

STATE-OF-THE-ART REVIEW

Life's Essential 8

Optimizing Health in Older Adults



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ABSTRACT

The population worldwide is getting older as a result of advances in public health, medicine, and technology. Older individuals are living longer with a higher prevalence of subclinical and clinical cardiovascular disease (CVD). In 2010, the American Heart Association introduced a list of key prevention targets, known as "Life's Simple 7" to increase CVD-free survival, longevity, and quality of life. In 2022, sleep health was added to expand the recommendations to "Life's Essential 8" (eat better, be more active, stop smoking, get adequate sleep, manage weight, manage cholesterol, manage blood pressure, and manage diabetes). These prevention targets are intended to apply regardless of chronologic age. During this same time, the understanding of aging biology and goals of care for older adults further enhanced the relevance of prevention across the range of functions. From a biological perspective, aging is a complex cellular process characterized by genomic instability, telomere attrition, loss of proteostasis, inflammation, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication. These aging hallmarks are triggered by and enhanced by traditional CVD risk factors leading to geriatric syndromes (eg, frailty, sarcopenia, functional limitation, and cognitive impairment) which complicate efforts toward prevention. Therefore, we review Life's Essential 8 through the lens of aging biology, geroscience, and geriatric precepts to guide clinicians taking care of older adults. (JACC Adv 2023;2:100560) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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ABBREVIATIONS AND ACRONYMS

AHA = American Heart Association

BP = blood pressure

CAD = coronary artery disease

CV = cardiovascular

CVD = cardiovascular disease

DASH = Dietary Approaches to Stop Hypertension

DM = diabetes mellitus

LDL-C = low-density lipoprotein-cholesterol

QOL = quality of life

Chronological age is the single most important risk factor for the development of chronic diseases, including cardiovascular disease (CVD).¹ In the last few decades, population worldwide has seen unprecedented growth, with resultant increase in the prevalence of clinical and subclinical CVD.¹⁻⁴ In 2010, the American Heart Association (AHA) introduced the concept of “Life’s Simple 7” to provide key prevention targets for improved cardiovascular (CV) health: physical activity, dietary quality, smoking, weight, blood glucose, cholesterol, and blood pressure (BP).⁵ In 2022, it was expanded to “Life’s Essential 8”

with the addition of sleep health.⁶ Implementation of Life’s Essential 8 in older adults has unique challenges due to heterogeneity of biological aging, multimorbidity, and coexisting geriatric syndromes such as frailty, sarcopenia, functional limitation, and cognitive impairment. In addition, despite optimization of these essentials, there is also interest in identification of strategies informed by geroscience.

Aging is a multifactorial, complex, biologically malleable processes that entails key molecular signals, identified as “aging hallmarks”: genomic instability, telomere attrition, loss of proteostasis, inflammation, deregulated nutrient-sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, systemic inflammation, gut dysbiosis, and altered intercellular communication.⁷ These aging hallmarks collectively contribute to each individual’s ‘aging phenotype’ with associated decline in the ability of physiological systems to respond to stressors.⁸ As a consequence, these pathways contribute to geriatric syndromes and chronic conditions including CVD (**Central Illustration**).^{9,10} Therefore, prevention of CVD can be considered foundational for healthy aging. Recently, geroscience insights suggest ways to slow decline and delay development of chronic diseases from its physiologic foundations.⁸

We review AHA’s “Life’s Essential 8” through the lens of aging physiology, geroscience, and unique challenges older adults face. Moreover, we consider prevention as it applies across the geriatric framework referred to as ‘Geriatric 5Ms.’ Geriatric 5Ms include: 1) *mind*; 2) *mobility*; 3) *medications*; 4) *multicomplexity*; and 5) *what matters most*.¹⁰

HIGHLIGHTS

- Biological aging is driven by a complex molecular and cellular process characterized by key aging hallmarks that are often accelerated by traditional CVD risk factors leading to development of not only CVD but also various geriatric syndromes that possess unique challenge.
- Optimization of Life Essential 8 components impact aging process at multiple molecular and cellular levels and contribute to healthy aging, increased lifespan, and health span.
- Future studies of gero-therapeutics may identify interventions that can improve cardiovascular health, as well as healthy aging and longevity.

