Special Report

Lifestyle Medicine: A Brief Review of Its Dramatic Impact on Health and Survival

Balazs I Bodai, MD, FACS; Therese E Nakata, STAR Provider, CWFPBN; William T Wong, MD; Dawn R Clark, MD, FACOG; Steven Lawenda, MD, ABFM; Christine Tsou, MD; Raymond Liu, MD; Linda Shiue, MD; Neil Cooper, MD; Michael Rehbein, MD, FACP; Benjamin P Ha, MD, ABFM; Anne McKeirnan, MD, FACOG; Rajiv Misquitta, MD; Pankaj Vij, MD, FACP; Andrew Klonecke, MD; Carmelo S Mejia, MD; Emil Dionysian, MD, FACOS; Sean Hashmi, MD, FACM; Michael Greger, MD, FACLM; Scott Stoll, MD, FABPMR; Thomas M Campbell, MD

Perm J 2018;22:17-025

E-pub: 09/20/2017

https://doi.org/10.7812/TPP/17-025

ABSTRACT

By ignoring the root causes of disease and neglecting to prioritize lifestyle measures for prevention, the medical community is placing people at harm. Advanced nations, influenced by a Western lifestyle, are in the midst of a health crisis, resulting largely from poor lifestyle choices. Epidemiologic, ecologic, and interventional studies have repeatedly indicated that most chronic illnesses, including cardiovascular disease, cancer, and type 2 diabetes, are the result of lifestyles fueled by poor nutrition and physical inactivity.

In this article, we describe the practice of lifestyle medicine and its powerful effect on these modern instigators of premature disability and death. We address the economic benefits of prevention-based lifestyle medicine and its effect on our health care system: A system on the verge of bankruptcy. We recommend vital changes to a disastrous course. Many deaths and many causes of pain, suffering, and disability could be circumvented if the medical community could effectively implement and share the power of healthy lifestyle choices. We believe that lifestyle medicine should become the primary approach to the management of chronic conditions and, more importantly, their prevention. For future generations, for our own health, and for the Hippocratic Oath we swore to uphold ("First do no harm"), the medical community must take action. It is our hope that the information presented will inspire our colleagues to pursue lifestyle medicine research and incorporate such practices into their daily care of patients. The time to make this change is now.

INTRODUCTION

Many consider lifestyle medicine to be a relatively new subspecialty, although it has been practiced for thousands of years.[1] Unlike conventional medicine, the focus of lifestyle medicine is not on the treatment of chronic diseases but rather on their prevention. Chronic diseases are presently the leading cause of morbidity and mortality and are responsible for most of our health care expenditure.[2] Most of these chronic conditions are preventable and are the result of an unhealthy lifestyle.[3] More than 80% of chronic conditions could be avoided through the adoption of healthy lifestyle recommendations.[3-5] Eighty percent of the population wants to live in a better state of health but do not know how to pursue it.[6] Minimal information is given by health care practitioners on how to implement an effective, long-term plan to achieve health.[3] The ongoing acceptance and adoption of a healthy lifestyle remains our greatest challenge. Implementation of lifestyle recommendations can save lives because lifestyle-related diseases are now the leading cause of mortality in the "modernized" world.[7] An aggressive analysis is needed to review the impact of lifestyle on our health.

So why are we sick and dying prematurely? Cardiovascular disease (CVD) and cancer have come to be known as the two "killer diseases" and account for more than half of all deaths in the US.[8] We are experiencing these diseases in the wealthiest nation in the world, which spends more on health care per capita than any other advanced economy and yet has some of

Balazs I Bodai, MD, FACS, is the Director of The Breast Cancer Survivorship Institute in Sacramento, CA. E-mail: balazs.bodai@kp.org. **Therese E Nakata, STAR Provider, CWFPBN,** is the Program Manager of The Breast Cancer Survivorship Institute in Sacramento, CA. E-mail: therese.e.nakata@kp.org. **William T Wong, MD,** is a Psychiatrist at the Redwood City Medical Center in CA. E-mail: william.t.wong@kp.org. **Dawn R Clark, MD, FACOG,** is the Chief Facilitator of the Physician Wellness Program and an Obstetrician/Gynecologist at the San Dimas-Baldwin Park Medical Center in San Dimas, CA. E-mail: dawn.r.clark@kp.org. **Steven Lawenda, MD, ABFM,** is an Internist at the Antelope Valley Medical Center in Lancaster, CA. E-mail: steven.a.lawenda@kp.org. **Christine Tsou, MD,** is an Internist at the San Jose Medical Center in CA. E-mail: christine.tsou@kp.org. **Raymond Liu, MD,** is the Chief of Hematology-Oncology at the San Francisco Medical Center in CA. E-mail: raymond.liu@kp.org. **Linda Shiue, MD,** is an Internist and the Director of Culinary Medicine at the San Francisco Medical Center in CA. E-mail: linda.w.shiue@kp.org. **Neil Cooper, MD,** is a Radiologist at the Glenlake Medical Center in Atlanta, GA. E-mail: neil.b.cooper@kp.org. **Michael Rehbein, MD, FACP,** is a Pediatrician and Assistant Physician-in-Charge for Outpatient Service at the Stockton Medical Office in CA. E-mail: michael.rehbein@kp.org. **Benjamin P Ha, MD, ABFM,** is the Associate Area Medical Director for Family Medicine at the Bakersfield Medical Center in CA. E-mail: benjamin.p.ha@kp.org. **Anne McKeirnan, MD, FACOG,** is an Obstetrician/Gynecologist at the San Diego Medical Center in CA. E-mail: anne.p.mckeirnan@kp.org. **Rajiv Misquitta, MD,** is a Primary Care Physician at the South Sacramento Medical Center in CA. He is also an Elected Representative on The Permanente Medical Group Board of Directors. E-mail: rajiv.misquitta@kp.org. **Pankaj Vij, MD, FACP,** is the Medical Director of the Kaiser Permanente Weight Management Program in Pleasanton, CA. E-mail: Pankaj.k.vij@kp.org. **Andrew Klonecke, MD,** is a Nuclear Medicine Specialist at the Sacramento Medical Center and at the Roseville Medical Center in CA. E-mail: andrew.klonecke@kp.org. **Carmelo S Mejia, MD,** is an Internist at the Skyline Medical Offices in Salem, OR. E-mail: carmelo.mejia@kp.org. **Emil Dionysian, MD, FACOS,** is an Orthopedic Surgeon at the Lakeview Medical Offices and at the Orange County Medical Center in Anaheim, CA. E-mail: emil.dionysian@kp.org. **Sean Hashmi, MD, FACM,** is an Internist at the Woodland Hills Medical Center in CA. E-mail: sean.x.hashmi@kp.org. **Michael Greger, MD, FACLM,** is a Physician and Founder of NutritionFacts.org in Kensington, MD. E-mail: mhg1@cornell.edu. **Scott Stoll, MD, FABPMR,** is the Co-Founder and Chairman of the Plantrician Project in Rieglesville, PA. E-mail: stollx7@gmail.com. **Thomas M Campbell, MD,** is an Instructor of Clinical Family Medicine at the University of Rochester School of Medicine and Dentistry and the Co-Founder and Clinical Director of the University of Rochester Program for Nutrition in Medicine in NY. E-mail: thomas_campbell@urmc.rochester.edu.

the poorest health outcomes.[2] The most important problem is our poor lifestyle choices based on misinformation.[1,4]

There has been a dramatic shift in the leading causes of death in the US in the past 100 years. Whereas infectious diseases were the primary cause of death in the early 20th century, CVD and cancer have now assumed dominance in mortality (Figure 1).[9] Additionally, obesity and diabetes are inflammatory conditions that not only contribute to CVD and cancer but also serve as profound comorbidities; their shared etiologies promote one another. Both are sentinel signals of seriously eroding health, each harboring its own morbidities. This can be changed through a shift in how we take charge of managing our health and the health of our patients—through lifestyle medicine.

In this article, we address the pervasive effects of inflammation, obesity, and type 2 diabetes and their cost on the health care system. We review evidence on how implementation of lifestyle medicine recommendations may lead to a paradigm shift not only in health care delivery but also on its dramatic impact on chronic conditions.

Lifestyle medicine addresses basic recommendations, which may extend lives and may allow patients to live longer, in better health, with fewer disabilities, and with an improved quality of life. The intervention recommendations in lifestyle medicine are healthy eating, active living, healthy weight, and emotional resilience (see Figure 2 and the Sidebar: A Special Note on Emotional Resilience). Also represented in Figure 2 is what we refer to as the "red zone"—the percentage of the Western population that fails to adhere to such recommendations. Lifestyle determines in substantial ways the state of health; a poor lifestyle leads to poor health, and a good lifestyle generally leads to good health.

The quadrants of total health can be affected by the adoption of whole, plant-based foods; a moderate level of exercise; and emotional resilience. Whole, plant-based food maximizes the consumption of nutrient-dense foods and minimizes animal-based products (including dairy) and processed foods with added sugar, salt, and oil. Consuming whole, plant-based foods is synonymous with an anti-inflammatory diet.[10] A whole-foods, plant-based diet promotes the increased consumption of leafy greens, vegetables, fruits, legumes, and whole grains as staple foods.[3,11,12] The benefits of a whole-foods, plant-based diet have been shown to substantially influence the development of CVD as well as many common malignancies.[13-15] In addition, an anti-inflammatory diet has beneficial effects on obesity and diabetes, recognized as risk factors for CVD and numerous cancers.[3,11,16-21] The benefits of adopting a healthy lifestyle have been extensively documented. A less-than-optimal lifestyle is associated with the development of chronic conditions and can have a profound impact on the prognosis of such diseases. We summarize the evidence relevant to CVD and three of the most common malignancies: colorectal, prostate, and breast cancer.

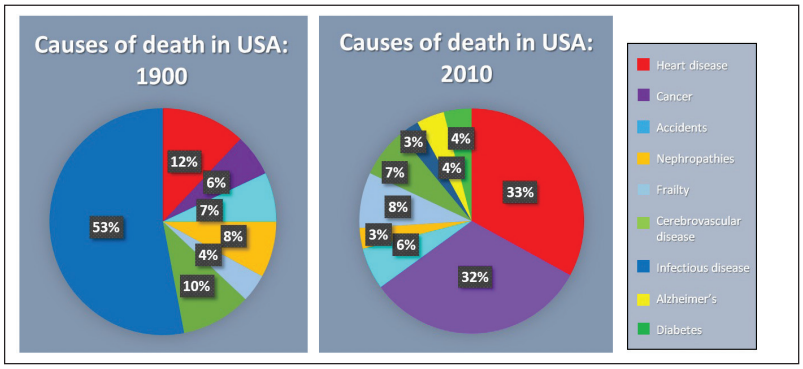

Figure 1. Leading causes of death in the US, 1900 and 2010.[a]

[a] Source: Centers for Disease Control and Infection data from Jones et al.[9]

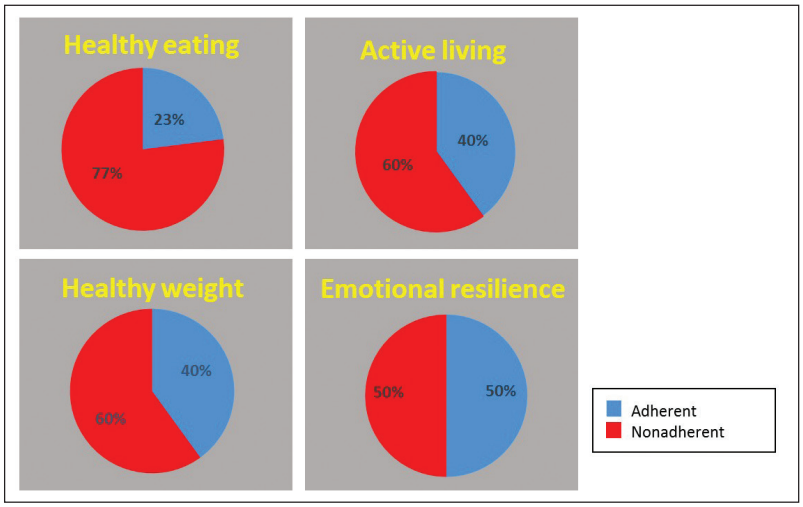

Figure 2. Quadrants of total health.

