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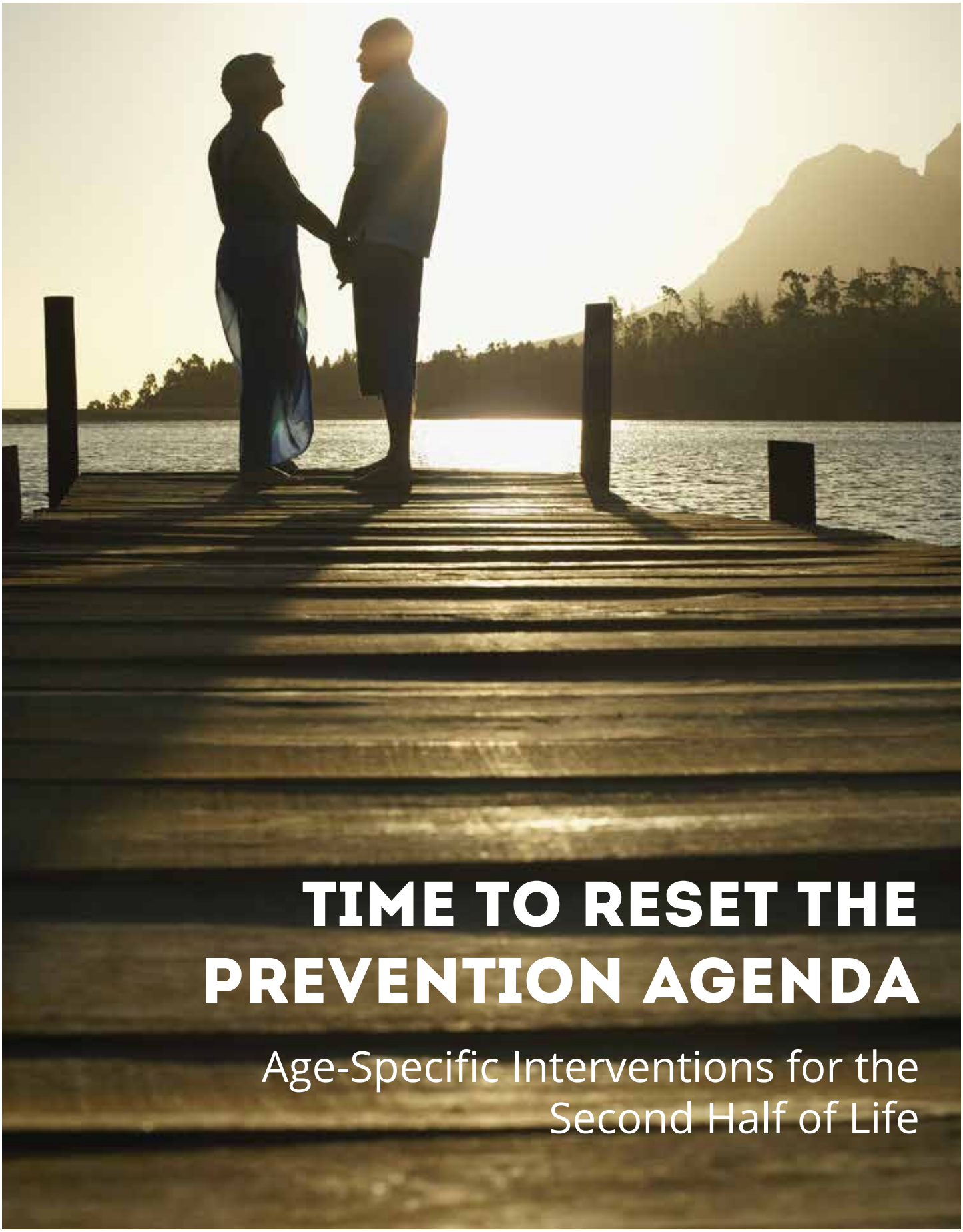

TIME TO RESET THE PREVENTION AGENDA

Age-Specific Interventions for the Second Half of Life

SEPTEMBER 2015

CONTENTS

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EXECUTIVE SUMMARY

Social, economic, and medical progress in recent history have resulted in dramatic improvements to life expectancy and subsequently, a global aging population. Although global mortality has continued to fall, this has been accompanied by increasing morbidity from non-communicable diseases (NCDs) and age-specific conditions including cardiovascular disease, diabetes, cancer, dementia, untreated mental health conditions, and musculoskeletal disorders.

With advancing age, these impact functional independence and quality of life, and threaten ongoing improvements. In addition, these conditions can often occur simultaneously, adding complexity to their management. Illness and poor health are not inevitable outcomes of aging, though. Substantial potential exists to modify this current relationship and diminish the economic and social burden of an aging population.

In order to promote health and longevity, and achieve the maximal possible compression of morbidity, interventions must be considered in age-specific contexts across the lifespan, from early childhood through adolescence, adulthood, and old age. With advancing age comes changes in health status, health risks, and functional status.

Currently, a lack of age-specific recommendations for older adults account for these changes and underlying cumulative risks.

This paper summarizes available scientific evidence to synthesize recommendations that favorably influence morbidity and mortality for older adults each decade over 50.

Recommendations outline specific types of exercise, dietary patterns, and other interventions to promote healthy aging throughout adulthood and old age. These recommendations will require ongoing refinement. In order to do so, investment is needed in research to fill the many gaps informing them.