BE MORE ACTIVE (EXERCISE)

Staying active has health benefits irrespective of age, exercise capacity, or functional status, yet, older adults, especially women, are most likely to be sedentary.¹¹ The prevalence of inactivity increases from 26.9% in those aged 65 to 74 years to 35.3% in those ≥ 75 years.¹² On average, older adults spend 9 hours or more being sedentary, accounting for 65 to 80% of waking hours per day.¹³ Physical inactivity has detrimental consequences in older adults beyond the CV system. It exacerbates sarcopenia, frailty, metabolic syndrome leading to loss of independence, and poor quality of life (QOL).¹⁴⁻¹⁶ Furthermore, sedentary behavior accelerates the hallmarks of aging in muscle cells.¹⁷ Although exercise is important for health, restoration of age-appropriate physiology may not occur even after resuming a physically active routine.¹⁶

PHYSICAL ACTIVITY CONSIDERATIONS FOR OLDER ADULTS. Multiple factors contribute to physical inactivity in older adults. Aging reduces exercise capacity and capability due to age-related changes in multiple organ systems.¹⁸ In addition, multimorbidity, cognitive impairment, and polypharmacy worsen physical function and vice versa.^{19,20}

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors’ institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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TABLE 1 Highlights of Each Life's Essential 8 Component Pertaining to the Care of Older Adults

Eat better	<ul style="list-style-type: none"> • Emphasis should be on dietary quality and adequate protein-energy intake to avoid malnutrition. • Mediterranean diet and DASH diet have important beneficial impact on CVD and its risk factors. • There is no convincing evidence for the use of supplements.
Be more active	<ul style="list-style-type: none"> • Physical activity has multisystem antiaging effects. • Goal is to avoid inactivity. Any activity counts. • Multicomponent tailored exercise regimen focusing on aerobic, resistance, balance, and flexibility exercise provides the best outcomes.
Get more sleep	<ul style="list-style-type: none"> • Poor sleep quality accelerates aging. • Older adults should get 7-9 hours of sleep. • Lifestyle and behavioral intervention along with cognitive behavioral therapy are mainstay of treatment. • Pharmacologic options are avoided because of adverse risk benefit ratio.
Quit tobacco	<ul style="list-style-type: none"> • Benefits seen at all ages including advanced age. • Screen and counsel for smoking cessation at each visit. • Nicotine alone or in combination with bupropion, bupropion, and varenicline remain effective for smoking cessation at older ages.
Manage weight	<ul style="list-style-type: none"> • Weight-loss therapy that minimizes muscle and bone loss is recommended for older adults • A combination of an energy-deficit diet rich in protein with increased physical activity and behavioral therapy is the cornerstone of weight loss program.
Control cholesterol	<ul style="list-style-type: none"> • Older adults benefit from lipid lowering therapy for primary and secondary prevention of CVD irrespective of age.
Manage blood sugar	<ul style="list-style-type: none"> • Avoid intensive glycemic control in older adults due to risk of adverse effects such as hypoglycemia. • Exercise and pharmacotherapy with metformin and SGLT-2 inhibitors have important glycemic and antiaging properties.
Manage blood pressure	<ul style="list-style-type: none"> • Goal blood pressure <130/80 • Start low, go slow, and get there • Avoid orthostatic hypotension

CVD = cardiovascular disease; DASH = Dietary Approaches to Stop Hypertension; SGLT-2 = sodium-glucose cotransporter-2.

independence, and QOL while decreasing multimorbidity, and polypharmacy.^{21,25,26} Moreover, use of senolytics, drugs with the ability to clear senescent cells, mimic some of the properties of exercise and may therefore also reduce musculoskeletal decline associated with aging.^{27,28}

RECOMMENDATIONS FOR PHYSICAL ACTIVITY IN OLDER ADULTS. “Life’s Essential 8” recommends 150 minutes of moderate or 75 minutes of vigorous physical activity per week regardless of age, sex, or race.⁵ However, achieving these goals may not always be feasible or safe. Careful consideration of individual characteristics such as preferences, functional status, cognitive limitation, exercise capacity, and fall risk can determine best type and duration of exercise (Table 1).

The benefits of physical activity are driven by exercise intensity.^{22,29} However, the most important goal for older adults is to avoid inactivity. The greatest benefit is seen in those who go from a sedentary lifestyle to any activity, that is, walking for 5 minutes several times a day.^{29,30} In order to perform aerobic activity safely, other modes of exercises focusing on strength, balance, and mobility are often required.^{31,32} Physical therapists, exercise physiologists, and nurses play an important role in implementation of progressive exercise. For those with mobility limitations, seated range of motion exercise, controlled breathing, stretching, and yoga can be safe and helpful.^{33,34} Strength (eg, stretch bands), balance (eg, chair stands, standing on 1 foot,), and flexibility

training improves gait, speed/power of movement, and reduce risk of falls by improving muscle mass and strength, balance, and bone strength.³⁵⁻³⁷ These are usually initiated at low intensity for short durations (ie, 5-10 minutes) and then advanced in length and then intensity as tolerated.