ENDEMIC CONDITIONS OF THE WESTERN WORLD

In the Western world, we subject ourselves to a poorly recognized, self-inflicted death sentence. We have become victims of three major conditions endemic to the Western World: inflammation, obesity, and type 2 diabetes, which are intricately interrelated and largely result from poor lifestyle choices. Combined, these diseases are lethal. That's the bad news. The good news is that we can now affect these "invaders" of our health through lifestyle changes. Recent reports have addressed the importance of lifestyle interventions (maintaining a healthy body mass index [BMI], a healthy diet, increasing physical activity, and managing stress) on chronic disease management.[3,12,16,18,20,21]

A Special Note on Emotional Resilience

Emotional resilience is defined as one's ability to respond to an adverse situation and, more importantly, a return to the "pre-event" baseline state of health. Factors impairing or affecting emotional resilience include depression, anxiety, stress, insomnia, and the presence of comorbidities, namely, additional chronic conditions. Depression and anxiety are the most common issues that negatively affect emotional resilience in the Western population. Stress is difficult to measure scientifically because of its omnipresence in everyday life. Depression, in particular, is recognized as a leading cause of disability, forecast to be the second-largest contributor to the worldwide burden of disease by 2020.[1] Many of the components of emotional resilience are interrelated, not just among themselves but also with other medical issues, most notably, obesity. The association of obesity and depression has been confirmed by several recent large meta-analysis studies.[2,3]

Depression is a recognized risk factor for the development of cardiovascular disease (CVD, as much as a twofold increase) and serves as a prognostic indicator for poorer outcomes in those already with a diagnosis of CVD.[4,5] Depression in patients after an acute myocardial infarction has been associated with a threefold increase in mortality.[4] The relationship of depression and CVD is reciprocal; each increases the risk of the other. Recent investigations have addressed the interrelationship of depression, stress, and CVD; depression and CVD may result from the cumulative effects of stress on the body.[6] Stress provokes the body's immune system to react by initiating a response to outside irritants, much the same as it does in reaction to bacterial, viral, or chemical intrusions. At the core of the immune response are white blood cells known as macrophages, resulting in the production of cytokines that aid communication in the immune system, promoting the establishment of a chronic inflammatory state and ongoing endothelial cell damage (see Figure 3). Physical activity may decrease such cellular injury.[7]

Depression and anxiety are also seen at higher levels in patients diagnosed with colorectal and prostate cancer.[8,9] Depression remains a major health concern, which is often underdiagnosed and, therefore, undertreated in patients with cancer.[10] Caregivers are increasingly recognizing the importance of screening for and treating depression in patients with breast cancer, but such efforts must be extended to other malignancies.[5] A recent study, the largest to date, addresses the importance of strong social connections; socially integrated women who practiced a healthier lifestyle, perhaps minimizing their stress levels, had decreased recurrence rates and an increase in overall disease-free survival after a diagnosis of breast cancer.[11] Emotional resilience addresses one's potential to return to a "previous normal" and is enhanced by an intense support system. Unfortunately, a substantial number of patients face a cancer diagnosis, treatment, and their outcomes alone and without support from their clinicians in the promotion of a healthier lifestyle.

Interestingly, the gut microbiome is also involved or at least has been implicated, with emotional resilience, affecting anxiety and depression.[12] Processed foods lead to intestinal permeability, which, as previously described, allows toxins to affect distant organs, including the nervous system.[13] It is recognized that lifestyle alterations, including a healthy diet and the pursuit of exercise, can have a positive impact on emotional resilience as well as cardiovascular health.[14] In addition, the influence of exercise in the treatment of depression and anxiety has been well documented and is not limited to the cancer community. Physical activity decreases symptoms of depression and anxiety, and physical inactivity increases the potential for the development of such conditions.[6] The association of psychological distress in the quality of life in patients with cancer has been noted, as well as an increase in the mortality of those with any malignancy.[15,16]

Current technology allows for the analysis of the effect of stress on the body at the molecular level.[17,18] Telomere caplets at the end of each chromosome assist in the regulation of appropriate genetic replication. Each time a cell divides, telomere base pairs shorten, resulting in a lessening of their effective regulation of normal cell replication. Chronic stress and poor health, such as the development of CVD and cancer, are linked. Shortening of telomeres has been associated with the onset of malignancies and the process of aging, which itself is a major risk factor for the development of cancer. Chronic stress has been demonstrated to result in such "shortening damage" of telomeres.[19]

References

1. Lopez AD, Murray CC. The global burden of disease, 1990-2020. Nat Med 1990 Nov;4(11):1241-3. DOI: https://doi.org/10.1038/3218.
2. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: A systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry 2010 Mar;67(3):220-9. DOI: https://doi.org/10.1001/archgenpsychiatry.2010.2.
3. Nicholson A, Kuper H, Hemmingway H. Depression as an aetiologic and prognostic factor in coronary heart disease: A meta-analysis of 6362 events among 146 538 participants in 54 observational studies. Eur Heart J 2006 Dec;27(23):2763-74. DOI: https://doi.org/10.1093/eurheartj/ehl338.
4. Hare DL, Toukhsati SR, Johansson P, Jaarsma T. Depression and cardiovascular disease: A clinical review. Eur Heart J 2014 Jun 1;35(21):1365-72. DOI: https://doi.org/10.1093/eurheartj/eht462.
5. Tuso P. Treatment progress indicator: Application of a new assessment tool to objectively monitor the therapeutic progress of patients with depression, anxiety, or behavioral impairment. Perm J 2014 Summer;18(3):55-9. DOI: https://doi.org/10.7812/tpp/13-091.
6. Miller GE, Blackwell E. Turning up the heat: Inflammation as a mechanism linking chronic stress, depression, and heart disease. Curr Dir Psychol Sci 2006;15(6):269-72. DOI: https://doi.org/10.1111/j.1467-8721.2006.00450.x.
7. Carek PJ, Laibstain SE, Carek SM. Exercise for the treatment of depression and anxiety. Int J Psychiatry Med 2011;41(1):15-28. DOI: https://doi.org/10.2190/PM.41.1.c.
8. Medeiros M, Oshima CT, Forones NM. Depression and anxiety in colorectal cancer patients. J Gastrointest Cancer 2010 Sep;41(3):179-84. DOI: https://doi.org/10.1007/s12029-010-9132-5.
9. Korfage IJ, Essink-Bot ML, Janssens AJ, Schröder FH, de Koning HJ. Anxiety and depression after prostate cancer diagnosis and treatment: 5-year follow-up. Br J Cancer 2006 Apr 24;94(8):1093-8. DOI: https://doi.org/10.1038/sj.bjc.6603057.
10. Massie MJ. Prevalence of depression in patients with cancer. J Natl Cancer Inst Monogr 2004;(32):57-71. DOI: https://doi.org/10.1093/jncimonographs/lgh014.
11. Kroenke CH, Michael YL, Poole EM, et al. Postdiagnosis social networks and breast cancer mortality in the After Breast Cancer Pooling Project. Cancer 2017 Apr 1;123(7):1228-37. DOI: https://doi.org/10.1002/cncr.30440.
12. Galland L. The gut microbiome and the brain. J Med Food 2014 Dec;17(12):1261-72. DOI: https://doi.org/10.1089/jmf.2014.7000.
13. Kelly JR, Kennedy PJ, Cryan JF, Dinan TG, Clarke G, Hyland NP. Breaking down the barriers: The gut microbiome, intestinal permeability and stress-related psychiatric disorders. Front Cell Neurosci 2015 Oct 14;9:392. DOI: https://doi.org/10.3389/fncl.2015.00392.
14. Mosovich SA, Boone RT, Reichenberg A, et al. New insights into the link between cardiovascular disease and depression. Int J Clin Pract 2008 Mar;62(3):423-32. DOI: https://doi.org/10.1111/j.1742-1241.2007.01640.x.
15. Brown LF, Kroenke K, Theobald DE, Wu J, Tu W. The association of depression and anxiety with health-related quality of life in cancer patients with depression and/or pain. Psychooncology 2010 Jun;19(7):734-41. DOI: https://doi.org/10.1002/pon.1627.
16. Russ TC, Stamatakis E, Hamer M, Starr JM, Kivimäki M, Batty GD. Association between psychological distress and mortality: Individual participant pooled analysis of 10 prospective cohort studies. BMJ 2012 Jul 31;345:e4933. DOI: https://doi.org/10.1136/bmj.e4933.
17. Hofker MH, Fu J, Wijmenga C. The genome revolution and its role in understanding complex diseases. Biochim Biophys Acta 2014 Oct;1842(10);1889-95. DOI: https://doi.org/10.1016/j.bbadis.2014.05.002.
18. Wilson BJ, Nicholls SG. The Human Genome Project, and recent advances in personalized genomics. Risk Manage Healthc Policy 2015 Feb 16;8:9-20. DOI: https://doi.org/10.2147/rmhp.s58728.
19. Epel ES, Blackburn EH, Lin J, et al. Accelerated telomere shortening in response to life stress. Proc Natl Acad Sci U S A 2004 Dec 7;101(49):17312-5. DOI: https://doi.org/10.1073/pnas.0407162101

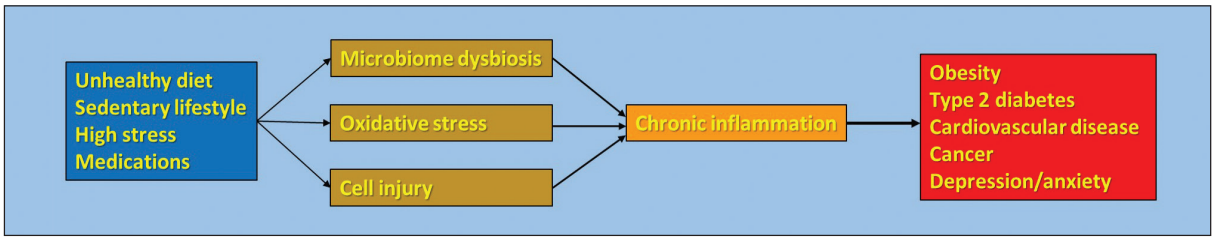

Figure 3. Steps in the pathogenesis of inflammation leading to progression of chronic diseases.

Such interventions are based on large-scale, prospective studies, which provide evidence-based conclusions.[6,13,18-21]

Inflammation

We live in a world that initiates, promotes, and accelerates chronic inflammation. Inflammation has been implicated as a causative factor in nearly all chronic diseases.[22] From an evolutionary perspective, the body's inflammatory response was vital for survival before modern sanitation processes (water purification, sewage systems, and the recognition of hygiene issues such as hand washing). Today, we live longer, and thus inflammatory responses are more likely to confuse and overwhelm the body's defense systems. Many attributes of our Western lifestyle incite an inflammatory response, and such continued lifestyle exposures perpetuate unmitigated inflammation.

Obesity

Obesity is the second endemic condition we face. Two of three Westerners are either overweight or obese (Figure 2). Furthermore, obesity is an inflammatory disease.[23] Adequate physical activity and normalizing weight decreases the inflammatory reaction of the body and may help mitigate the massive immune response to infectious agents that serve as a stimulus for carcinogenesis. Inflammatory proteins (Interleukin-6, tumor necrosis factor, and C-reactive protein, among others) are elevated in obese patients because of excess adipose tissue.

The current focus of obesity is centered on CVD, yet cancer is far more feared and less frequently addressed. A 2008 Surveillance, Epidemiology, and End Results (SEER) Program Study[21] estimated that nearly 90,000 cases of cancer were caused by obesity. Estimates are that the continuing trend in obesity will lead to an additional 500,000 deaths by the year 2030.[21] Additionally, obese individuals are more likely to live in a state of chronic inflammation.[23]

The common link between inflammation and obesity may well reside in the gastrointestinal (gut) microbiome. The physiology of the gut remains poorly defined. However, recent advances in molecular tools, such as gene sequencing, have allowed a more intricate understanding of the role of the gut microbiome as an endocrine organ that manufactures hundreds, if not thousands, of chemicals that influence the regulation of multiple distant organs.[24] Such compounds play a substantial role in the development of a "leaky" gut, which allows toxins to enter the bloodstream and results in inflammation and promotion of CVD, obesity, Type 2 diabetes, and chronic diseases.[25-30] The gut microbial complex appears to be a major factor responsible for metabolic and inflammatory diseases, linking inflammation and obesity to additional factors such as alterations in lipid metabolism and insulin signaling. The accumulation of fat promotes a chronic inflammatory state that results in the activation and recruitment of immune cells, which leads to an ongoing, self-perpetuating process.[31] A major hallmark of obesity is documentation of the occurrence of inflammation.[32] The result is a state of chronic inflammation promoting the disease states of our modern civilization. The steps in the pathogenesis of inflammation are depicted in Figure 3 in their most simplified form to help readers understand chronic disease progression.