Furthermore, personalized approaches to healthy aging must be complemented with population-wide approaches such as incorporating changes to the physical environment, emerging technologies, and advances in behavioral economics and genomic predictions. Broad cross-sector partnerships will aid these efforts and help ensure greater longevity is an opportunity, rather than a burden, for society.

> “In order to promote health and longevity, and achieve the maximal possible compression of morbidity, **interventions must be considered** in age-specific contexts across the lifespan”

01

Introduction

An Aging World

A baby born in the year 1900 could not expect to live past the age of 50. Today, the global average life expectancy at birth is 71 years, with the highest average in Japan at 84 years.[1] Immense social and economic progress throughout the 20th century has contributed to these dramatic improvements.[2] Notably, better living standards, cleaner drinking water, improvements in immunization and disease management, and more nutritious diets have led to a steady decline in death and disability from infectious diseases.[3]

Today, as life expectancy continues to increase, the worldwide population is aging. By 2050, the number of people aged 60 and above will have increased from 841 million to more than 2 billion (see Figure 1 below); for the first time in history, this population will be larger than that of children less than 14 years of age.[4] Among European Union (EU) nations, projections are that by 2060, life expectancy at age 65 will reach 22.4 additional years for men and 25.6 for women.[5]

The Challenge of an Aging Population

Increases in life expectancy can be explained by declining mortality rates at all ages. In many cases, however, this decrease has been accompanied by increased morbidity and reduced quality of life with advancing age.[5] The global burden of disease may have shifted away from infectious diseases as the leading causes of death and disability, but today largely preventable, non-communicable diseases (NCDs) such as diabetes, heart disease, and cancer – often referred to as chronic diseases – are driving up death and disability rates.[3]

An aging population brings with it unique challenges to individuals, families, and society. Twenty-three percent of the global disease burden is attributable to disorders among people aged 60 and above, a substantial proportion due to NCDs.[6] Major diseases and conditions afflicting the elderly impact longevity, functional independence, and quality of life. In addition to the NCDs mentioned above, these include frailty and impaired mobility, dementia and cognitive decline, depression, and musculoskeletal disorders.

