them unacceptable among the scientific and professional communities. On the other hand, the wide variety and overwhelming presence of anti-aging clinics and practices that offer anti-aging treatments to their patients has led to a trend achieving healthier living by life-style modification, increased exercise activities and dietary adherences, which in turn encourages community health consciousness and possibly improves health outcomes in the long run.

Medical (scientific) anti-aging clinics, on the other hand, should be specialized in the entire spectrum of anti-senescent intervention technologies or at least offer collaborations with appropriate specialists, and should have system in place to direct patients towards the above-mentioned AAI clusters - if desired and clinically indicated.

We here attempt to answer the initially stated questions:

- Is there scientific evidence for anti-aging medical recommendations?
- As stated above, founded on several scientific publications, there is ample evidence of reducing morbidity and possibly, even mortality, whether it may be caused by dietary changes, life style modifications, weight loss, implementing an exercising regimen or certain supplements. Lowered morbidity and mortality materialize synonymously to anti-aging properties.
- Are there health and/or community benefits of anti-aging clinics?
- Based on the fact that there is on overwhelming interest in a healthier aging and there are several anecdotal reports of anti-aging, regenerative medicine, and life-prolonging interventions presented in the lay press, the education provided by anti-aging clinics and experts significantly uplifted community health consciousness. Promoting anti-aging diagnostics and medicine as part of a routine healthcare by utilizing modern technology for the early detection, prevention, treatment, and reversal of age-related diseases is associated with overall benefits within those communities that implement these efforts into routine medical practices [13]. The aging population also requires additional educational efforts by health care providers leading to prevention, early detection, therapy, and reduction of health risks.
- Is the sale of anti-aging products a hoax to lure patients into expensive memberships or sales or does it improve overall health?
- Several but not all compounds that have been studied showed promising anti-aging effects such as NMN or NAD not only in experimental animal models [85] but also in human trials [86,87], so did Vitamin D [88], resveratrol [89], turmeric [90], and nitric oxide [91], among others. Further studies are warranted to verify specific effects of certain agents on age-related conditions such as cancer or cardiovascular diseases. At least some of the so-called anti-aging compounds have demonstrated health benefits [92,93].

Of interest, health care insurance providers primarily still focus on reactive medicine rather than on prevention and anti-aging. Currently, anti-aging therapies - whether these are supplements or stem cell therapies - are neither approved by Federal regulatory bodies nor paid for by health insurers. Therefore, antiaging is a personal choice on personal costs, which can be extensive and unfortunately, might be restricted to those you can afford it at the current time [94]. On the other hand, life-style adjustments and most supplements do not require a lot of financial resources.

- What is the future of anti-aging medicine?

The addition of controlled clinical trials testing different supplements on measurable anti-aging effects will further shed light onto the potential of certain agents to delay or reverse processes of aging. DNA-modification technology known as CRISPR has the potential to rejuvenate cells and reverse ageing [95]. Regenerative medicine using stem cells likely will have a prominent role in reversal of age-related degeneration, repair of damage tissues, and possibly anti-aging and longevity effects [64].

Conclusion

Educational efforts by health care providers on processes of aging, early prevention, risk factor reduction and treatment will contribute to improved awareness and life-style changes within communities to gain longer and healthier lives with less frailty, improved mobility, and increased quality of life into high ages. Dedicated medical (scientific) anti-aging clinics that provide and support the entire concept of life-style modifications with supplementation and medical therapy supporting healthy aging are required to provide a holistic approach for geriatric research and clinically applicable anti-aging therapies. Medical (scientific) anti-aging clinics should be welcomed and appreciated as long as they provide scientific facts and evidence-based medicine to promote health and defy age-related morbidity and mortality.

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