Diabetes

The rate of diabetes has steadily risen in the past decade.[33] It is recognized as the leading cause of target organ complications (limb amputations, end-stage renal failure, and adult-onset blindness). Diabetes is also a major risk factor for CVD. With its increasing prevalence and long-term complications, diabetes has become one of the costliest medical conditions in the US. Between 2007 and 2012, costs associated with diabetes increased an alarming 48%.[2] Obesity, as described earlier, has been associated with chronic inflammation, insulin resistance, and the development of type 2 diabetes.[34] Diabetes has been identified to be far beyond a metabolic disease and is now acknowledged to be an inflammatory condition.[35,36]

The increasing prevalence and costs associated with diabetes have resulted in the need for improved efforts directed at prevention. Exercise and weight reduction are well established as important priorities in prevention, with strong supportive evidence.[37-40] Recent attention to diet quality as it pertains to diabetes prevention has focused on the reduction of refined sugar consumption, and rightfully so; each serving per day of sugar-sweetened beverages (eg, soft drinks) has been associated with a 25% increased risk of diabetes.[41]

Refined sugar consumption is an important focus, but currently lacking in the conversation on diabetes prevention is the importance of animal product consumption. A large study of more than 60,000 North Americans showed a stepwise increase in the prevalence of diabetes with increasing animal product consumption. Those eating no animal products at all (vegans) had the lowest diabetes prevalence overall, at 2.9%, with omnivores having the highest prevalence at 7.6%. Even when risk factors such as age, BMI, and physical activity were adjusted for, there persisted a statistically significant reduction of 49%

in the risk of later development of diabetes.[21] Data from the Nurses and Physicians' Health Studies (more than 4 million person-years combined) demonstrated that the substitution of just 5% of calories from animal to plant protein reduced the risk of diabetes by 23%.[42] Data looking at processed meats (bacon, sausage, hot dogs, and deli meat) and egg consumption in relation to diabetes risk have been impressive. A meta-analysis of processed meat consumption revealed that each serving of processed meat daily was associated with a 51% increased risk of diabetes.[43] A separate meta-analysis looking at egg consumption demonstrated that high egg consumption was associated with a 68% increase in the risk of diabetes development.[44]

Prevention is ideal, but the reality is that more than 29 million Americans already have diabetes, making prevention management the priority. The past decades have focused on glycemic management with medications. However, recent studies question this approach, including a meta-analysis of 13 randomized controlled trials, which found that intensive glycemic management with medications resulted in a doubling of the risk of severe hypoglycemia, with no overall mortality or cardiovascular mortality benefit.[45] A separate review of 328 articles, 11 meta-analyses, and 5 randomized controlled trials all published in the last decade cast doubt on the supposed benefits of fewer microvascular complications with intensive glycemic management; specifically, no significant benefit was found with respect to the risk of dialysis/transplantation/renal death, blindness, or neuropathy.[46] Medications used in the treatment of diabetes also carry a wide range of side effects, which include the following: diarrhea, vitamin B12 deficiency, lactic acidosis (caused by metformin), hypoglycemia, weight gain (sulfonylureas and insulin), heart failure, an increase in fractures (thiazolidinediones), pancreatitis, yeast infections, urinary tract infections, and acute kidney injury.[47]

With legitimate concerns about the utility and safety of the intensive management of diabetes with medications, it is essential and timely to note that lifestyle changes are as effective as, and perhaps more so than, medications, with no side effects. The most effective lifestyle changes have been exercise and diets based on whole, plant foods (fruits, vegetables, whole grains, beans, nuts, and seeds). Regarding exercise, a meta-analysis of 27 studies found that regular exercise, regardless of type (aerobic, resistance, or combined), resulted in the improvement of hemoglobin A_{1C} control by an average of 0.8%,[48] a benefit comparable to current diabetes medications.[47]

Dietary studies focused on diabetes have demonstrated consistent results when based on whole, plant foods. A randomized controlled trial of 99 patients compared a whole-foods, plant-based diet with the American Diabetes Association diet and found that although both diets improved glycemic control, the plant-based diet group had superior results.[49] In the plant-based diet group, hemoglobin A_{1C} control improved by 1.23 points,[49] an effect comparable to, if not superior to, that of the most currently prescribed medications.[47] A larger study analyzed 232 patients with diabetes who were placed on a plant-based diet as part of a residential dietary intervention program. More than 90% of patients were able to decrease or discontinue their diabetes medications in just 7 days while improving or maintaining control of their diabetes.[50] A review of 14 randomized diet trials concluded that the best results occurred with plant-based diets.[51]

The annual health care costs attributable to obesity alone exceed $100 billion.[2] Add to this the rapid rise in the costs of treating type 2 diabetes, which total approximately $101 billion annually.[2,52] Escalation of health care costs from other complications of obesity and type 2 diabetes are inevitable as these conditions continue to result in substantial future complications that will require further expensive medical care. Inflammation, obesity, and diabetes are intricately related, fuel one another, and will drive health care expenses beyond affordability.

Cardiovascular Disease

Despite major advances in the treatment of cardiac events, CVD remains the leading cause of death and disability in the US.[53-55] More than 600,000 deaths (1 in 4) are attributable to heart disease each year, and CVD accounts for more than $70 billion annually (approximately 17% of the total health care expenditure).[56-58] By the year 2030, 40% of the US population is projected to have some form of CVD, and care will exceed $800 billion, making it our most costly disease.[56]

The understanding of the pathogenesis of atherosclerosis has recently undergone a dramatic update. The role of chronic inflammation in its development, particularly in the setting of obesity, serves as the foundation for the most current theory.[59,60] Atherosclerosis appears to be the result of oxidative damage to the endothelial cells that line the vascular system, including, of course, the coronary arterial anatomy.[61] The damage to the endothelial layer of the coronary arteries is a progressive process beginning with inflammation secondary to oxidative stresses that result from the oxidation of low-density lipoproteins, energizing the low-density lipoproteins to penetrate the endothelial layer; this process leads to the subsequent development of plaques, the rupture of which may result in a myocardial infarction or often sudden death.[61,62]

Dietary components consumed by the Western population promote CVD by directly affecting the gut microbiota.[63] In particular, consumption of red meats, which are high in L-carnitine, elevate serum levels of trimethylamine oxide (TMAO) because of the hepatic conversion of its microbially derived precursor, trimethylamine.[63] Reducing red meat consumption results in decreased TMAO production, which downregulates the macrophagic uptake of oxidation of low-density lipoproteins. Levels of TMAO are reduced in patients who are following an anti-inflammatory diet. Although measurement of TMAO levels is not readily available, future technology may soon develop a test measuring TMAO and allow for the early intervention of individuals at risk of atherogenic threats before they progress to the point of sudden death.[61] Some authors offer an in-depth discussion of the biochemical basis and pathogenesis of oxidative stress and vascular injury.[59-62]

A lifestyle program that incorporates a whole, plant-based diet has been shown to reverse CVD, a feat largely elusive to medications and technologic advances. Numerous studies have demonstrated that lifestyle interventions can have a major impact on the development of, and even the reversal of, CVD.[1,13,62,64] Evidence has accumulated

associating a healthy dietary pattern with lower rates of cardiac events, and an extensive review has been presented endorsing the cardioprotective effects of a diet that endorses the increased consumption of plant-based foods.[65] Lifestyle management offers support for the adoption of a diet consisting of mostly plants to prevent CVD.[11] A whole-foods, plant-based diet offers additional protection against CVD because of the beneficial effect that polyphenols have on the endothelial layer of the vasculature, including the negation of oxidation of low-density lipoproteins and its impact on inflammation.[11,61,66-68] Large epidemiologic studies support the fact that those following an anti-inflammatory, plant-based diet may decrease the risk of CVD development by nearly 25%.[69,70] The promotion of a diet contrary to the standard American diet—embracing the increased consumption of plant-based foods and the avoidance of red meat, highly processed foods, added sugars, salt, and fat—appears to be beneficial in the improvement of cardiovascular health.[71]

Recent scientific advances have allowed us to characterize the human genome, opening the door to the genetic expression of disease in its earliest development.[72,73] Regarding CVD, a recently published study demonstrated the effect of lifestyle modification on pro-inflammatory gene expression.[74] The impact of our understanding of disease at the epigenomic level presents an opportunity to intervene in the development of chronic diseases and increase the odds for cure. Lifestyle interventions (tobacco cessation; adoption of a whole-foods, plant-based diet; and exercise) focusing on CVD have been documented as remarkably effective.[75] Even in patients with a high genetic risk profile, a favorable lifestyle has been associated with a 50% decreased risk of CVD development.[76]

Physical activity in individuals at increased risk of CVD has been noted to significantly decrease mortality.[61,75,77] Those who are least fit may, in fact, gain the most benefit from exercise and thus realize a more statistically significant impact on their survival.[78] Interestingly, many common malignancies share similar pathologic characteristics that are akin to CVD—notably, inflammation and obesity.

CANCER

Despite enormous research efforts and funds expended, cancer continues to be a major cause of death. Each year, 17.5 million cancers are diagnosed and 8.7 million deaths caused by cancer occur worldwide.[79] In the US, 1.6 million Americans receive a diagnosis of cancer, and more than 600,000 deaths are attributable to this disease.[80] In the next few years, the world population will exceed 7.5 billion, which is expected to drive these figures even higher.[81] The current belief is that most cancers are the result of inherited genetic abnormalities, yet 90% of malignancies are rooted in our lifestyle and environmental exposures. Many of these exposures are modifiable; we can avoid tobacco and alcohol, decrease our exposure to ultraviolet light, increase our level of physical activity, and, perhaps most importantly, alter our diets.

In the US, October is National Breast Cancer Awareness Month; September is set aside for prostate cancer awareness; and March is dedicated to colorectal cancer awareness. These awareness campaigns are laudable; however, their emphasis on early detection, treatment, and survivorship does not address the more crucial issue that many such cancers can actually be prevented by lifestyle changes. For instance, obesity is a well-recognized risk factor for the development of a large number of malignancies, as well as for cancer recurrence and mortality.[82,83] In 2016, the US will have more than 14 million persons alive as survivors of cancer. In comparison, in 1971, there were 3 million cancer survivors. By 2020, there will be 20 million people in whom some form of cancer has been diagnosed who are alive and well. More than 75% of all cancer patients currently live beyond 5 years.[84] As such, there is ample time for patients to implement lifestyle changes that may further contribute to their overall disease-free, long-term survival.

Colorectal Cancer

In 2015, there were 1.7 million cases of colorectal carcinoma with 832,000 deaths worldwide.[79] More than 140,000 people in the US will receive a diagnosis of colorectal carcinoma in 2016, and more than 50,000 will die.[80] Colorectal cancer is the third most commonly diagnosed non-sex-specific cancer. Less than 20% of colorectal carcinomas have a genetic basis[85]; therefore, most colorectal cancer cases have been linked to environmental exposures (eg, food-borne mutagens) and chronic intestinal inflammation.[86] Perhaps no malignancy other than colorectal carcinoma demonstrates so dramatically the connection between inflammation and the development of neoplasms. Patients with chronic inflammatory bowel disease (ulcerative colitis and Crohn disease) are at an increased risk of breast cancer development,[87] adding to the ever-growing body of evidence linking chronic inflammation to the progression of cancer. The risk of colorectal cancer developing increases with the duration and extent of inflammatory bowel disease.[87] The microbiome of the gut has also been implicated in the development of sporadic colorectal carcinoma.[25,88]

Risk factors for the development of colorectal cancer include a sedentary lifestyle, obesity, and the dietary components that form the basis of the standard American diet (large consumption of red meats and highly processed foods and low amounts of fruit, vegetables, legumes, and fiber intake).[89] Low-fiber diets, such as the standard American or "Westernized" diet that promotes inflammation, have been linked to the increased risk and development of colorectal cancer.[90] In addition, patients with colorectal cancers appear to have more comorbidities at the time of diagnosis than patients with other malignancies.[91] For example, patients with diabetes have a 26% increased risk of developing colon cancer and a 30% increased risk of dying because of it compared with patients without diabetes.[92] Data exist that modifiable lifestyle issues (diet and activity) are increasingly associated with the risk of colorectal cancer development, perhaps more so than any other malignancy.[93,94]