GET HEALTHY SLEEP

Healthy sleep is important for maintaining health at all ages. Sleep has distinct dimensions: timing, continuity or efficiency, duration, and satisfaction/quality.³⁸ Sleep architecture undergoes several changes with aging. Sleep in later years is characterized by increased latency, reduced efficiency, fragmentation, awakening, phase advancement, and periodic limb movements.³⁹⁻⁴¹

Sleep duration between 7 and 9 hours is associated with reduced risk of coronary artery disease (CAD), stroke, CVD, and all-cause mortality.^{42,43} Poor sleep quality is associated with CV risk factors such as metabolic syndrome, frailty, functional impairment, falls, cognitive decline, depression and poor QOL, diet quality and physical inactivity.⁴⁴⁻⁴⁹ The effects of poor sleep may be mediated through impaired autonomic tone, endothelial dysfunction, inflammation, altered systemic/cardiac hemodynamics, and pro-coagulation milieu.^{50,51}

SLEEP CONSIDERATIONS FOR OLDER ADULTS. Normal age-related changes in sleep patterns predispose to sleeping disturbances that impact more than 50% of older adults.^{39,52} Social identities and

statuses, sociocultural factors, and physical/built environment factors that intersect with age also affect sleep health.⁵³ Sleep health can additionally be compromised by precipitating factors such as primary sleep disorders (eg, sleep apnea syndromes, insomnia), medical illnesses, medications, alcohol use, psychosocial (eg, bereavement, caregiving roles, social isolation, lifestyle transitions), and physical stressors.^{45,54}

Senescent cell accumulation seen with aging, obesity, and comorbidities contribute to changes in circadian rhythm, resulting in impaired cellular homeostasis.^{55,56} Declines in sleep quantity and quality accelerate biological aging.^{55,57} Therefore, efforts to restore and maintain sleep quality and age-appropriate duration can have important effects on the health, function, and QOL.^{43,45}

RECOMMENDATIONS TO PROMOTE SLEEP HEALTH IN OLDER ADULTS. Life's Essential 8 recommends 7 to 9 hours of sleep.^{5,6} Similar to younger adults, recommendations for sleep health-promoting behaviors include: avoid substances (eg, limiting caffeine after lunch time, avoid nicotine and alcohol within 3-4 hours of bedtime), avoid evening fluids or diuretics, engage in regular physical activity, manage stress, make environmental changes (eg, dark bedroom at cool temperature), regularize sleep-wake timing, and avoid naps or be intentional about their timing and duration.⁵⁸ In older adults, review of medications can identify those that can affect sleep quality and/or architecture (eg, central nervous system stimulants, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors, lipophilic beta-adrenergic blockers, centrally acting alpha adrenergic agonists, and glucocorticoids).⁵⁹

Healthy sleep habits are often not enough treatment.⁶⁰ Cognitive behavioral therapy is the first-line of treatment for insomnia at all ages.^{60,61} Other modalities such as bright light therapy, acupuncture, and mindfulness-based stress reduction techniques may be helpful.⁶²⁻⁶⁴ Behavioral interventions carry fewer risks of adverse effects than pharmacological interventions. In older adults, pharmacological interventions should be avoided. Specifically, benzodiazepines and "Z-drugs" such as zolpidem should be avoided due to the high risk of falls, fracture, and dementia.⁶⁵ There has been increasing use of melatonin to address sleep difficulties in older adults, however evidence is limited.⁶⁶ (Table 1) There is early interest in the role of senolytics targeting cellular senescence to improve circadian rhythm and prevent age-related decline in sleep duration and quality.⁶⁶

EAT BETTER (NUTRITION)

The healthy eating index of older adults ranges from 47.7 to 65.8 (out of 100), reflecting suboptimal diet.^{67,68} Adherence to a healthy eating pattern is associated with reduced CVD and mortality, as well as improving frailty, sarcopenia, polypharmacy, mobility limitations, cognitive, and mental health.⁶⁹⁻⁷³

In older adults, poor dietary quality and malnutrition are key issues. Malnutrition, defined as a deficiency of energy and nutrients, affects 6% of older adults in the community and 50% in rehabilitation facilities.^{74,75} Aging increases the risk for malnutrition through complex factors including loss of appetite, impaired smell and taste, impaired dentition, difficulty swallowing, loss of mobility necessary to acquire and prepare healthy food, cognitive decline, social isolation, depression, financial food insecurity, and diminished nutrition absorption.^{76,77} Therefore, dietary interventions in older adults range from emphasis on dietary quality to prioritizing adequate protein-energy intake.