FIGURE 1. PROJECTED POPULATION INCREASE FROM 2015 TO 2050

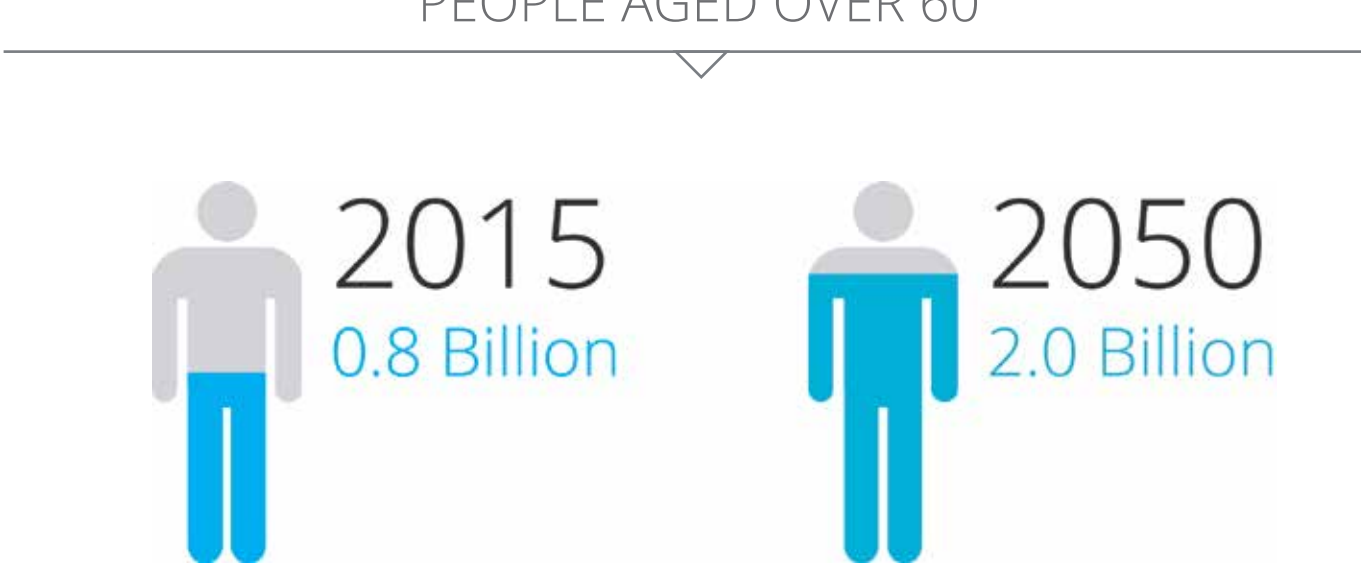
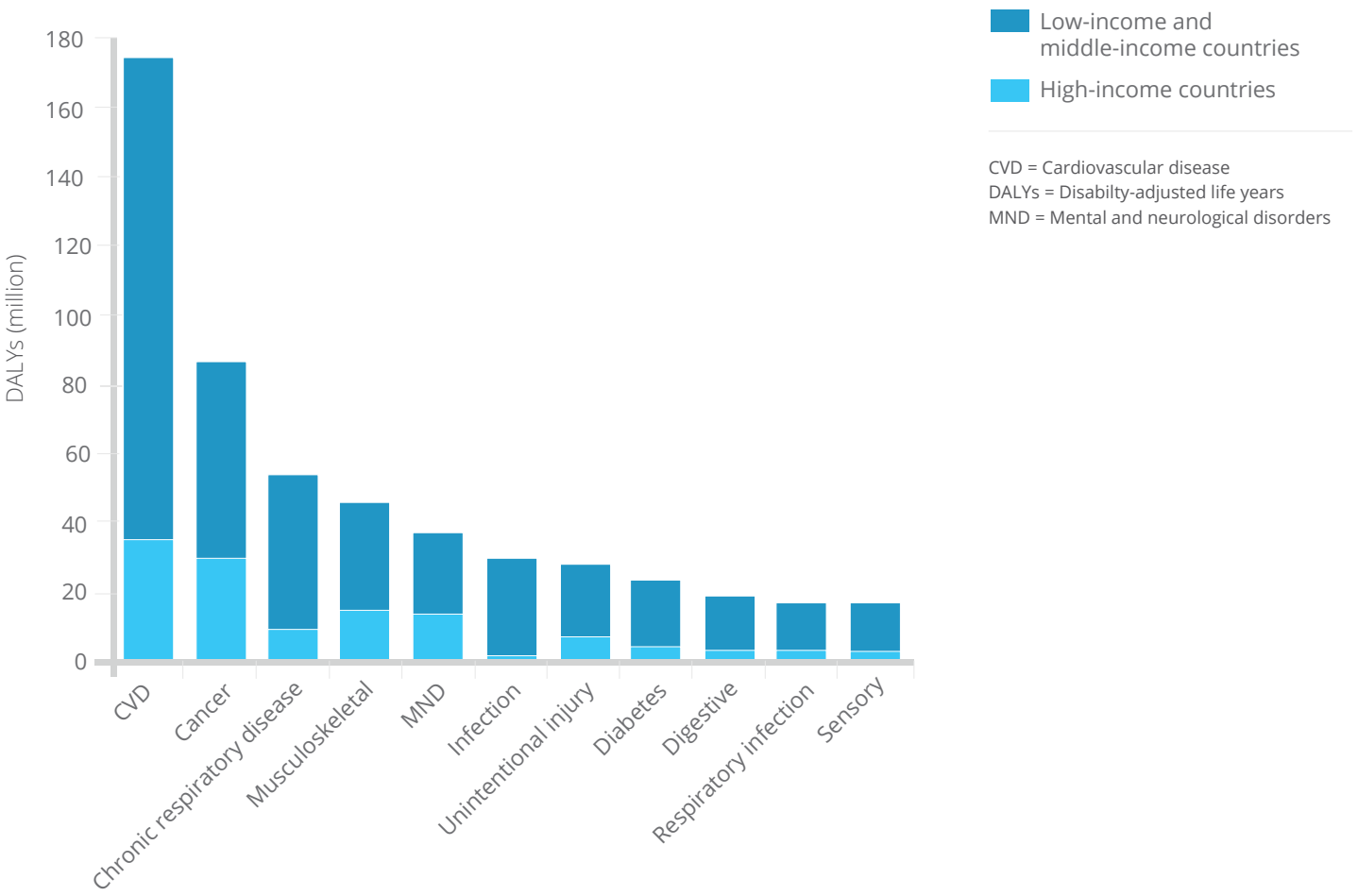


FIGURE 2. LEADING CONTRIBUTORS TO DISEASE BURDEN AMONG ADULTS 60 YEARS OF AGE AND OLDER [6]



Aging in Poor Health: an Economic and Global Health Security Issue

Increased longevity without improvements in population health increases the demand for services and, thus, health care costs over a longer period.[5] In the United States (US), the number of adults over 65 years of age is expected to more than double to 71 million by 2030. Approximately 80% of older adults currently have at least one NCD, and 50% have at least two.[7] In South Africa, people 50 years of age and older insured with Discovery Health account for 52% of hospital admission costs, despite representing less than 25% of the insured population.[8] If these trends continue, health- and aging-related services will face unprecedented strains.

Because NCDs require lifelong management, the high costs associated with them threaten the ability of individuals to seek medical care and the ability of governments to provide universal health coverage, with dire implications for productivity and economic growth.[9] An older person is less likely to remain in the workforce if he or she is in poor health. Thus, changes to pension systems and retirement policies will be needed, along with a reorientation of health care systems that previously neglected the needs of an aging population.[10]

Demographic projections expand on the economic and social challenges that await us. The EU population is expected to increase by almost 5%, from 507 million in 2013 to 526 million in 2050, with the greatest growth among those over 80.

Older people have greater health care needs than do younger people. As a result, spending on health care and long-term care is expected to increase by approximately 2 percentage points of the gross domestic product (GDP) of EU nations. At the same time, the old-age dependency ratio – the number of people aged 65 or above relative to those between 15 and 64 years of age – is expected to almost double such that EU nations would shift from having four to having two working-age people for every person over 65 years of age.[5]

The Opportunity to Intervene

Illness and poor health are not inevitable outcomes of aging. Substantial potential exists to modify the current relationship between age and health.[6] Many of the conditions affecting longevity can be mitigated through risk-reduction strategies throughout life. These strategies seek to address underlying risk factors, including physical inactivity, poor diet, tobacco use, excess alcohol use, non-adherence to chronic disease medications, abstention from preventive screenings, lack of immunization, and cognitive impairment. If longevity is accompanied by healthy life years, the burden of an aging population need not be as dire as predicted. Moreover, a healthy aging population can confer great benefits to the workforce, the economy, and society.