Prostate Cancer

Prostate cancer is the most commonly diagnosed malignancy in men, affecting 1.6 million worldwide and resulting in the death of nearly 370,000 in 2015.[79] In the US, nearly 150,000 men received a diagnosis of prostate cancer in 2016, and close to 40,000 will die of this cancer.[80] Somewhat alarming is a recent report that the incidence of metastatic prostate cancer has increased by 72% since 2004.[95] Of particular concern is that the largest increase in new cases was

in the age range of 55 to 69 years, ironically the same group most likely to benefit from early treatment.[96] If this increase is, as some postulate, caused by a more aggressive presentation of the disease, then the importance of lifestyle changes may further increase in relevancy. As with many other malignancies, diet and obesity contribute to chronic inflammatory processes that lead to disease aggressiveness.[81,97] Furthermore, obesity has been implicated in not only the development but also the progression of prostate cancer.[81,97]

Prostate cancer patients are often advised to make lifestyle changes. Such changes could be beneficial but need further verification. In one study,[98] changes in prostate-specific antigen levels were monitored in a small group of patients. The experimental group was subjected to an intensive lifestyle intervention program, which included a vegan diet, soy protein, supplemental vitamins (E and C), selenium, exercise (30 minutes of walking 6 d/wk), and a support group/stress management program for 1 hour per week. Prostate-specific antigen levels decreased 4% in the experimental group and increased 6% in the control group.[99] In addition, blood taken from both groups demonstrated that the serum of the experimental group inhibited growth of prostate cancer cells nearly 8-fold more intensively than the serum of the control group. Furthermore, these comprehensive nutrition and lifestyle changes have been shown to downregulate prostate gene expression in men after a diagnosis of early-stage prostate cancer.[99]

The incidence and mortality of prostate cancer appear to be associated with a Western lifestyle, and a strong corollary relationship has been noted with the intake of animal foods.[97,100] Men in developing countries who drift toward a Western-oriented lifestyle experience an increased incidence of prostate cancer. Furthermore, migration studies have demonstrated that those populations that live in low-cancer-risk geographic areas assume Western rates of cancer within 1 to 2 decades of immigration to the West. This observation is not limited to prostate cancer but involves the development of other malignancies as well.[81]

Breast Cancer

The most common malignancy among women in 2016 was breast cancer, affecting 2.4 million women worldwide and taking the lives of more than 520,000.[79] In 2017, nearly 250,000 women will receive a diagnosis of breast cancer and more than 40,000 will die in the US.[80] Breast cancer is the most feared disease by many women, yet heart disease is the leading cause of death in women in the US.[3] Interestingly, less than 50% of women are aware that heart disease is the leading cause of death.[3]

As with previously addressed malignancies, breast cancer can be attributed in part to a lifestyle fueled by a poor diet that often results in obesity.[101] Sinicrope and Dannenberg[101] addressed this topic in a recent publication. Obesity leads to insulin resistance, resulting in elevated blood levels of insulin and insulin-like growth factor (IGF) and a decrease in sex hormone-binding globulin. Consequently, the availability of estradiol increases, which may fuel the development and aggressiveness of breast cancers. Fatty tissues (adipocytes) have been demonstrated to be an independent endocrinogenic organ capable of manufacturing and storing estrogenic compounds that contribute to multiple malignancies. Importantly, fatty tissues also store a dozen or more inflammatory proteins that promote carcinogenesis.[101] In a recent study, low-dose aspirin was shown to reduce inflammation, resulting in a lower incidence of breast cancer.[102]

Not only is obesity a risk factor for breast cancer development, it is an independent prognostic factor for distant metastases and an increased risk of death.[103] Comorbidities also have a role in oncogenesis. Patients with diabetes have a 23% increased risk of breast cancer developing and a 38% increased risk of dying of the disease compared with patients without diabetes.[92] A substantial proportion of breast cancer patients are both obese and sedentary, emphasizing the need for lifestyle interventions that may improve prognosis and ultimate outcomes.[3]

Understanding of breast cancer and the influence of dietary consumption patterns has recently advanced. Dietary recommendations, including an increase in fiber intake, have been made to aid in the prevention of this cancer.[104,105] Recently the human "estrobolome" has been discovered as the set of gut bacterial genes that metabolize estrogen.[106] Dysbiosis of the gastrointestinal tract is involved in the re-cycling of estrogen through the enterohepatic circulation, increasing its potency, which may further fuel the development of breast cancer.[107,108] Estrogen levels are further decreased by the increased consumption of fiber intake because fiber inhibits the absorption of estrogen in the gastrointestinal tract.[104,109] The American Institute for Cancer Research reported in 2014, from worldwide data, that diet, physical activity, and weight control are major contributors to long-term survival after a diagnosis of breast cancer.[110] Furthermore, a 2011 meta-analysis of postdiagnosis exercise in patients with breast cancer involving more than 12,000 patients demonstrated a 34% decrease in risk of death caused by breast cancer, a 24% decrease in recurrence, and a 41% decrease in the risk of all-cause mortality.[111] This conclusion is the result of the review of 67 published articles addressing lifestyle changes as they relate to the reduction of breast cancer recurrence.[112]

Additional studies have documented that physical activity not only increases survival and decreases recurrence but also improves overall quality of life in patients with breast cancer and in patients with colon cancer.[113-115] Another study followed nearly 1500 women diagnosed with early-stage breast cancer. These patients were followed for up to 9 years and demonstrated a 50% decreased death rate in those who adhered to a high fruit and vegetable intake (5 servings/d) and a regular physical activity regimen (30 minutes, 5 times weekly) compared with those who did not.[116] Although the exact mechanism of the action of exercise and its impact on cancer recurrence remains elusive, some have pointed to the possibility that exercise may affect the inflammatory response of the body, resulting in a decreased rate of recurrence.[117] Regular exercise may also have a protective role in the initial development of breast cancer.[118]

DISCUSSION

For far too long, patients have experienced chronic illnesses because our health care system has not taken a proactive role in promoting healthy eating, active living, and the promotion of emotional resilience (see Sidebar: A Special Note on Emotional Resilience). The medical community has been proud to announce major achievements in health care and their impact, yet a recent analysis on cardiovascular mortality brings into question such advances; the

decreasing rate of CVD that has been noted since the 1970s appears to be declining at a slower pace.[119] Advances in CVD survival no longer approach the prior rate of decline despite improvements in treatment. Perhaps the management of CVD should focus more on lifestyle recommendations and prevention than on treatment once the disease has become symptomatic. In addition, it has been suggested that the recently noted decline in cancer incidence may be related to the recession of 2008, which may have decreased screening accessibility for many.[120] It is increasingly recognized that the real issue in health care—lifestyle—should become the primary prescription for the leading causes of disease that result in the highest rates of mortality.[4-7,9,22] The slow progress in decreasing mortality rates from CVD incriminates an unhealthy diet and a sedentary lifestyle as major contributing factors.[121]

Ample evidence exists to support the avocation of a diet on the basis of the recommendations outlined in Table 1.[3,7,116,122-127]

Lifestyle medicine addresses principles that are the cornerstone of health and well-being. The current practice of prescribing medications or performing surgery for nearly every illness must be revisited. A paradigm shift to lifestyle medicine needs urgent implementation. Dramatic effects using lifestyle interventions have been demonstrated in patients with chronic conditions. Several large studies have conclusively shown that diet and exercise modifications not only substantially improve long-term survival but also result in a portrait more nearly approaching total health.[5,105,116,122,128,129] As an example, a prospective study of 23,000 participants evaluated adherence to 4 simple recommendations[5]: No tobacco use, 30 minutes of exercise 5 times per week, maintaining a BMI of less than 30 kg/m^2, and eating a healthy diet as previously described. Participants who adhered to these 4 recommendations had an overall 78% decreased risk of development of a chronic condition during an 8-year timeframe. Furthermore, in participants adhering to these recommendations, there was a 93% reduced risk of diabetes mellitus, an 81% reduced risk of myocardial infarction, and a 36% reduction in the risk of the development of cancer.[5]

Table 1. Daily dietary recommendations[1]

Decrease substantially or eliminate	Increase or consume heavily
Inflammatory effects	**Anti-Inflammatory effects**
Low nutrient and/or high calorie	**High nutrient/low calorie**
Meat: beef, pork, lamb, chicken, turkey, seafood	Leafy greens
Processed meats: salami, bologna, ham, turkey, chicken	Vegetables: cruciferous, squash, garlic
Animal dairy: milk, cheese, yogurt, kefir, sour cream, cottage cheese, butter	Mushrooms
Sugar substitutes and refined sugars: aspartame, high-fructose corn syrup	Fruits: berries, bananas, pomegranates
Processed foods: refined grains (white bread, cookies, fried potato chips)	Legumes: green beans, lentils, soybeans, sugar snap peas
Soft drinks, alcohol	Whole grains: quinoa, wheat, oat, rice, pasta, barley, corn
	Seeds: flax, chia, pumpkin, sesame
	Plant-based "dairy": soy, almond, rice milk
	High nutrient/high fat: Limited consumption
	Nuts: walnuts, pecans, almonds, etc

[1] Bodai BI, Tuso P. Breast cancer survivorship: A comprehensive review of long-term medical issues and lifestyle recommendations. Perm J 2015 Spring;19(2):48-79. DOI: https://doi.org/10.7812/TPP/14-241.

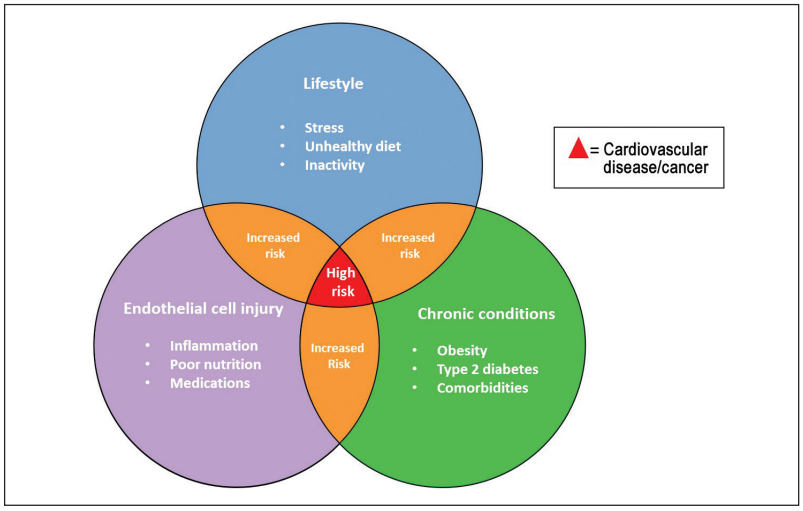

Figure 4. Effects of cellular damage, chronic conditions, and lifestyle practices appear to raise the risk of cardiovascular disease and cancer.

The additive effects of cellular damage, chronic conditions, and lifestyle practices appear to place us at an ever-increasing risk of CVD and cancer (Figure 4). Risk factors are interactive and should be recognized as such. Those who fall into the high-risk category in Figure 4 need urgent attention and lifestyle interventions.

Medications, particularly in chronic or repeated sequences, may also play an important role in the development of malignancies. The overprescription of antibiotics has received recent attention in the promotion of "super strain" bacteria that are resistant to most currently available antibiotics. Prostate cancer risk increased with the use of penicillin, quinolones, sulfonamides, and tetracycline; breast cancer risk was demonstrated to modestly increase with exposure to sulfonamides.[130] This increased risk may well be caused by the drugs' influence and/or the depletion of the natural microbiome resulting in a state of dysbiosis.