RECOMMENDATIONS TO IMPROVE DIETARY QUALITY FOR OLDER ADULTS. A healthy balanced diet consists of whole grains, fruits and vegetables, lean protein, nuts, seeds, and cooking in nontropical oils such as olive oil.⁵ Various diets have beneficial impacts on life span. Some have focused on the content, such as Mediterranean diet, Dietary Approaches to Stop Hypertension (DASH) diet, plant-based diet, Ketogenic diet, Baltic Sea diet, Nordic diet, and others on the timing of food intake, such as intermittent fasting.⁷⁸ Diets rich in fibers and antioxidants have been associated with more favorable biological aging in the form of telomere shortening, DNA responses to oxidative damage, DNA methylation patterns, mitochondrial function, stem cell survival, and inflammation.^{78,79} While more intervention studies are needed, greater adherence to any healthy eating pattern over long term is required to lower the risk of total and cause-specific mortality.^{80,81}

Improved dietary quality may be achieved by counseling on beneficial dietary patterns. The Mediterranean and DASH diets have the most robust evidence for prevention of CVD, cancer, and diabetes mellitus (DM).⁸²⁻⁸⁴ Both of these diets are very similar, with the exception of emphasis on reduction of sodium, sugar, and saturated fats in DASH diet.⁸⁵ Certain vegetarian eating patterns such as lacto-ovo vegetarian and pescatarian diets, which both exclude meat and poultry, also positively impact CV health.⁸⁶

SUPPLEMENTS. Older adults are at risk for micronutrient deficiencies, however, routine multivitamin supplementation for CVD prevention is not recommended.^{87,88} Similarly, over the counter, N-3 polyunsaturated fatty acid (omega-3 fatty acid) supplementation, is not effective in CVD prevention.^{89,90} However, a prescription-only omega-3 fatty acids (eicosapentaenoic acid ethyl ester) reduces CV events in individuals with established CVD and elevated triglyceride levels.⁹¹ Finally, despite the popularity of vitamin D supplementation, it has not been shown to reduce risk of bone fractures, falls, frailty, or CV events.⁹²⁻⁹⁴

QUIT TOBACCO (SMOKING CESSATION)

Nicotine use is lowest among people aged 65 years and older (11.8%) as compared to the individuals aged 25 to 44 years (22.9%) and 45 to 64 years (20.4%), nevertheless, remains a cause of excess mortality and morbidity at advancing age.^{95,96} The effects of smoking on the CV system are mediated via promotion of atherogenesis through a complex interplay of inflammation, oxidation of lipids, pro-thrombosis, insulin resistance, and increased release of catecholamines.⁹⁶

SMOKING CONSIDERATIONS FOR OLDER ADULTS. Smoking affects older adults disproportionately because of the longer duration of cumulative injury, leading to higher associated rates of CVD, pulmonary disease, and cancers.^{97,98} Smoking accelerates the aging process through free radical damage, shortening of telomere length, development of concurrent pathologies, and therefore, contributes to age-related syndromes such as frailty, functional impairment, cognitive decline, and poor QOL.^{98,99}

At all ages, quitting tobacco dramatically reduces CVD risk, cognitive decline, pulmonary disease, and cancer.^{100,101} The magnitude of reduction of smoking-related morbidity and mortality directly relates to duration and amount of tobacco use.^{97,102} The CV benefits of smoking cessation begin within 20 minutes.¹⁰³ The risk of myocardial infarction decreases within 24 hours, and excess risk of CAD is half that of a smoker at 1 year. At 5 years, stroke risk decreases to same as nonsmokers and risk of CAD becomes same as nonsmokers at 15 years.¹⁰³

Quitting tobacco can be challenging for older adults because it has been a part of their lifestyle for decades. Recognition of the immediate benefits of smoking cessation, dangers of smoking, including fire risk, should be emphasized. For those with cognitive impairment, involvement of caregivers is key to successful smoking cessation. Other barriers include

previous failed attempts, lack of awareness, lack of resources, and support.¹⁰⁴ Short-term declines in motor abilities and cognition following cessation may impair QOL and contribute to continued tobacco dependence.¹⁰⁵ As a result, older adults are half as likely to quit compared to younger adults, however, remain abstinent at similar rates following cessation.¹⁰⁶

RECOMMENDATIONS FOR SMOKING CESSATION IN OLDER ADULTS. Effective interventions include counseling by a physician, nurse, pharmacists or cessation specialist, (multiple sessions better than a single session), group behavioral interventions, and telephone counseling.¹⁰⁷ Cognitive behavioral therapy is successful in cessation and maintenance of abstinence in older adults and can be used in conjunction with pharmacotherapy¹⁰⁸ (Table 1).

Nicotine replacement therapy has the best data in older adults, with cessation rates ranging from 10% to 25%.¹⁰⁹ Nicotine is available in multiple modalities (ie, transdermal patches, gums, lozenges, sublingual tablets, inhalers, and nasal sprays). Caution should be taken for patients with dysphagia and aspiration risk as gums and lozenges may not be tolerated.