The Need to Consider Health Promotion and Disease Prevention From a Life-Course Perspective

To promote both health and longevity and achieve the maximum possible compression of morbidity, health promotion and disease prevention interventions must be considered in age-specific contexts across the lifespan, from early childhood through adolescence, adulthood, and old age. The World Health Organization (WHO) provides guidance on underlying biological, behavioral, and psychosocial processes that operate throughout a person's lifetime, affecting disease risk and health outcomes in later life.[11]

There is evidence, for example, that exposure to risk factors for cardiovascular disease (CVD), such as smoking, hypertension, high body mass index (BMI), and high low-density lipoprotein cholesterol, from as early as the first decade of life impacts future cardiovascular health.[12]

This paper focuses on health promotion and disease prevention among people 50 years of age and older, who can now expect almost 50 additional years of life. Recommendations to promote health and longevity must take into account functional status, changes in overall health profile, and accumulated health risks with age. Multi-morbidity is common with age and adds complexity to disease management. The presence of one condition can affect the presentation or management of another. For example, depressive symptoms have been associated with poor self-management of type 2 diabetes.[13] Late-onset major depression combined with cognitive impairment increases the risk of Alzheimer's disease, with an estimated 40% of individuals developing dementia within 3 to 5 years of depression diagnosis.[14] With each new diagnosis, however, comes an opportunity to intervene.

> “Moreover, a healthy aging population can confer great benefits to the workforce, the economy, and society”

Definition: Compression of Morbidity

Compression of morbidity describes the delay of disease onset and, therefore, a shortened duration of disease. For example, if someone were to develop type 2 diabetes at age 55 and die at age 85, this would mean 30 years lived with the disease. In an environment where health promotion and disease prevention efforts were in place throughout the lifespan, the same person might have not developed diabetes until age 65 and might also have lived to age 90. The compression of morbidity comes from the reduced duration of diabetes experienced (25 years) and the extended lifespan (5 more years). This effect has been shown to varying magnitudes on a population level.[15] Quality of life with advancing age and the extent of financial and social burden will depend largely on morbidity, and how to minimize years lived with disability.

> Recommendations to promote health and longevity must take into account functional status, changes in overall health profile, and accumulated health risks with age

02

Interventions to Extend Life and Promote Healthy Aging

> Existing health care guidelines for midlife and old age rarely take into account the underlying cumulative risks and rarely provide guidance for approaches specific to age

Existing health care guidelines for midlife and old age rarely take into account the underlying cumulative risk and rarely provide guidance for approaches specific to age and functional level; and where recommendations do exist, they have not been combined into coherent, focused packages of value for people as they age. Therefore, this paper attempts to provide a summary of available scientific evidence to address the needs described above and outline specific interventions that favorably influence morbidity and mortality from age 50 on. The implications of this paper are global, though where recommendations may differ between national contexts, a US-focused approach was taken.

Methodology

What disease-preventing interventions should be recommended throughout adulthood to extend life and improve the quality of years lived? We sought to answer this question by reviewing the scientific evidence for interventions that modify individual-level risk factors contributing to the greatest disease burden for adults aged 50 years and above. In addition, we consulted with leading experts on aging. More detailed methodology is provided in the Appendix.

Interventions that promote healthy aging were reviewed and subsequently categorized into the following:

1) Those that predominantly impact morbidity or quality of life. These interventions relate to immunization status, mental health, and age-specific conditions of cognitive decline, dementia, frailty, and musculoskeletal disorders.

2) Those that impact longevity; that is, where a clear mortality benefit was observed. These interventions relate to level of physical activity, dietary patterns, tobacco use, alcohol intake, medication adherence, cancer screening, and immunization status.

These results were then distilled into decade-specific recommendations for the ages of 50 and above.

Measures of Intervention Impact[16]

Odds Ratio (OR): OR indicates the relative change in the risk of a preventable event. It is the odds of an event (such as death) occurring in one group divided by the odds of it occurring in another group.

Relative Risk (RR): RR is the risk of an event occurring in an experimental group divided by the risk of the same event occurring in a control group. For most clinical trials, RR and OR can be considered interchangeable.

Hazard Ratio (HR): HR is a measure of how often a particular event happens in one group compared to how often it happens in another group, over time.

When events occur in the intervention group less frequently than in the control group, the OR, RR, or HR will be less than 1. If the opposite is observed, the intervention impact will be greater than 1.

Results

Preventive interventions that have a proven impact on morbidity and mortality among individuals aged 50 years and older are presented in Tables 1 and 2, respectively.