The potential carcinogenicity of red and processed meats has drawn extensive attention since the Interventional Agency for Research on Cancer evaluated these products.[131] Consuming a whole, plant-based

food (anti-inflammatory) diet promotes high-nutrient foods with fewer calories per pound compared with low-nutrient foods.[3] This will result in a healthy BMI, potential weight loss, and a lower risk of development of CVD and some of the most common malignancies. Vegetables, fruits, legumes, whole grains, and healthy fats should become our staple foods and have been recommended as key components of a healthy lifestyle to avert the three chronic conditions that are responsible for the majority of deaths in the US (Figure 1). Recently, the association of animal vs plant protein intake with all-cause mortality has been documented. Specifically, high consumption of animal protein was associated with an increased risk of cardiovascular mortality and all-cause mortality.[132] In this same study, high consumption of plant-based protein demonstrated an overall decrease in all-cause mortality.[132]

Genetic variants have been associated with susceptibilities to the development of chronic disease. However, evidence is available that the hereditability of such variants may, in fact, be only modest.[31] Thus, credibility is added to the fact that most chronic conditions are, in reality, the result of lifestyle. An invitation to the development of chronic conditions is related to shifts in the human microbiome as represented by Western influence. Evidence for a strong correlation between the gut microflora and disease is exponentially expanding, particularly relevant to the development of CVD and cancer.[133-135] Along with our growth of knowledge comes an opportunity to intervene in the prevention of disease. An incredible shift in cancer care has recently become recognized because of technologic advances, and priming of the immune system has now been shown to be effective in treating patients with a wide variety of malignancies. Epigenomics may play a major role in our immunogenetic capabilities, and, as such, lifestyle modifications, demonstrated to have an influence on the modulation of genetic expression profiles, are worthy of further investigation. Dietary and lifestyle changes can and should be pursued to avert poor outcomes.[136]

Profit motives play a large role in the food industry as well as "Big Pharma" and health care; therefore, the delivery of information and the care of patients may themselves become the victims of politics. Most chronic conditions are influenced by lifestyle and account for 75% or more of health care costs.[4,137] Since 2010, nearly 18% of the US gross national product has been spent on health care, which exceeded $3.0 trillion in 2015.[138,139] Few of these dollars have been spent on identifying the true underlying causes of patients' chronic conditions. Lifestyle recommendations, as the primary treatment of disease, fail to be recognized as a priority. If we continue our current path of treating risk factors and advanced diseases, costs for care will continue to escalate and the health care system will approach bankruptcy in the near future.[4] As a consequence, lives will be lost. The enormous cost of health care directed toward CVD and cancer account for up to one-third of the health care fiscal burden in the US. If 1 in 10 of the US population would adopt a healthy lifestyle, the amount of money saved could well fund others more in need. A 10% reduction in such costs may results in billions of dollars saved.

Given the benefits of lifestyle medicine interventions, it would seem that our health care system would rush to embrace this movement; however, nothing could be further from the truth. Through the decades, leading proponents of lifestyle interventions have faced resistance or marginalization. Such resistance to change has to do with barriers on multiple levels affecting patients, clinicians, administrators, government, and society in general. Most patients typically gather their food and nutrition information from popular media rather than from clinicians, many of whom may have limited knowledge of lifestyle interventions. In addition, much of this may reflect the limited time available in a typical office visit. Perhaps a more important issue stems from the formal education in medical school, residency, or fellowship programs, which lack a focus on scientific evidence supporting the importance of nutrition related to a healthy lifestyle.[140,141] Health care practitioners as well as administrators are often focused on the bottom line and find it challenging to direct resources toward new and innovative practices given low reimbursement rates for counseling on lifestyle changes. Adding to this, they may fear that patients will find such changes difficult and not sustainable. We are long overdue for a "rethink" about health care to achieve a more directive role in the lifestyle intervention of patients.

Currently, multiple forces maintaining the status quo exist at the systemic level. Special interest groups, including certain lobbyists, maintain barriers by spending monies to influence governmental and professional targets. For example, national dietary guidelines are watered down out of a concern over the economic interests of certain industries instead of reflecting on the evidence-based recommendations regarding the consumption of meat and dairy products. On the societal level, the hedonistic aspects of food are promoted over their health and nutritional aspects.

Despite the status quo, there is a groundswell of interest in lifestyle medicine and a hunger for change. There exists reason for optimism. The growing interest in wellness programs and the mainstreaming of yoga, tai chi, and mindfulness practices are examples of such changing attitudes. Integrating lifestyle medicine into clinical practice in the areas of food, nutrition, exercise, and stress reduction is becoming more commonplace. Multiple organizations, including health care systems and large successful corporations, have come to realize the enormous benefits of a healthy lifestyle not only to wellness but also positively influencing enhanced productivity.

The establishment of lifestyle medicine as an effective therapy will ultimately depend on a strategic plan to embrace the basic concepts addressed. We propose and advocate for a series of multiple approaches with a focus on potential future ventures. In an ideal setting, establishing a lifestyle medicine clinic within a health care organization would be a major step toward the promotion of patient wellness. Establishing a trained, interested team of dedicated professionals would be key to a successful patient experience. Although many different lifestyle medicine approaches have been implemented, they all share some common characteristics: A physician trained in lifestyle techniques, supportive staff, patient educators who are strong in plant-based diets, and access to behavioral health. Such a team approach can be used to encourage, educate, and support patients for motivation to achieve their goals.

It will take time to break down the barriers that exist. We recommend the allocation of resources dedicated to the expansion and further development of such programs. More research documenting the efficacy and cost-saving benefits of innovative lifestyle clinics is needed. True preventive care must include tools and information on lifestyle recommendations. It is time for the medical community to intervene and provide the proper treatment when confronting preventable conditions. Many conditions are reversible with education and ongoing support to patients regarding lifestyle changes. Addressing the root cause of diseases and taking immediate corrective action may avert the health care crisis and restore a solid foundation for patients and the medical community. The practice of medicine is ever evolving, and the medical community must keep pace of new information as it becomes available to implement best practices. Creating change takes courage and a willingness to think creatively as we begin to shift our medical system from one characterized by sick care to one deserving of the label of health care.

In conjunction with building specific clinic workflows, we would recommend and endorse activities so that all practitioners possess at least an awareness and a basic understanding of what lifestyle modifications can do to prevent, treat, and even reverse chronic diseases. Large health care organizations must obligate themselves to such programs. Numerous health care practitioners may not have the essential information available to share with patients. Some, particularly in a solo-practice environment, may not have time to address lifestyle issues or have access to support such a program, despite their best intentions to do so. Many of our colleagues are uncomfortable in addressing lifestyle issues as they feel they are not qualified in such concerns, despite the fact that many of their patients seek such information. Multiple courses are available, at numerous conferences and through programs online, where practitioners can easily gain the knowledge they need to promote a healthy lifestyle.

Moving Forward: Healthy Lifestyle Recommendations and Resources for Daily Practice

Practitioner education regarding benefits of healthy lifestyle recommendations

- Plant-based nutrition certification, Cornell University
- American College of Lifestyle Medicine certification
- Lifestyle conference attendance (eg, The Plantrician Project: www.plantricianproject.org)
- Endorsement by providers to adopt such practices
- Online resources: T Colin Campbell Center for Nutrition Studies (http://nutritionstudies.org); Physicians Committee for Responsible Medicine (www.pcrm.org)

Identification of team members engaged in promotion of a healthy lifestyle

- Physician colleagues
- Dietitians trained in whole-foods, plant-based nutrition
- Social workers
- Behavioral therapists
- Lifestyle coaches

Promotion of exercise programs

- Walk to Thrive (https://kpwalktothrive.org/)
- Exercise coaches

Endorsement of alternative approaches to health and well-being

- Yoga
- Meditation
- Dance
- Aromatherapy

Establishment of and participation in cooking demonstrations and classes in the clinic and community—patient provision of resources

- Health education handouts and pamphlets addressing health and wellness
- Community-provided educational materials
- Reputable Web site resources
- Vigorous endorsement by providers to adopt such practices

Healthy lifestyle interventions need not be limited to the clinic environment. Numerous opportunities to share information with a direct impact on overall health are readily available. Community events, such as religious celebrations and festivals, present a major forum for valuable information dissemination. Most large and influential companies have come to realize the importance of a healthy lifestyle for their employees and now understand the increased effectiveness and productivity associated with good health. Social media, perhaps the most powerful contemporary means of connectivity, provides incredible opportunities to disseminate information promoting a healthy lifestyle. Although not all practitioners may be able to incorporate lifestyle goals into their practice, at least having the information easily available and knowing how to access such tools is a major step forward (see Sidebar: Moving Forward: Healthy Lifestyle Recommendations and Resources for Daily Practice).

CONCLUSION

Escalating health care costs and the impact on care delivery are enormous and underestimated. Projections of chronic diseases lack an accurate forecast because of our ongoing endorsement of a poor Western lifestyle. We have become a society that has embraced a lifestyle of convenience and availability, fueled by technology and misinformation. We are no longer forced to search for foods and nutrients; computers and electronics have replaced physical activity.

A potential decline in life expectancy in the US in the current century was forecast 12 years ago.[142] That prediction has now come to fruition, verified by the latest statistics, which demonstrate a decrease in life expectancy by 0.1% years in 2015.[143] This is the first decline noted since the 1990s. The evidence is irrefutable, and the message is clear. We must prevent disease in all aspects of our lives and in the lives of the people we love. It is time to change our health destiny by shifting our attitude toward a healthy lifestyle. It is time to move from a state of disease to a state of health. It is time to eat healthy, be active, and decrease stress.

We must address the impact of lifestyle changes on our future generations. Numerous studies have shown that the positive

impact of a healthy lifestyle carries forward as children mature. The youngest of our population must be exposed to a healthy lifestyle from their earliest ages because CVD risk factors begin in childhood.[144] Such recommendations have been demonstrated to lead to a significant decrease in annual mortality owing to not only CVD but also type 2 diabetes.[145]

We are charged with providing patients the information they need to live a long, healthy life, which can be readily accomplished through the practice of lifestyle medicine. It has been stated that we, as caregivers, owe our patients this information to stay well and healthy.[3] Changing medicine to a culture that teaches lifestyle empowers patients to take control of their own health. Nutritional education is key to the implementation of a healthy lifestyle. Authors of several recent articles address this and have come forth with solid recommendations, educational resources, and guidelines to aid physicians in achieving these objectives.[11,146] Positive recommendations are presented as how physicians can educate themselves and present an effective treatment plan to patients, which include multiple options.[146]

As an aging population, we are faced with confronting inflammation, obesity, and diabetes, resulting in a dysbiotic microbiome, which contributes to our contemporary chronic conditions. Most deaths from chronic illness in the US are preventable and related to how we live. The system has failed to implement well-documented strategies and has fallen short of addressing risk factors that continue to contribute to long-term disabilities that greatly influence the potential to extend our lifespan—in an enjoyable manner.

We have addressed current concerns regarding a healthy lifestyle; such factors are being increasingly recognized as prognostic indicators of health. Weight loss, a major concern in the US, is a priority of most people yet is often a goal unachieved. Adherence to a healthy lifestyle, including a whole-foods, plant-based diet regimen and moderate exercise, has been shown to result in long-term weight loss comparable to that with conventional "reduced"-calorie diets, but with better results in overall health. A focus on lifestyle includes understanding the quadrants of health: Healthy eating, active living, healthy weight, and emotional resilience. This can be achieved by adopting a healthy lifestyle, and our goal is to deliver this message.

We should all be concerned about the wellness of each other. It's time to save our patients as well as ourselves. Medicine, as currently practiced, is approaching a strategic inflection point; a need for change must be recognized and instituted. Practitioners, insurance providers, and governmental agencies must inform the population that we have identified the root causes of many of our diseases and must implement a plan to halt and reverse these conditions. The misconception that many chronic illnesses are simply the result of aging must be corrected. Maladies such as hypertension, heart disease, diabetes, and osteoarthritis are not inevitable outcomes of aging, but are an end product of poor lifestyles. To those of us looking for solutions to our health care crisis, the gaping need for lifestyle medicine in daily practice is evident. Initiatives must be identified and put in place that focus on wellness promotion. We are running out of time to reverse a destructive trend. Our survival and the survival of the next generation are at risk. The modernization of our civilization has led to the birth of many current diseases, largely because of the adoption of a 21st-century lifestyle. Our health problems are manmade and, therefore, solvable. We must multiply our wisdom regarding the future of health, our health care, and our survival. We constantly strive to protect endangered species from extinction, while, in fact, it may well be that we ourselves are far closer to extinction.

It is our hope and anticipation that this article will motivate and inspire our colleagues to share their stories and successes with implementing lifestyle medicine programs in their Regions, service areas, clinics, and practices. We are aware of faculty at numerous campuses, many of whom are coauthors of this paper, who have implemented successful projects that have incorporated lifestyle practices with excellent clinical results. Sharing "best practice" models will result in the most effective care of our patients. Because many of our colleagues are educated in the science of lifestyle medicine, this should serve as a call to action. The impact of such projects, when adequately publicized, may result in a dramatic impact on the future of health care delivery, and more importantly the long-term well-being of our patients. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgment

Kathleen Louden, ELS, of Louden Health Communications provided editorial assistance.

How to Cite this Article

Bodai BI, Nakata TE, Wong WT, et al. Lifestyle medicine: A brief review of its dramatic impact on health and survival. Perm J 2018;22:17-025. DOI: https://doi.org/10.7812/TPP/17-025.