Bupropion is equally efficacious and can be used alone or in combination with nicotine replacement therapy. However, there are insufficient data for smoking cessation in older adults and should be used with caution, especially with impaired renal or liver function, due to the risk of side effects and mild anticholinergic properties.^{65,109} Varenicline is a partial agonist of alpha4-beta2 neuronal nicotinic acetylcholine receptor. It is safe, well-tolerated, and most effective smoking cessation pharmacotherapy in older adults.^{98,107} The most common adverse effects include nausea, sleep disturbances, and abnormal dreams.¹¹⁰

MANAGE WEIGHT (OBESITY)

Nearly 40% of men and women aged >60 years are obese and the prevalence, especially in women, continues to rise.¹¹¹ Older adults are particularly susceptible to sarcopenic obesity wherein fat mass increases with concomitant reduction in muscle mass and strength.¹¹² Sarcopenic obesity affects 12 to 48% of older adults.¹¹³ Although epidemiologic studies suggest obesity may be protective in older adults, this "obesity paradox" may be misleading. Worse outcomes with lower body weight may reflect confounding from smoking, diseases causing weight loss (reverse causation, eg, cancer), and varying periods of follow-up.¹¹⁴ Obesity is known to accelerate biological aging including telomere shortening and an altered

epigenetic landscape typical of age-related dysfunction.^{115,116}

WEIGHT CONSIDERATIONS FOR OLDER ADULTS.

Aging is associated with changes in body composition. Fat mass increases with the accumulation of visceral and intermuscular adipose tissue, while fat-free mass decreases.^{117,118} This ectopic fat is associated with elevated inflammatory molecules such as IL-6 and TNF- α and contributes to inflammation of aging and insulin resistance.^{119,120} The most important contributor to the accumulation of body fat is decrease in major components of total energy expenditure (resting metabolic rate, thermal effect of food, physical activity). Approximately 50% of the reduction is due to physical inactivity.¹¹⁸ Age-related hormonal changes such as decreased growth hormone and testosterone secretion, reduced responsiveness to thyroid hormone, and resistance to leptin with decreased ability to down-regulate appetite also account for shifts in proportion of fat and fat-free mass.^{118,121}

RECOMMENDATIONS FOR MANAGING WEIGHT IN OLDER ADULTS.

Life's Essential 8 recommends maintenance of a healthy body weight with a body mass index <25 kg/m².⁵ Weight loss in individuals with obesity, regardless of age, sex, or race improves physical function and QOL.¹¹⁸ Lifestyle interventions are effective at all ages.¹²² A realistic weight loss goal for older adults is a 5 to 10% reduction in body weight. The combination of an energy-deficit diet (energy deficit ~500-750 kcal/day), rich in high-quality protein (1 g/kg/day) with increased physical activity results in moderate weight loss.^{118,123} Interventions aimed at weight loss should consider worsening body composition from baseline and focus on loss of adiposity with maintenance or increase of bone and muscle.¹²⁴ (Table 1) Tailored programs that account for biologic sex (eg, greater protein needs for men) should be considered. A specific behavioral strategy includes self-monitoring, goal setting, social support, and stimulus control.¹²⁵ The program should be nutritionally adequate and applicable to ethnic and cultural background, and physical and cognitive capabilities of the individual.

In preclinical models, energetic restriction has demonstrated reduced risk for all-cause mortality and CVD due to favorable effects on aging-related molecular mechanisms.^{126,127} Intermittent fasting is a popular approach to lose weight by reduction in calorie intake.^{128,129} Safety and CV outcomes of intermittent fasting have not been evaluated in older adults, and it may have a negative effect on lean mass retention.^{129,130}

Clinical trials studying pharmacotherapy in obesity treatment have enrolled few older adults (2%-8.8%).¹³¹⁻¹³⁴ There is insufficient evidence to determine efficacy and safety of weight loss medications in this population. Weight loss medications, in addition, may have detrimental adverse effects and add to the burden of polypharmacy. When selecting a weight management medication, several factors must be considered including each drug's efficacy, side effects, cautions, warnings, patient's comorbidities, and should be a shared decision with a comprehensive lifestyle intervention. Bariatric surgery is the most effective intervention especially in patients with severe obesity, however, evidence concerning its efficacy and safety in older adults is limited.¹³⁵ Preclinical data suggest that senolytics may alleviate the development of obesity and metabolic syndrome by promoting favorable deposition of fat to subcutaneous region rather than visceral deposition, thereby increasing insulin sensitivity and reduction of metabolic syndrome in mice.¹³⁶

CONTROL CHOLESTEROL (HYPERLIPIDEMIA)

The role of lipids, in particular, low-density lipoprotein cholesterol (LDL-C), in the development of atherosclerosis is well-established.¹³⁷ However, there is conflicting evidence for the association of LDL-C with CVD in older adults.^{138,139}

CHOLESTEROL PHYSIOLOGY CONSIDERATIONS FOR OLDER ADULTS.