TABLE 1. INTERVENTIONS THAT AFFECT MORBIDITY

INTERVENTION/EVIDENCE OF BENEFIT	MEASURED IMPACT	OPTIMAL PARAMETERS
IMMUNIZATION		
Administration of chickenpox vaccine (for those who did not have the disease in childhood) and shingles vaccine to individuals aged 50+ reduces morbidity risk.[17]	N/A	**INTERVENTION(S):** Vaccination per national guidelines **INITIATION:** No optimal age **DURATION:** Single administration
Administration of pneumococcal vaccine to adults aged 65 and older reduces risk of developing pneumonia and associated complications.[18]	N/A	**INTERVENTION(S):** Vaccination per national guidelines **INITIATION:** Age 65 **DURATION:** Single administration
MENTAL AND COGNITIVE HEALTH		
Management of major depression (through medication and/or psychotherapy) among 60- to 94-year-olds by primary care providers reduces suicidal ideation, depressive symptoms, and all-cause mortality.[19,20]	Suicidal ideation down 12.9% (raw rate vs 3% in control group); HR 0.55 for all-cause mortality	**INTERVENTION(S):** No evidence for optimal intervention by age group **INITIATION:** No optimal age of initiation, but should begin as early as possible **DURATION:** Subject to individual needs
Multi-domain intervention for adults 60-77 years of age at risk of dementia results in improved cognition. Intervention includes modifying diet to meet Finnish national guidelines (including 5-10% weight loss if appropriate), physical activity training (strength training 1-3 times per week, aerobic exercise 2-5 times per week), cognitive training (focus on executive processes, working memory, episodic memory, mental speed), and vascular risk monitoring (blood pressure, BMI).[21]	25% improvement in cognition as measured through neuro-psychological test battery (NTB) Z score	**INTERVENTION(S):** Multi-domain to address multiple risk factors **INITIATION:** No evidence for optimal time of initiation, though earlier is likely better **DURATION:** No evidence for optimal duration; benefit evident from 2-year multi-domain intervention

TABLE 1. INTERVENTIONS THAT AFFECT MORBIDITY, CONT.

INTERVENTION/EVIDENCE OF BENEFIT	MEASURED IMPACT	OPTIMAL PARAMETERS
FRAILTY, MUSCULOSKELETAL DISORDERS		
30 minutes/day of moderate-intensity walking, 10 minutes' strength training (focused on lower extremities), and 10 minutes' balance and flexibility training for 70- to 89-year-olds at risk for disability improves mobility.[22]	Reduction in major (HR 0.82) and persistent (HR 0.72) mobility disability	**INTERVENTION(S):** Multi-component exercise program (30-45 minutes at least 3 times/week) to improve strength, balance, flexibility, aerobic capacity **INITIATION:** No evidence for or against optimal starting age, but earlier is likely better than later **DURATION:** At least 5 months
15 minutes of Tai Chi twice daily over a 15-week period for those aged 70 and above reduces risks of falls and improves indicators of frailty.[23]	47.5% reduced risk of falls	
Group exercise program involving 1 hour of class 2 times/week (including stretching, moderate-paced walking, conditioning, muscle relaxation, controlled breathing, and guided imagery) over 12 months reduces incidence of falls.[24]	22% fewer falls vs control group; 31% fewer falls among those who had fallen in past year	
1-hour exercise class weekly (individually tailored and focused on balance, strength, bone, endurance, flexibility, gait, functional skills, fall avoidance, backward-chaining, functional floor exercises) and 30 minutes of home exercises twice weekly (focus on lower limb strength) over 36 weeks reduced falls and fall-related injuries.[25]	31% fewer falls vs control group	
Group exercise program (30 minutes, 3 times/week) that involved strengthening exercises, balance and stability exercises, and active range of motion exercises and encouraged walking outside the home at least twice per week reduced incidence of falls and 12-month mortality.[26]	Incident rate ratio 0.68 (falls); RR 0.45 (mortality)	
Home safety visits by occupational therapists to provide fall-prevention advice and equipment reduces falls incidence and injuries from falls over a 12-month period.[27]	41% reduced incidence of falls vs control group	
Supplementation of calcium and vitamin D (at least 1200mg calcium and 800 International Units [IU] vitamin D daily) assists in preventing musculoskeletal disorders such as osteoporosis and fractures.[28]	12% reduction in all fracture types (RR 0.88)	**INTERVENTION(S):** Adequate protein to prevent malnutrition and maintain muscle mass, calcium and vitamin D supplements to prevent bone loss and fractures **INITIATION:** After age 50 (or around menopause for women) and priority for those aged 65 and above (when incidence increases) **DURATION:** No evidence for or against optimal duration, although optimizing diet should always be relevant
Average daily intake of protein 1-1.2 g/kg body weight/day for healthy adults aged 65 and above maintains lean body mass and muscle function.[29]	N/A[a]	

[a] Recommendations from expert committee consensus.