Dedication

We dedicate this article to T Collin Campbell, PhD, whom many consider the patriarch of the whole-foods, plant-based diet and author of The China Study, *a landmark work on health, and who has stated that "everything in food works together to create health or disease."*

References

1. Minich DM, Bland JS. Personalized lifestyle medicine: Relevance for nutrition and lifestyle recommendations. Scientific World Journal 2013 Jun 26;2013:129841. DOI: https://doi.org/10.1155/2013/129841.
2. Dieleman JL, Baral R, Birger M, et al. US spending on personal health care and public health, 1993-2013. JAMA 2016 Dec 27;316(24):2627-46. DOI: https://doi.org/10.1001/jama.2016.16885.
3. Bodai BI, Tuso P. Breast cancer survivorship: A comprehensive review of long-term medical issues and lifestyle recommendations. Perm J 2015 Spring;19(2):48-79. DOI: https://doi.org/10.7812/TPP/14-241.
4. Hyman MA, Ornish D, Roizen M. Lifestyle medicine: Treating the causes of diseases. Altern Ther Health Med 2009 Nov-Dec;15(6):12-4.
5. Ford ES, Bergmann MM, Kröger J, Schienkiewitz A, Weikert C, Boeing H. Healthy living is the best revenge: Findings from the European Prospective Investigation Into Cancer and Nutrition-Potsdam study. Arch Intern Med 2009 Aug 10;169(15):1355-62. DOI: https://doi.org/10.1001/archinternmed.2009.237.
6. Alpert JS. Failing grades in the adoption of healthy lifestyle choices. Am J Med 2009 Jun;122(6):493-4. DOI: https://doi.org/10.1016/j.amjmed.2009.01.010.
7. Murray CJ, Atkinson C, Bhalla K, et al; US Burden of Disease Collaborators. The state of US health, 1990-2010: Burden of diseases, injuries, and risk factors. JAMA 2013 Aug 14;310(6):591-608. DOI: https://doi.org/10.1001/jama.2013.13805.
8. Twombly R. Cancer surpasses heart disease as leading cause of death for all but the very elderly. J Natl Cancer Inst 2005 Mar 2;97(5):330-1. DOI: https://doi.org/10.1093/jnci/97.5.330.
9. Jones DS, Podolsky SH, Greene JA. The burden of disease and the changing task of medicine. N Engl J Med 2012 Jun 21;366(25):2333-8. DOI: https://doi.org/10.1056/NEJMp1113569.
10. Watzl B. Anti-inflammatory effects of plant-based foods and of their constituents. Int J Vitam Nutr Res 2008

Dec;78(6):293-8. DOI: https://doi.org/10.1024/0300-9831.78.6.293.

11. Tuso PJ, Ismael MH, Ha BP, Bartolotto C. Nutritional update for physicians: Plant-based diets. Perm J 2013 Spring;17(2):61-6. DOI: https://doi.org/10.7812/TPP/12-085.
12. Blaney D, Diehl H. The optimal diet: The official CHIP cookbook. Hagerstown, MD: Autumn House Publishing; 2009 Jan 1.
13. Ornish D, Scherwitz LW, Billings JH, et.al. Intensive lifestyle changes for reversal of coronary heart disease. JAMA 1998 Dec 16;280(23):2001-7. DOI: https://doi.org/10.1001/jama.280.23.2001.
14. Esselstyn CB Jr. Resolving the coronary artery disease epidemic through plant-based nutrition. Prev Cardiol 2001 Autumn;4(4):171-7. DOI: https://doi.org/10.1111/j.1520-037x.2001.00538.x.
15. Esselstyn CB Jr, Gendy G, Doyle J, Golubic M, Roizen MF. A way to reverse CAD? J Fam Pract 2014 Jun;63(7):356-364b.
16. Wang Y, Beydoun MA. Meat consumption is associated with obesity and central obesity among US adults. Int J Obes (Lond) 2009 Jun;33(6):621-8. DOI: https://doi.org/10.1038/ijo.2009.45.
17. Berkow SE, Barnard N. Vegetarian diets and weight status. Nutr Rev 2006 Apr;64(4):175-88. DOI: https://doi.org/10.1111/j.1753-4887.2006.tb00200.x.
18. Farmer B, Larson BT, Fulgoni VL 3rd, Rainville AJ, Liepa GU. A vegetarian dietary pattern as a nutrient-dense approach to weight management: An analysis of the national health and nutrition examination survey 1999-2004. J Am Diet Assoc 2011 Jun;111(6):819-27. DOI: https://doi.org/10.1016/j.jada.2011.03.012.
19. Ornish D, Brown SE, Scherwitz LW, et al. Can lifestyle changes reverse coronary heart disease? The Lifestyle Heart Trial. Lancet 1990 Jul 21;336(8708):129-33. DOI: https://doi.org/10.1016/0140-6736(90)91656-U.
20. Tonstad S, Butler T, Yan R, Fraser GE. Type of vegetarian diet, body weight, and prevalence of type 2 diabetes. Diabetes Care 2009 May;32(5):791-6. DOI: https://doi.org/10.2337/dc08-1886.
21. Polednak AP. Estimating the number of US incident causes attributable to obesity and the impact on temporal trends in incident rates for obesity-related cancers. Cancer Detect Prev 2008;32(3):190-9. DOI: https://doi.org/10.1016/j.cdp.2008.08.004.
22. Hunter P. The inflammation theory of disease EMBO reports 2012. 13;11:968-70.doi:10.1038/embor.2012.142
23. Cancello R, Clément K. Review article: Is obesity an inflammatory illness? Role of low-grade inflammation and macrophage infiltration in human white adipose tissue. BJOG 2006 Oct:1141-7. DOI: https://doi.org/10.1111/j.1471-0528.2006.01004.x.
24. Clarke G, Stilling RM, Kennedy PJ, Stanton C, Cryan JF, Dinan TG. Minireview: Gut microbiota: The neglected endocrine organ. Mol Endocrinol 2014 Aug;28(8):1221-38. DOI: https://doi.org/10.1210/me.2014-1108.
25. Marchesi JR, Adams DH, Fava F, et al. The gut microbiota and host health: A new clinical frontier. Gut 2016 Feb;65(2):330-9. DOI: https://doi.org/10.1136/gutjnl-2015-309990.
26. Tang WH, Wang Z, Levison BS, et al. Intestinal microbial metabolism of phosphatidylcholine and cardiovascular risk. N Engl J Med 2013 Apr 25;368(17):1575-84. DOI: https://doi.org/10.1056/nejmoa1109400.
27. Rajendhran J, Shanker M, Dinakaren V, Rathinavel A, Gunasekaran P. Contrasting circulating microbiome in cardiovascular disease patients and healthy individuals. Int J Cardiol 2013 Oct 12;168(5):5118-20. DOI: https://doi.org/10.1016/j.ijcard.2013.07.232.
28. Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 2006 Dec 21;444(7122):1027-31. DOI: https://doi.org/10.1038/nature05414.
29. Larsen N, Vogensen FK, van den Berg FW, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. PLoS One 2010 Feb 5;5(2):e9085. DOI: https://doi.org/10.1371/journal.pone.0009085.
30. Windey K, De Preter V, Verbeke K. Relevance of protein fermentation to gut health. Mol Nutr Food Res 2012 Jan;56(1):184-96. DOI: https://doi.org/10.1002/mnfr.201100542.
31. Boulangé CL, Neves AL, Chilloux J, Nicholson JK, Dumas ME. Impact of the gut microbiota on inflammation, obesity, and metabolic disease. Genome Med 2016 Apr 20;8(1):42. DOI: https://doi.org/10.1186/s13073-016-0303-2.
32. Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. Ann Rev Immunol 2011;29:415-45. DOI: https://doi.org/10.1146/annurev-immunol-031210-101322.
33. Klonoff DC. The increasing incidence of diabetes in the 21st century. J Diabetes Sci Technol 2009 Jan;3(1):1-2. DOI: https://doi.org/10.1177/193229680900300101
34. Goldfine AB, Shoelson SE. Therapeutic approaches targeting inflammation for diabetes and associated cardiovascular risk. J Clin Invest 2017 Jan 3;127(1):83-93. DOI: https://doi.org/10.1172/JCI88884.
35. Navarro JF, Mora C. Role of inflammation in diabetic complications. Nephrol Dial Transplant 2005 Dec;20(12):2601-4. DOI: https://doi.org/10.1093/ndt/gfi155.
36. Wellen KE, Hotamisligil GS. Inflammation, stress, and diabetes. J Clin Invest 2005 May;115(5):1111-9. DOI: https://doi.org/10.1172/jci25102.
37. Tuomilehto J, Lindström J, Eriksson JG, et al; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001 May 3;344(18):1343-50. DOI: https://doi.org/10.1056/nejm200105033441801.
38. Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002 Feb 7;346(6):393-403. DOI: https://doi.org/10.1056/nejmoa012512.
39. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. Diabetes Care 1997 Apr;20(4):537-44. DOI: https://doi.org/10.2337/diacare.20.4.537.
40. Saito T, Watanabe M, Nishida J, et al; Zensharen Study for Prevention of Lifestyle Diseases Group. Lifestyle modification and prevention of type 2 diabetes in overweight Japanese with impaired fasting glucose levels: A randomized controlled trial. Arch Intern Med 2011 Aug 8;171(15):1352-60. DOI: https://doi.org/10.1001/archinternmed.2011.275.
41. Imamura F, O'Connor L, Ye Z, et al. Consumption of sugar sweetened beverages, artificially sweetened beverages, and fruit juice and incidence of type 2 diabetes: Systematic review, meta-analysis, and estimation of population attributable fraction. BMJ 2015 Jul 21;351:h3576. DOI: https://doi.org/10.1136/bmj.h3576.
42. Malik VS, Li Y, Tobias DK, Pan A, Hu FB. Dietary protein intake and risk of type 2 diabetes in US men and women. Am J Epidemiol 2016 Apr 16;183(8):715-28. DOI: https://doi.org/10.1093/aje/kwv268.
43. Micha R, Michas G, Mozaffarian D. Unprocessed red and processed meats and risk of coronary artery disease and type 2 diabetes—An updated review of the evidence. Curr Atheroscler Rep 2012 Dec;14(6):515-24. DOI: https://doi.org/10.1007/s11883-012-0282-8.
44. Djoussé L. Relation of eggs with incident cardiovascular disease and diabetes: Friends or foes? Atherosclerosis 2013 Aug;229(2):507-8. DOI: https://doi.org/10.1016/j.atherosclerosis.2013.05.003.
45. Boussageon R, Bejan-Angoulvant T, Saadatian-Elahi M, et al. Effect of intensive glucose lowering treatment on all cause mortality, cardiovascular death, and microvascular events in type 2 diabetes: Meta-analysis of randomised controlled trials. BMJ 2011 Jul 26;343:d4169. DOI: https://doi.org/10.1136/bmj.d4169.
46. Rodríguez-Gutiérrez R, Montori V. Glycemic control for patients with type 2 diabetes mellitus: Our evolving faith in the face of evidence. Circ Cardiovasc Qual Outcomes 2016 Sep;9(5):504-12. DOI: https://doi.org/10.1161/circoutcomes.116.002901.
47. American Diabetes Association. 8. Pharmacologic approaches to glycemic treatment. Diabetes Care 2017 Jan;40(Suppl 1):S64-S74. DOI: https://doi.org/10.2337/dc17-S011. Erratum in: Diabetes Care 2017 Jul;40(7):985. DOI: https://doi.org/10.2337/dc17-er07b.
48. Snowling NJ, Hopkins WG. Effects of different modes of exercise training on glucose control and risk factors for complications in type 2 diabetic patients: A meta-analysis. Diabetes Care 2006 Nov;29(11):2518-27. DOI: https://doi.org/10.2337/dc06-1317.
49. Barnard ND, Cohen J, Jenkins DJ, et al. A low-fat vegan diet improves glycemic control and cardiovascular risk factors in a randomized clinical trial in individuals with type 2 diabetes. Diabetes Care 2006 Aug;29(8):1777-83. DOI: https://doi.org/10.2337/dc06-0606.
50. McDougall J, Thomas LE, McDougall C, et al. Effects of 7 days on an ad libitum low-fat vegan diet: The McDougall Program cohort. Nutr J 2014 Oct 14;13:99. DOI: https://doi.org/10.1186/1475-2891-13-99. Erratum in: Nutr J 2017 Feb 10;16(1):12. DOI: https://doi.org/10.1186/s12937-017-0234-9.
51. Wolfram T, Ismail-Beigi F. Efficacy of high-fiber diets in the management of type 2 diabetes mellitus. Endocr Pract 2011 Jan-Feb;17(1):132-42. DOI: https://doi.org/10.4158/ep10204.ra.
52. Rowley WR, Bezold C, Arikan Y, Byrne E, Krohe S. Diabetes 2030: Insights from yesterday, today, and future trends. Popul Health Manag 2017 Feb;20(1):6-12. DOI: https://doi.org/10.1089/pop.2015.0181.
53. Roberston RM. Women and cardiovascular disease: The risks of misperception and the need for action. Circulation 2001 May 15;103(19):2318-20. DOI: https://doi.org/10.1161/01.cir.103.19.2318.
54. Mensah GA, Brown DW. An overview of cardiovascular disease burden in the United States. Health Aff (Millwood) 2007 Jan-Feb;26(1):38-48. DOI: https://doi.org/10.1377/hlthaff.26.1.38.
55. Thom T, Haase N, Rosamond W, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2006 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2006 Feb 14;113(6):e85-151. DOI: https://doi.org/10.1161/circulationaha.105.171600. Erratum in: Circulation 2006 Apr 11;113(14):e696. DOI: https://doi.org/10.1161/circulationaha.106.174501. Erratum in: Circulation 2006 Dec 5;114(23):e630. DOI: https://doi.org/10.1161/circulationaha.106.180110.
56. Heidenreich PA, Trogdon JG, Khavjou OA, et al; American Heart Association Advocacy Coordinating Committee; Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Arteriosclerosis; Thrombosis and Vascular Biology; Council on Cardiopulmonary; Critical Care; Perioperative and Resuscitation; Council on Cardiovascular Nursing; Council on the Kidney in Cardiovascular Disease; Council on Cardiovascular Surgery and Anesthesia, and Interdisciplinary Council on Quality of Care and