With aging, lipid metabolism becomes dysregulated via complex multifaceted mechanisms.¹⁴⁰ Total cholesterol and LDL-C levels initially increase with age until the early 50s followed by a plateau or even decrease in subsequent years.¹⁴¹⁻¹⁴³ Significant sex differences in plasma lipid levels are observed with aging, with decreased estrogen levels in postmenopausal women leading to increased triglyceride levels compared with men.^{144,145} Changes in body composition associated with aging, insulin resistance, decreased circulating levels of growth hormone contribute to changes in lipid profiles over time.^{142,146} Lower cholesterol levels in older adults may also reflect survivorship bias: individuals with lower cholesterol levels live longer. Moreover, low LDL-C may also be confounded by a catabolic condition such as cancer, renal disease, or dementia.

RECOMMENDATIONS FOR CONTROLLING CHOLESTEROL IN OLDER ADULTS.

Most recently, 2018 American College of Cardiology/AHA guideline recommended statin use for primary prevention in patients with LDL-C \geq 190 mg/dL, DM, or a 10-year atherosclerotic CVD risk \geq 7.5% with risk enhancers.¹⁴⁷ Atherosclerotic CVD

risk is validated for age 20 to 79 years.¹⁴⁷ On the other hand, cardiovascular risk score-3 risk calculator is valid up to the age of 85 years.¹⁴⁸

Coronary artery calcium score is a valuable prognostic tool in older adults. The negative predictive value of zero coronary artery calcium score for predicting CAD events and mortality increases with age and can be used as an impactful prognostic marker for de-risking at older ages.¹⁴⁹

Adherence to a healthy lifestyle aids in cholesterol lowering. Statins are important for secondary prevention, and to reduce first CVD event at least to age 75 years.¹⁵⁰⁻¹⁵² Observational data suggest lower risk for CV events for primary prevention over age 75 years with statin.^{152,153} Few trials have included individuals aged 75 and older. The PROSPER (Prospective Study of Pravastatin in the Elderly at Risk) trial, the first dedicated trial to older individuals (70-82 years), demonstrated an overall improvement in CVD outcomes with pravastatin treatment in a mixed primary and secondary prevention population.¹⁵⁴ Subsequent analysis of primary prevention data from Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin and Heart Outcomes Prevention Evaluation-3 demonstrated a significant 26% relative reduction in CVD events and death among individuals aged ≥ 70 years.¹⁵⁵ Moreover, meta-analysis of 28 major statin trials that included over 186,000 participants (both primary and secondary prevention) and found a 12% reduction in vascular mortality per 1.0 mmol/L reduction in LDL-C, though benefits were attenuated in those over age 75 without pre-existing CVD.¹⁵¹ Two ongoing randomized controlled trials, the STAREE (Statin Therapy for Reducing Events in the Elderly; [NCT02099123](#)) trial and the PREVENTABLE (Pragmatic Evaluation of Events and Benefits of Lipid-Lowering in Older Adults; [NCT04262206](#)) trial will address the role of statins for primary prevention in those aged 75 years and older. In addition to lowering cholesterol, statins may have antiaging properties through modulation of telomerase activity.¹⁵⁶ That being said, in older adults with life-limiting illnesses and polypharmacy concerns, the potential net benefits of statin treatment for primary prevention are likely attenuated.

The utility of non-statin drugs, ezetimibe added to simvastatin, or PCSK9 inhibitor, extend to older adults as well.^{157,158} Novel therapeutics such as inclisiran and bempedoic acid offer additional treatment options, though evidence in older adults is limited.^{159,160}

Statins are safe and well tolerated even at advanced ages.^{151,161} Less serious muscle symptoms

are commonly observed with statin treatment >90% of which can be attributable to the so-called “nocebo effect.”¹⁶² Nevertheless, it is important to consider how such ‘aches and pains’ may impact an older adult with mobility limitations and careful follow-up for side effects, considering dose adjustment, or rotating to another statin if these should occur.