TABLE 2. INTERVENTIONS THAT AFFECT MORTALITY

INTERVENTION/EVIDENCE OF BENEFIT	IMPACT	OPTIMAL PARAMETERS
PHYSICAL ACTIVITY		
Vigorous physical activity (e.g., running, jogging, cycling, swimming, tennis, aerobic workouts) more than once per week reduces all-cause mortality among adults more than 50 years of age.[30]	HR 0.44	**INTERVENTION(S):** Moderate and vigorous physical activity performed frequently (≥300 min/week) is most effective **INITIATION:** No evidence on optimal age, though early is likely better **DURATION:** ≥5-15 years to see mortality benefit
Mild physical activity (e.g., laundry, home repairs) 1-3 times/month reduces all-cause mortality among those over 50 years of age.[30]	HR 0.76	
There is a dose-response, inverse relationship between number of minutes per week of moderate or vigorous activity and all-cause mortality.[31]	HR 0.66 (10-149 min) HR 0.53 (150-299 min) HR 0.46 (300+ min)	
Running an average of 76 minutes/week and completing 287 minutes/week vigorous exercise among adults aged 50 and above.[11]	3.3 years' extended life	
Moderate activity that ranges in intensity from 3 to 6 metabolic equivalents (METs) and expend about 1000 (kilo)calories/week of energy (equivalent to walking about 30 minutes/day) showed a mortality reduction over 5-15 years.[32]	20%-40% mortality reduction	
Aerobic physical activity to achieve weight loss for obese individuals reduces mortality (but not among average-weight or overweight individuals).[33]	RR 0.84	
Physical activity for weight loss among people with diabetes.[33]	3-4 months' prolonged survival for every 1-kg weight loss	
DIETARY PATTERNS		
Adherence to DASH (Dietary Approaches to Stop Hypertension) diet by women aged 34-59 years reduces risk of fatal coronary heart disease (CHD) and stroke over 24-year follow-up.[34]	RR 0.76 (CHD); RR 0.82 (stroke)	**INTERVENTION(S):** Regular diet that resembles Mediterranean or DASH diet (high intake of vegetables, fruit, nuts, legumes; moderate intake of whole grains, fish, monounsaturated fats, dairy; low intake of meat, alcohol; sodium intake 3-6 g/day); no evidence on different dietary patterns for different age groups **INITIATION:** No evidence of optimal age; likely earlier the better. Particularly important at time of hypertension diagnosis **DURATION:** No evidence, though longer is likely better
High adherence to Mediterranean diet reduces all-cause mortality among adults aged 51-70 years over a 10-year period.[35]	20%-21% mortality reduction; HR 0.79	
Higher adherence to Mediterranean diet reduces mortality among adults 20-86 years of age with CHD over a 3.78-year period.[36]	27% mortality reduction	
Mediterranean diet reduces all-cause mortality among those aged 70-90 years, with higher reduction among those who also were nonsmokers and consumed a moderate amount of alcohol.[37]	HR 0.77; >50% among nonsmokers, moderate alcohol users	

TABLE 2. INTERVENTIONS THAT AFFECT MORTALITY, CONT.

INTERVENTION/EVIDENCE OF BENEFIT	IMPACT	OPTIMAL PARAMETERS
Average salt intake (6.7-12.6 g day) decreases mortality and risk of cardiovascular events compared with lower and higher intakes.[38]	HR 1.16 (high vs average intake); HR 0.91 (average vs low intake)	
3-6 g/day sodium intake reduces mortality and risk of cardiovascular events in those aged 35-70 years; strong association among those with existing hypertension.[39]	OR 1.15 (intake <7 g/day)	
TOBACCO USE		
Quitting tobacco use before age 50 can completely eliminate excess risk of mortality due to smoking. Quitting after age 50 or 60 reduces risk of all-cause mortality among former smokers.[40]	HR 0.54 (after age 50) HR 0.61 (after age 60)	**INTERVENTION(S):** No evidence for or against quitting interventions for specific age groups **INITIATION:** As early as possible **DURATION:** Excess mortality risk is completely eliminated after about 10 years for light smokers and 20 years for heavy smokers[41]
Quitting smoking by individuals with CHD reduces all-cause mortality.[42]	36% mortality reduction, RR 0.64	
Quitting at age 30, 40, or 50 incrementally reduces mortality.[43]	10 years' extended life (quit at 30) 9 years' extended life (quit at 40) 6 years' extended life (quit at 50)	
Among former smokers aged 60 and above, excess mortality decreases with time since quitting, as measured by mortality rate advancement periods (RAPs), i.e. the age difference by which a risk factor advances mortality.[44]	3.9 yr RAP (quit <10 yrs ago) 2.7 yr RAP (quit 10-19 yrs ago)	
ALCOHOL USE		
Reducing or abstaining from drinking alcohol lowers odds of death compared with continued heavy drinking.[45]	OR 0.61 (reduce) OR 0.35 (abstain)	**INTERVENTION(S):** No evidence for or against specific programs or for specific ages (benefit is likely from abstinence no matter how it is achieved) **INITIATION:** No evidence, but early is likely better, especially before diseases such as cirrhosis are evident **DURATION:** No evidence, but ≥1.5 years of abstinence after development of cirrhosis is necessary before significant benefit is seen

TABLE 2. INTERVENTIONS THAT AFFECT MORTALITY, CONT.