Outcomes Research. Forecasting the future of cardiovascular disease in the United States: A policy statement from the American Heart Association. Circulation 2011 Mar 1;123(8):933-44. DOI: https://doi.org/10.1161/hhf.0b013e318291329a.

57. Writing Group Members, Mozaffarian D, Benjamin EJ, Go AS, et al; American Heart Association Statistics Committee; Stroke Statistics Subcommittee. Heart disease and stroke statistics—2016 update: A report from the American Heart Association. Circulation 2016 Jan 26;133(4):e38-360. DOI: 10.1161/CIR.0000000000000350. Erratum in: Circulation 2016 Apr 12;133(15):e599. DOI: https://doi.org/10.1161/CIR.0000000000000409.
58. Song Z, Blumenthal DM. Expanding payment reform in Medicare: The cardiology episode-based payment model. JAMA 2016 Nov 15;316(19):1973-4. DOI: https://doi.org/10.1001/jama.2016.16146.
59. Mathieu P, Lemieux I, Deprés JP. Obesity, inflammation, and cardiovascular risk. Clin Pharmacol Ther 2010 Apr;87(4):407-16. DOI: https://doi.org/10.1038/clpt.2009.311.
60. Libby P, Ridker PM, Hansson GK; Leducq Transatlantic Network on Atherothrombosis. Inflammation in atherosclerosis: From pathophysiology to practice. J Am Coll Cardiol 2009 Dec 1;54(23):2129-38. DOI: https://doi.org/10.1016/j.jacc.2009.09.009.
61. Tuso P, Stoll SR, Li WW. A plant-based diet, atherogenesis, and coronary artery disease prevention. Perm J 2015 Winter;19(1):62-7. DOI: https://doi.org/10.7812/TPP/14-036.
62. Esselstyn CB Jr. Is the present therapy for coronary artery disease the radical mastectomy of the twenty-first century? Am J Cardiol 2010 Sep 15;106(6):902-4. DOI: https://doi.org/10.1016/j.amjcard.2010.05.016.
63. Koeth RA, Wang Z, Levison BS, et al. Intestinal microbiota of L-carnitine, a nutrient in red meat, promotes atherosclerosis. Nat Med 2013 May;19(5):576-85. DOI: https://doi.org/10.1038/nm.3145.
64. Ornish D. Avoiding revascularization with lifestyle changes: The Multicenter Lifestyle Demonstration Project. Am J Cardiol 1998 Nov 26;280(10B):72T-76T. DOI: https://doi.org/10.1016/s0002-9149(98)00744-9.
65. Franklin BA, Cushman M. Recent advances in preventive cardiology and lifestyle medicine: A themed series. Circulation 2011 May 24;123(20):2274-83. DOI: https://doi.org/10.1161/circulationaha.110.981613.
66. Eichelmann F, Schwingshackl L, Fedirko V, Aleksandrova K. Effect of plant-based diets on obesity-related inflammatory profiles: A systematic review and meta-analysis of intervention trials. Obes Rev 2016 Nov;17(11):1067-79. DOI: https://doi.org/10.1111/obr.12349.
67. Mink PJ, Scrafford CG, Barraj LM, et al. Flavonoid intake and cardiovascular disease mortality: A prospective study in postmenopausal women. Am J Clin Nutr 2007 Mar;85(3):895-909.
68. Mente A, de Koning L, Shannon HS, Anand SS. A systematic review of the evidence supporting a causal link between dietary factors and coronary heart disease. Arch Intern Med 2009 Apr 13;169(7):659-69. DOI: https://doi.org/10.1001/archinternmed.2009.38.
69. Schwingshackl L, Hoffmann G. Diet quality as assessed by the healthy eating index, the alternate healthy eating index, the dietary approaches to stop hypertension score, and health outcomes: A systematic review and meta-analysis of cohort studies. J Acad Nutr Diet 2015 May;115(5):780-800.e5. DOI: https://doi.org/10.1016/j.jand.2014.12.009.
70. Dinu M, Abbate R, Gensini GF, Casini A, Sofi F. Vegetarian, vegan diets and multiple health outcomes: A systematic review with meta-analysis of observational studies. Crit Rev Food Sci Nutr 2017 Nov 22;57(17):3640-3649. DOI: https://doi.org/10.1080/10408398.2016.1138447.
71. Harland J, Garton L. An update of the evidence relating to plant-based diets and cardiovascular disease, type 2 diabetes and overweight. Nutr Bull 2016 Dec;41(4):323-38. DOI: https://doi.org/10.1111/nbu.12235.
72. Hofker MH, Fu J, Wijmenga C. The genome revolution and its role in understanding complex diseases. Biochim Biophys Acta 2014 Oct;1842(10):1889-95. DOI: https://doi.org/10.1016/j.bbadis.2014.05.002.
73. Wilson BJ, Nicholls SG. The Human Genome Project, and recent advances in personalized genomics. Risk Manag Healthc Policy 2015 Feb 16;8:9-20. DOI: https://doi.org/10.2147/rmhp.s58728.
74. Ellsworth DL, Croft DT, Weyandt J, et al. Intensive cardiovascular risk reduction induces sustainable changes in expression of genes and pathways important to vascular function. Circulation: Cardiovascular Genetics 2014 Apr;7(2):151-60. DOI: https://doi.org/10.1161/circgenetics.113.000121.
75. Chow CK, Jolly S, Rao-Melacini P, Fox KA, Anand SS, Yusuf S. Association of diet, exercise, and smoking modification with risk of early cardiovascular events after acute coronary syndrome. Circulation 2010 Feb 16;121(6):750-8. DOI: https://doi.org/10.1161/circulationaha.109.891523.
76. Khera AV, Emdin CA, Drake I, et al. Genetic risk, adherence to a healthy lifestyle, and coronary disease. N Engl J Med 2016 Dec 15;375(24):2349-58. DOI: https://doi.org/10.1056/nejmoa1605086.
77. Nocon M, Heimann T, Müller-Riemenschneider F, Thalau F, Roll S, Willich SN. Association of physical activity with all-cause and cardiovascular mortality: A systematic review and meta-analysis. Eur J Cardiovasc Prev Rehabil 2008 Jun;15(3):239-46. DOI: https://doi.org/10.1097/hjr.0b013e3282f55e09.
78. Franklin BA, McCullough PA. Cardiorespiratory fitness: An independent and additive marker of risk stratification and health outcomes. Mayo Clin Proc 2009 Sep;84(9):776-9. DOI: https://doi.org/10.4065/84.9.776.
79. Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990-2015. A systematic analysis for the Global Burden of Disease Study. JAMA Oncol 2017 Apr 1;3(4):524-48. DOI: https://doi.org/10.1001/jamaoncol.2016.5688.
80. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017 Jan;67(1):7-30. DOI: https://doi.org/10.3322/caac.21387.
81. Anand P, Kunnumakkara AB, Sundaram C, et al. Cancer is a preventable disease that requires major lifestyle changes. Pharm Res 2008 Sep;25(9):2097-116. DOI: https://doi.org/10.1007/s11095-008-9690-4.
82. Ligibel J. Lifestyle factors in cancer survivorship. J Clin Oncol 2012 Oct 20;30(30):3697-704. DOI: https://doi.org/10.1200/jco.2012.42.0638.
83. Kyrgiou M, Kalliala I, Markozannes G, et al. Adiposity and cancer at major anatomical sites: Umbrella review of the literature. BMJ 2017 Feb 28;356:j477. DOI: https://doi.org/10.1136/bmj.j477.
84. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. CA Cancer J Clin 2016 Jul;66(4);271-89. DOI: https://doi.org/10.3322/caac.21349.
85. Rustgi AK. The genetics of hereditary colon cancer. Genes Dev 2007 Oct 15;21(20):2525-38. DOI: https://doi.org/10.1101/gad.1593107.
86. Terzić J, Grivennikov S, Karin E, Karin M. Inflammation and colon cancer. Gastroenterology 2010 Jun;138(6):2101-14.e5. DOI: https://doi.org/10.1053/j.gastro.2010.01.058.
87. Tsai MS, Chen HP, Hung CM, Lee PH, Lin CL, Kao CH. Hospitalization for inflammatory bowel disease is associated with increased risk of breast cancer: A nationwide cohort study of an Asian population. Ann Surg Oncol 2015;22(6):1996-2002. DOI: https://doi.org/10.1245/s10434-014-4198-0.
88. Ou J, Carbonero F, Zoetendal EG, et al. Diet, microbiota, and microbial metabolites in colon cancer risk in rural Africans and African Americans. Am J Clin Nutr 2013 Jul;98(1):111-20. DOI: https://doi.org/10.3945/ajcn.112.056689.
89. Platz EA, Willet WC, Colditz GA, Rimm EB, Spiegelman D, Giovannucci E. Proportion of colon cancer risk that might be preventable in cohort of middle-aged US men. Cancer Causes Control 2000 Aug;11(7):579-88. DOI: https://doi.org/10.1023/A:1008999232442.
90. Bultman SJ. Emerging roles of the microbiome in cancer. Carcinogenesis 2014 Feb;35(2):249-55. DOI: https://doi.org/10.1093/carcin/bgt392.
91. Edwards BK, Noone AM, Mariotto AB, et al. Annual report to the nation on the status of cancer, 1975-2010, featuring prevalence of comorbidity and impact on survival among persons with lung, colorectal, breast, or prostate cancer. Cancer 2014 May 1;120(9):1290-314. DOI: https://doi.org/10.1002/cncr.28509.
92. De Bruijn KM, Arends LR, Hansen BE, Leeflang S, Ruiter R, van Eijck CH. Systematic review and meta-analysis of the association between diabetes mellitus and the incidence and mortality in breast and colorectal cancer. Br J Surg 2013 Oct;100(11):1421-9. DOI: https://doi.org/10.1002/bjs.9229.
93. Van Blarigan EL, Meyerhardt JA. Role of physical activity and diet after colorectal cancer diagnosis. J Clin Oncol 2015 Jun 1;33(16):1825-34. DOI: https://doi.org/10.1200/jco.2014.59.7799.
94. Campbell PT, Patel AV, Newton CC, Jacobs EJ, Gapstur SM. Associations of recreational physical activity and leisure time spent sitting with colorectal cancer survival. J Clin Oncol 2013 Mar 1;31(7):876-85. DOI: https://doi.org/10.1200/jco.2012.45.9735.
95. Weiner AB, Matulewicz RS, Eggener SE, Schaeffer EM. Increasing incidence of metastatic prostate cancer in the United States (2004-2013). Prostate Cancer Prostatic Dis 2016 Dec;19(4):395-7. DOI: https://doi.org/10.1038/pcan.2016.30.
96. Carter HB, Albertsen PC, Barry MJ, et al. Early detection of prostate cancer: AUA guideline. J Urol 2013 Aug;190(2):419-26. DOI: https://doi.org/10.1016/j.juro.2013.04.119.
97. Freedland SJ, Aronson WJ. Examining the relationship between obesity and prostate cancer. Rev Urol 2004 Spring;6(2):73-81.
98. Ornish D, Weidner G, Fair WR, et al. Intensive lifestyle changes may affect the progression of prostate cancer. J Urol 2005 Sep;174(3):1065-70. DOI: https://doi.org/10.1097/01.ju.0000169487.49018.73.
99. Ornish D, Magbanua MJ, Weidner G, et al. Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention. Proc Natl Acad Sci U S A 2008 Jun 17;105(24):8369-74. DOI: https://doi.org/10.1073/pnas.0803080105.
100. Yang M, Kenfield SA, Van Blarigan EL, et al. Dietary patterns after prostate cancer diagnosis in relation to disease-specific and total mortality. Cancer Prev Res (Phila) 2015 Jun;8(6):545-51. DOI: https://doi.org/10.1158/1940-6207.capr-14-0442.
101. Sinicrope FA, Dannenberg AJ. Obesity and breast cancer prognosis: Weight of the evidence. J Clin Oncol 2011 Jan 1;29(1):4-7. DOI: https://doi.org/10.1200/JCO.2010.32.1752.
102. Clarke CA, Canchola AJ, Moy LM, et al. Regular and low-dose aspirin, other non-steroidal anti-inflammatory medications and prospective risk of HER2-defined breast cancer: The California Teachers Study. Breast

Cancer Res 2017 May 1;19(1):52. DOI: https://doi.org/10.1186/s13058-017-0840-7.