MANAGE BLOOD SUGAR (DM)

Life's Essential 8 recommends controlling blood sugar for optimum CV health, which is relevant to older adults as well.^{5,163} About 50% and 30% of older adults >65 years have prediabetes and diabetes, respectively.¹⁶⁴ Older adults with diabetes are more likely to be Blacks and Hispanics, and as a result, have increased prevalence of CVD.¹⁶⁵⁻¹⁶⁸ In addition, DM increases the risk of geriatric syndromes such as urinary incontinence, falls, sarcopenia, frailty, chronic pain, dementia, and polypharmacy.¹⁶⁷ Furthermore, older adults have the highest rates of hospitalization due to hyperglycemia and hypoglycemia, visual impairment, and diabetes-related renal disease.^{163,165,169}

BLOOD SUGAR CONSIDERATIONS FOR OLDER ADULTS. Aging is associated with dysregulated glucose metabolism manifesting as elevated fasting and postprandial glycemic levels irrespective of presence or absence of diabetes.^{170,171} Body composition changes throughout life, and as mentioned above, is characterized by increased ectopic fat deposition. Accumulation of visceral fat, especially intra-abdominal, is the major driver of insulin resistance through increased pro-inflammatory cytokines.^{119,170} In addition, age-related impaired insulin secretion, reduced insulin sensitivity, and promotion of pancreatic B-cell death contribute to the development of DM.¹⁷⁰

RECOMMENDATIONS FOR MANAGING BLOOD SUGAR IN OLDER ADULTS. Glycemic control in older adults brings unique challenges due to comorbidities, cognitive, and functional heterogeneity. Studies have demonstrated increased risk of CV events, frailty, disability, cognitive impairment, and mortality with intensive glycemic control.¹⁶⁶ Moreover, tight glycemic control contributes to falls and fractures. Therefore, the goal for diabetes treatment in older adults is a simplified regimen that avoids hypoglycemia and hyperglycemia, and involves caregivers (5Ms medications) with a focus on health status and life expectancy.¹⁶³ Current guidelines from American Diabetes Association recommend an HbA1c of <7.5% in older adults with few chronic illness and intact

cognitive and physical function who do not have a life-limiting illness.¹⁷² Higher HbA1c goals may be most relevant to nursing home populations and those with very limited life expectancy (Table 1).

Advances in pharmacotherapeutics with improved CV outcomes have reinvanized the management of DM. With these newer agents, lower HbA1C levels can be targeted in healthy older adults without comorbidities.¹⁷³ Metformin is the first-line agent for treatment but is contraindicated in renal dysfunction (estimated glomerular filtration rate <30 mL/min/1.73 m²). Insulin and insulin secretagogues such as sulfonylureas should be used with caution due to the risk of hypoglycemia. Oral dipeptidyl peptidase 4 inhibitors are safe with low risk of hypoglycemia, though are costly and do not impact CVD outcomes. Glucagon-like peptide-1 receptor agonists have demonstrated CV benefits in patients with diabetes and established CVD.¹⁷⁴ These drugs are injectable and require adequate visual, motor, and cognitive skills for proper use. Sodium-glucose transporter-2 inhibitors are oral drugs that demonstrated reduction in CVD in patients with and without diabetes.¹⁷⁵

Senolytics have shown promise in reducing senescent cell burden, macrophages, and crown-like structures in adipose tissues in diabetics with kidney disease, suggesting that onset or progression of diabetes might be delayed with these drugs, though large-scale studies are needed.¹⁷⁶ On the other hand, existing antidiabetic drugs, metformin, and sodium-glucose cotransporter-2 inhibitors have shown anti-aging properties by attenuating multiple aspects of biological aging raising promise for their use as gerotherapeutics.^{177,178}

MANAGE BLOOD PRESSURE (HYPERTENSION)

Hypertension is highly prevalent in older adults, affecting nearly 80% of older adults ≥75 years, with highest prevalence in men and non-Hispanic Blacks.² Isolated systolic hypertension, defined as elevated systolic pressure with normal or reduced diastolic pressure is the predominant form of hypertension seen in older adults.¹⁷⁹

BLOOD PRESSURE CONSIDERATIONS FOR OLDER ADULTS. Aging is characterized by generalized endothelial dysfunction and arterial stiffening which occurs due to a loss of elastin, increase in collagen and calcification.^{180,181} These changes are accentuated by age-induced chronic low-grade inflammation, irreversible mitochondrial oxidative stress from

accumulation of reactive oxygen species, and metabolic syndrome.^{179,182} Arterial stiffness, especially of large vessels, causes diminished baroreflex sensitivity leading to neurohormonal dysregulation and sympathetic activation.¹⁸³ Loss of distensibility of major central vessels and increased vascular resistance cause augmented reflected waves and elevated systolic pressure. Additionally, reduced arterial reservoir capacity and altered blood flow dynamics lead to low diastolic pressure and elevated pulse pressure.^{179,181}

Age-related increase in BP also arises from decline in renal function, increased salt sensitivity, and upregulation of ENaC channels, reduced nitric oxide bioavailability, increased endothelin-1, and reduced levels of aldosterone and renin.¹⁸⁴⁻¹⁸⁶ Environmental and lifestyle factors including low physical activity, poor diet, high salt intake, and weight gain further contribute to elevated BP. Common comorbidities, such as obstructive sleep apnea, renal dysfunction, and thyroid disorders, may present as secondary causes of hypertension and increase the likelihood of treatment resistant hypertension.¹⁸⁷