INTERVENTION/EVIDENCE OF BENEFIT	IMPACT	OPTIMAL PARAMETERS
MEDICATION ADHERENCE		
Non-adherence to antihypertensive medication carries higher odds of death from stroke at 2 years.[46]	OR 3.81	**INTERVENTION(S):** No evidence on ideal method; for individuals ≥70 years old, emphasis should be on reducing polypharmacy (simultaneous use of multiple medications)[47] **INITIATION:** No evidence, but should always be relevant **DURATION:** No evidence; ideal duration likely depends on natural history of target disease
CANCER SCREENING		
Colonoscopy reduces mortality from colorectal cancer.[48]	Estimated 60%-70% mortality reduction	**INTERVENTION(S):** Colonoscopy at regular intervals as indicated in national guidelines; for people at average risk virtual colonoscopy every 5 yrs, colonoscopy every 10 yrs in the US[49] **INITIATION:** 50 years of age (as per US guidelines)[50] **DURATION:** Until age 75 unless there is a history of abnormal results (as per US guidelines)[50]
Mammography reduces mortality from breast cancer among women who are screened for ≥10 years.[b,51]	15%-20% mortality reduction	**INTERVENTION(S):** Mammography screening as indicated in national guidelines, biennially in the US **INITIATION:** From age 50 (as per US guidelines)[52] **DURATION:** Until age 75 (as per US guidelines)[52]; mortality benefit seen after 10 years' screening
Regular Pap smears to screen for cervical cancer reduces mortality among women.[53]	80% mortality reduction	**INTERVENTION(S):** Pap smear at regular intervals as indicated by national guidelines (every 3-5 years, depending on results as per US guidelines) **INITIATION:** Age 21 (US guidelines)[54] **DURATION:** Until age 65 (US guidelines)[54]
IMMUNIZATION		
Routine primary prevention with influenza vaccine results in a mortality benefit for patients more than 65 years of age.[55]	OR 0.69	**INTERVENTION(S):** Seasonal vaccination per national guidelines **INITIATION:** Age 65 onward **DURATION:** Yearly, indefinitely
Regular yearly vaccination shows stronger mortality benefit over first-time vaccination during influenza epidemics.[56]	41% mortality reduction	

[b] At present, screening is recommended in clinical guidelines, though further research is necessary to determine the mortality benefits of mammography. Latest research indicates a positive correlation between screening and breast cancer incidence, but not with breast cancer mortality.[57]

03

Putting the Evidence Together:

Age-Specific Prevention Recommendations for Each Decade After 50

> Dietary patterns that resemble the Mediterranean and DASH diets are among the best for promoting health and reducing NCDs throughout life

To promote both longevity and quality of life, we propose the recommendations outlined on pages 24-25 for disease prevention and healthy aging for individuals as they age.

For the younger age groups, the major benefits of physical activity relate to maintaining a healthy weight, controlling blood pressure and cholesterol, reducing insulin resistance, and preventing NCDs such as obesity, CVD, cancer, and diabetes. The WHO recommends a minimum of 150 minutes of moderate-intensity aerobic physical activity per week.[58]

Dietary patterns that resemble the Mediterranean and DASH diets are among the best for promoting health and reducing NCDs throughout life. The Mediterranean diet emphasizes a high intake of vegetables, fruits, nuts, legumes, whole grains, fish, and monounsaturated fats, with a lower intake of dairy foods, meat, and alcohol. The DASH diet has a similar profile; it promotes fruits and vegetables, moderate intake of dairy products and animal proteins, and higher intake of plant proteins from legumes and nuts. There is a direct dose-response relationship between salt consumption and high blood pressure,[60] necessitating a moderate intake of salt throughout adulthood to mitigate CVD risk.

MODERATE-INTENSITY PHYSICAL ACTIVITY[59] (Approximately 3-6 METs) Requires a moderate amount of effort and noticeably accelerates the heart rate.	VIGOROUS-INTENSITY PHYSICAL ACTIVITY[59] (Approximately >6 METs) Requires a large amount of effort and causes rapid breathing and a substantial increase in heart rate.
EXAMPLES INCLUDE:	
Brisk walking Dancing Gardening Housework or domestic chores Traditional hunting and gathering Active involvement in games and sports with children / walking domestic animals General building tasks (e.g. roofing, thatching, painting) Carrying / moving moderate loads (<20 kg)	Running Walking / climbing briskly up a hill Fast cycling Aerobics Fast swimming Competitive sports and games (e.g. football, volleyball, hockey, basketball) Heavy shoveling or digging ditches Carrying / moving heavy loads (>20 kg)

Mortality is 2 to 3 times higher among smokers than among non-smokers and causes an average loss of 10 years of life.[43] Though smoking cessation should be emphasized at all times throughout the lifespan, to optimize the mortality benefit it should be prioritized for younger people. For those struggling to quit smoking, emphasis should be placed on reducing tobacco use in the interim. Research shows that the risk of heart failure and death for former smokers becomes similar to that for never-smokers after 15 years of

cessation, although this was not observed among heavy smokers (>32-pack-year history), who had a 45% higher risk of heart disease and a 38% higher risk of all-cause mortality than did never-smokers.[61]

Screening has become an invaluable tool for identifying certain cancers at an early stage before malignancies develop and when treatment can be more effective. In the adult population over 50 years old, major cancers for which screenings are recommended are colon, breast, and cervical cancer.