103. Ewertz M, Jensen MD, Gunnarsdóttir KÁ, et al. Effect of obesity on prognosis after early-stage breast cancer. J Clin Oncol 2011 Jan 1;29(1):25-31. DOI: https://doi.org/10.1200/jco.2010.29.7614.
104. Kotepui M. Diet and risk of breast cancer. Contemp Oncol (Pozn) 2016;20(1):13-9. DOI: https://doi.org/10.5114/wo.2014.40560.
105. Kushi LH, Doyle C, McCullough M, et al; American Cancer Society 2010 Nutrition and Physical Activity Guidelines Advisory Committee. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. CA Cancer J Clin 2012 Jan-Feb;62(1):30-67. DOI: https://doi.org/10.3322/caac.20140.
106. Adams S. Estrobolome disparities may lead to developing biomarkers that could mitigate cancer risk. J Natl Cancer Inst 2016;108(8):djw130. DOI: https://doi.org/10.1093/jnci/djw130.
107. Shapira I, Sultan K, Lee A, Taioli E. Evolving concepts: How diet and the intestinal microbiome act as modulators of breast malignancy. ISRN Oncol 2013 Sep 25;2013:693920. DOI: https://doi.org/10.1155/2013/693920.
108. Goedert JJ, Jones G, Hua X, et al. Investigation of the association between the fecal microbiota and breast cancer in postmenopausal women: A population-based case-control pilot study. J Natl Cancer Inst 2015 Jun 1;107(8):dvj147. DOI: https://doi.org/10.1093/jnci/djv147.
109. Kwa M, Plottel CS, Blaser MJ, Adams S. The intestinal microbiome and estrogen receptor-positive female breast cancer. J Natl Cancer Inst 2016 Apr 22;108(8):djw029. DOI: https://doi.org/10.1093/jnci/djw029.
110. What breast cancer survivors can do [Internet]. Washington, DC: American Institute for Cancer Research (AICR); 2014 Oct [cited 2017 Jul 27]. Available from: www.aicr.org.
111. Ibrahim EM, Al-Homaidh A. Physical activity and survival after breast cancer diagnosis: Meta-analysis of published studies. Med Oncol 2011 Sep;28(3):753-65. DOI: https://doi.org/10.1007/s12032-010-9536-x.
112. Hamer J, Warner E. Lifestyle modifications for patients with breast cancer to improve prognosis and optimize overall health. CMAJ 2017 Feb 1;189(7):E268-74. DOI: https://doi.org/10.1503/cmaj.160464.
113. Irwin ML, McTiernan A, Manson JE, et al. Physical activity and survival in postmenopausal women with breast cancer: Results from the women's health initiative. Cancer Prev Res (Phila) 2011 Apr;4(4):522-9. DOI: https://doi.org/10.1158/1940-6207.capr-10-0295.
114. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast 2013 Aug;22 Suppl 2:S30-7. DOI: https://doi.org/10.1016/j.breast.2013.07.006.
115. Meyerhardt JA, Heseltine D, Niedzwiecki D, et al. Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: Findings from CALGB 89803. J Clin Oncol 2006 Aug 1;24(22):3535-41. DOI: https://doi.org/10.1200/jco.2008.26.15_suppl.4039.
116. Pierce JP, Stefanick ML, Flatt SW, et al. Greater survival after breast cancer in physically active women with high vegetable-fruit intake regardless of obesity. J Clin Oncol 2007 Jun 10;25(17):2345-51. DOI: https://doi.org/10.1200/jco.2006.08.6819.
117. Morgan RJ Jr. Underserved topics in oncology: The role of physical activity in improving quality of life and decreasing recurrence risk in patients with cancer. J Natl Compr Canc Netw 2014 May;12(5):735-7. DOI: https://doi.org/10.6004/jnccn.2014.0075.
118. Fournier A, Dos Santos G, Guillas G, et al. Recent recreational physical activity and breast cancer risk in postmenopausal women in the E3N cohort. Cancer Epidemiol Biomarkers Prev 2014 Sep;23(9):1893-902. DOI: https://doi.org/10.1158/1055-9965.epi-14-0150.
119. Sidney S, Quesenberry CP Jr, Jaffe MG, et al. Recent trends in cardiovascular mortality in the United States and public health goals. JAMA Cardiol 2016 Aug 1;1(5):594-9. DOI: https://doi.org/10.1001/jamacardio.2016.1326.
120. Gomez SL, Canchola AJ, Nelson DO, et al. Recent declines in cancer incidence: Related to the Great Recession? Cancer Causes Control 2017 Feb;28(2):145-54. DOI: https://doi.org/10.1007/s10552-016-0846-y.
121. Lloyd-Jones DM. Slowing progress in cardiovascular mortality rates: You reap what you sow. JAMA Cardiol 2016 Aug 1;1(5):599-600. DOI: https://doi.org/10.1001/jamacardio.2016.1348.
122. Gonzales JF, Barnard ND, Jenkins DJ, et al. Applying the precautionary principle to nutrition and cancer. J Am Coll Nutr 2014;33(3):239-46. DOI: https://doi.org/10.1080/07315724.2013.866527.
123. Pan A, Sun Q, Bernstein AM, et al. Red meat consumption and mortality: Results from 2 prospective cohort studies. Arch Intern Med 2012 Apr 9;172(7):555-63. DOI: https://doi.org/10.1001/archinternmed.2011.2287.
124. Wang X, Ouyang Y, Liu J, et al. Fruit and vegetable consumption and mortality from all causes, cardiovascular disease, and cancer: Systematic review and dose-response meta-analysis of prospective cohort studies. BMJ 2014 Jul 29;349:g4490. DOI: https://doi.org/10.1136/bmj.g4490.
125. Allen NE, Appleby PN, Davey GK, Kaaks R, Rinaldi S, Key TJ. The associations of diet with serum insulin-like growth factor I and its main binding proteins in 292 women meat-eaters, vegetarians, and vegans. Cancer Epidemiol Biomarkers Prev 2002 Nov;11(11):1441-8.
126. Westley RL, May FE. A twenty-first century cancer epidemic caused by obesity: The involvement of insulin, diabetes, and insulin-like growth factors. Int J Endocrinol 2013;2013:632461. DOI: https://doi.org/10.1155/2013/63246.
127. Bellavia A, Larsson SC, Bottai M, Wolk A, Orsini N. Fruit and vegetable consumption and all-cause mortality: A dose-response analysis. Am J Clin Nutr 2013 Aug;98(2):454-9. DOI: https://doi.org/10.3945/ajcn.112.056119.
128. Demark-Wahnefried W, Campbell KL, Hayes SC. Weight management and its role in breast cancer rehabilitation. Cancer 2012 Apr 15;118(8 Suppl):2277-87. DOI: https://doi.org/10.1002/cncr.27466.
129. Ford ES, Bergmann MM, Boeing H, Li C, Capewell S. Healthy lifestyle behaviors and all-cause mortality among adults in the United States. Prev Med 2012 Jul;55(1):23-7. DOI: https://doi.org/10.1016/j.ypmed.2012.04.016.
130. Boursi B, Mamtani R, Haynes K, Yang YX. Recurrent antibiotic exposure may promote cancer formation—Another step in understanding the role of human microbiota? Eur J Cancer 2015 Nov;51(17):2655-64. DOI: https://doi.org/10.1016/j.ejca.2015.08.015.
131. Bouvard V, Loomis D, Guyton KZ, et al; International Agency for Research on Cancer Monograph Working Group. Carcinogenicity of consumption of red and processed meat. Lancet Oncol 2015 Dec;16(16):1599-600. DOI: https://doi.org/10.1016/s1470-2045(15)00444-1.
132. Song M, Fund TT, Hu FB, et al. Association of animal and plant protein intake with all-cause and cause-specific mortality. JAMA Intern Med 2016 Oct 1;176(10):1453-63. DOI: https://doi.org/10.1001/jamainternmed.2016.4182.
133. Tang WH, Hazen SL. The contributory role of gut microbiota in cardiovascular disease. J Clin Invest 2014 Oct;124(10):4204-11. DOI: https://doi.org/10.1172/jci72331.
134. Brown JM, Hazen SL. The gut microbial endocrine organ: Bacterially derived signals driving cardiometabolic diseases. Ann Rev Med 2015;66:343-59. DOI: https://doi.org/10.1146/annurev-med-060513-093205.
135. Plottel CS, Blaser MJ. Microbiome and malignancy. Cell Host Microbe 2011 Oct 20;10(4):324-35. DOI: https://doi.org/10.1016/j.chom.2011.10.003.
136. Deukota S, Chang EB. Nutrition, microbiomes, and intestinal inflammation. Curr Opin Gastroenterol 2013 Nov;29(6):603-7. DOI: https://doi.org/10.1097/mog.0b013e328365d38f.
137. Ornish D. Intensive lifestyle changes and health reform. Lancet Oncol 2009 Jul;10(7):638-9. DOI: https://doi.org/10.1016/s1470-2045(09)70175-5.
138. Iuga AO, McGuire MJ. Adherence and health care costs. Risk Manag Healthc Policy 2014 Feb 20;7:35-44. DOI: https://doi.org/10.2147/rmhp.s19801.
139. National Center for Health Statistics. Fast Stats [Internet]. Atlanta, GA: Centers for Disease Control and Prevention; 2016 [cited 2017 Jul 28]. Available from: www.cdc.gov/nchs/products/series.htm.
140. Adams KM, Butsch WS, Kohlmeier M. The state of nutrition education at US medical schools. J Biomed Educ 2015;2015:357627. DOI: https://doi.org/10.1155/2015/357627.
141. Lenders CM, Deen DD, Bistrian B, et al. Residency and specialties training in nutrition: A call for action. Am J Clin Nutr 2014 May;99(5 Suppl):1174S-83S. DOI: https://doi.org/10.3945/ajcn.113.073528.
142. Olshansky SJ, Passaro DJ, Hershow RC, et al. A potential decline in life expectancy in the United States in the 21st century. N Engl J Med 2005 Mar 17;352(11):1138-45. DOI: https://doi.org/10.1056/nejmsr043743.
143. Xu J, Murphy SL, Kochanek KD, Arias E. Mortality in the United States, 2015. NCHS data brief no. 267 [Internet]. Hyattsville, MD: National Center for Health Statistics; 2016 Dec 8 [cited 2017 Jul 27]. Available from: www.cdc.gov/nchs/data/databriefs/db267.pdf.
144. Macknin M, Kong T, Weier A, et al. Plant-based, no-added-fat or American Heart Association diets: Impact on cardiovascular risk in obese children with hypercholesterolemia and their parents. J Pediatr 2015 Apr;166(4):953-9.e1-3. DOI: https://doi.org/10.1016/j.jpeds.2014.12.058.
145. Micha R, Peñalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States. JAMA 2017 Mar 7;317(9):912-24. DOI: https://doi.org/10.1001/jama.2017.0947.
146. Hever J. Plant-based diets: A physician's guide. Perm J 2016 Summer;20(3):93-101. DOI: https://doi.org/10.7812/TPP/15-082.