Hypertension affects brain structure leading to cognitive impairment, neurodegenerative, and mood disorders. This in turn sets up a vicious cycle of poor insight, low treatment adherence, increased risk of polypharmacy, worsening cognition, functional status, and mortality.^{188,189} Hypertension control in older adults reduces CVD risk and associated mortality and has beneficial impact on delaying the onset and progression of cognitive impairment.^{190,191} Aging hallmarks are not well studied in the context of hypertension, and a few initial studies have demonstrated increased biomarkers of accelerated aging in these patients.¹⁹² Senolytics, such as navitoclax, dasatinib, and quercetin have demonstrated some efficacy in reducing myocardial senescent cells, vascular calcification, and interstitial fibrosis that may have a role in prevention of development of hypertension in future in humans.^{193,194}

RECOMMENDATIONS FOR MANAGING BLOOD PRESSURE IN OLDER ADULTS. Lifestyle modification should be encouraged and emphasized to prevent development and aid in BP management at every visit. Several trials (SHEP [Systolic Hypertension in the Elderly Program], HYET [Hypertension in Very Elderly Trial], STEP [Strategy of Blood Pressure Intervention in the Elderly Hypertensive Patients], SPRINT [Systolic Blood Pressure Intervention Trial]) have studied hypertension management in older adults with targets as low as systolic BP <120. Overall,

these trials demonstrated benefit for CV events, mortality, and dementia.^{190,195} Yet results remain inconclusive among those with advanced multimorbidity, frailty, cognitive decline, or institutionalization as these individuals were not included in the trials. Nevertheless, the 2017 American College of Cardiology/AHA hypertension guidelines recommend a target systolic BP of <130/80 mm Hg for most adults aged 65 years and older.¹⁹⁶ On the other hand, the 2018 European Society of Cardiology/European Society of Hypertension suggest a higher systolic BP goal of 130 to 139 mm Hg and diastolic BP of 70 to 79 mm Hg in adults between ages 65 and 80 years.¹⁹⁷

For patients with preserved functional status, BP targets in older adults should be similar to those in younger adults. For those who have significant cognitive and/or functional decline, frailty and limited life expectancy, a BP target of systolic BP 130 to 150 mm Hg may be reasonable if lower BP causes hypotension or other adverse reactions. The pharmacologic maxim of “start low, go slow, but get there” should be followed. Intensive BP lowering is most appropriate for older adults with high CV risk burden and life expectancy of 3 or more years as those with limited life expectancy may not live long enough to derive benefit^{102,198} (Table 1).

There are multiple first-line agents for BP treatment: thiazide diuretics, angiotensin-converting enzyme inhibitor, angiotensin II receptor blockers, and calcium-channel blocker. Thiazides have the highest risk of adverse events such as falls, acute renal injury, and should be used with caution.¹⁹⁹ Calcium channel blocker and angiotensin-converting enzyme inhibitor/angiotensin II receptor blockers may be beneficial in frail older patients, with the latter having a role in increasing lower limb muscle mass.²⁰⁰⁻²⁰² Alpha blockers, such as those commonly used for benign prostatic hyperplasia in men, and diuretics can induce or worsen orthostatic hypotension, increase risk of falls, and hip fracture.^{65,203} Other drugs to be used with caution are clonidine, methyldopa, nifedipine, and reserpine.⁶⁵

SOCIAL DETERMINANTS OF HEALTH IN OLDER ADULTS. In addition to Life's Essential 8 components, potentially modifiable social determinants of health also play an important role in preservation of CV health. Negative psychological conditions such as depression, anxiety, stress, social isolation and loneliness, pessimism, and so on adversely impact CV health, whereas positive psychological well-being improves CVH and associated mortality.²⁰⁴ Poor mental health in older adults may cause medication non adherence, substance misuse, inequalities in

access to health care, behavioral changes such as lack of motivation for exercise, and increased risk of medication adverse effects that may impact CVH directly or indirectly. Therefore, to improve CVH, a comprehensive and holistic approach addressing social determinants is necessary.²⁰⁵ Further studies exploring the impact of social determinants of health and potential intervention specifically in older adults are needed.

CONCLUSIONS

The risk of developing CVD varies considerably between individuals of the same chronological age. There is growing evidence indicating that variability in biological aging and reduced efficiency of homeostatic mechanisms that oppose aging may contribute to this clinical heterogeneity. A comprehensive, holistic, and individualized approach is required to treat the whole person with consideration of Geriatric 5Ms to ensure the extension of not only lifespan but also health span. Future studies of gero-therapeutics may identify interventions that can improve CV health, as well as healthy aging and longevity.

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