A light to moderate intake of alcohol is associated with a reduced risk of CHD, stroke, and diabetes, whereas greater consumption is associated with increased cardiovascular risks.[62] A moderate intake is considered 1 standard drink per day for women, and 1 to 2 for men (equivalent to 1.75 to 3.5 units of alcohol). Alcohol overuse and abuse are closely linked with liver cirrhosis, ischemic heart disease, stroke, falls, cancers (such as liver, mouth, and esophagus), and cognitive decline. Excess alcohol intake can predispose an individual to malnutrition and certain vitamin deficiencies.[63] In addition, excess alcohol use and mental health conditions are highly comorbid (more than one-third of alcohol abusers also suffer from psychiatric conditions), and alcohol itself has been shown to be a causal factor in depression.[64]

Although lifestyle changes to manage risk factors such as hypertension, high cholesterol, and insulin resistance that underlie NCDs should always be emphasized, a large body of evidence supports the use of medication in managing these conditions.[65-71] Encouraging adherence to prescribed regimens is essential for their effectiveness. In the case of hypertension, only 50% to 70% of patients are adherent to their treatment regimens, and less than two-thirds achieve the blood pressure control needed to prevent complications such as stroke.[72,73] Further evidence suggests that the effects of hypertension most impacting cognitive decline in late life may occur in midlife, between 48 and 67 years of age,[74] strengthening the need for optimal blood pressure control in midlife.

Immunization is important for all ages, for both the primary recipient and those nearby. The effects of certain infectious diseases (such as influenza and pneumococcal disease) can be most devastating to the elderly, but these diseases are also preventable through vaccination.

Regular exercise improves functional status and survival throughout adulthood. This is likely attributable to the increased cardiovascular fitness and aerobic capacity, muscle retention, and reduced systemic inflammation achievable with regular physical activity.[11] For adults of advanced age, the benefits of physical activity extend to preventing musculoskeletal disorders, dementia,[75] and cognitive decline.[76-78] There is general consensus that physical activity is strongly linked to healthy aging and can attenuate cognitive decline among middle-aged and older adults.[79] Physical activity is beneficial for healthy older adults and those with disability or disease, though medical advice should be sought for the latter. Those with existing health problems should be as physically active as their conditions allow.

As medication regimens increase in complexity, adherence rates decrease.[47] For people of advancing age and especially those with multiple NCDs, the emphasis should be on reducing polypharmacy, i.e., reducing the complexity of drug regimens, both in the number of medications and the frequency of dosing. Polypharmacy increases the risk of non-adherence and negative side effects; it is also a recognized contributor to the development of frailty in old age.[80] Reduction of polypharmacy will require the cooperation of the prescribing

physician and can likely be bolstered by engaging caretakers, family members, and pharmacists.

Mental well-being is essential for healthy aging. Research into subjective well-being and health indicates that greater eudemonic well-being, i.e., a sense of purpose and meaning in life, is associated with increased longevity.[81] The causes of depression among the elderly are likely a combination of genetic factors, age-related neurobiological changes, and stressful life events (such as the loss of a spouse).[15] Bereavement triples the risk of developing depression.[82] Financial strain, limitations in daily activities due to functional and cognitive decline, social isolation, and sleep disturbances such as insomnia are other risk factors for depression in the elderly.[15]

> Screening has become an invaluable tool for identifying certain cancers at an early stage before malignancies develop and when treatment can be more effective

Depression in late life is associated with an increased risk of suicide, greater self-neglect, and physical and cognitive decline.[83] Apart from direct suffering, mental health conditions can also increase dependence on tobacco and alcohol, and decrease adherence to medications. In one Finnish study of patients with hypertension, depression led to a 1.52 times higher number of "days not treated."[84] Depression increases mortality among patients with CVD[85] and increases health care spending, symptom burden, and poor self-management among people with type 2 diabetes.[86]

Lifestyle, genetic, and environmental factors across the lifespan influence cognitive aging and risk of dementia.[79] Changes in cognitive function with age can compromise individuals' ability to care for themselves properly, adhere to disease treatment, or carry out activities of daily living, impairing their sense of independence and purpose.[87]

Dementia increasingly is referred to as "type III diabetes," because the risk of developing the disease is strongly associated with modifiable vascular and lifestyle-related factors.[88] Roughly one-third of cases of Alzheimer's disease, the most common cause of dementia, can be attributed to seven modifiable risk factors: low education level, midlife hypertension, midlife obesity, diabetes, physical inactivity, smoking, and depression.[89] Interventions to improve cognitive function with age are likely to have a greater impact when multiple risk factors are addressed, particularly for individuals with existing dementia who are among those with the highest levels of multi-morbidity.[10]

Bilingualism and acquisition of a second language in adulthood have also been associated with improved late-life cognition.[90]

Oxidative stress and vascular impairment play a role in age-related cognitive decline. Antioxidant-rich diets, such as the Mediterranean diet, may therefore confer benefits on cognitive function with age. Improved cognition with age has been demonstrated among men aged 55 to 80 years and women aged 60 to 80 years following a Mediterranean diet with additional supplements of olive oil (1 L/week) or nuts (30 g/day).[91]

The aging process compromises nutritional status. Inherent physiological, social, and economic changes impact nutritional requirements and access to nutritious foods. This increases the risk of inadequate caloric and protein intake, contributing to age-related problems of osteoporosis, weakened

immunity, and sarcopenia – the gradual and progressive loss of muscle mass, strength, and physical endurance.[92,93] Further, impaired absorption of some vitamins and minerals, such as vitamin B12, zinc, and iron, can lead to micronutrient deficiencies.[94] Thus, with advancing age greater focus must be placed on ensuring adequate consumption of protein and micronutrient-dense foods to prevent malnutrition. Adequate protein and calorie consumption, along with exercise, is considered optimal for preserving muscle mass with age.[95]

Frailty is a recognized medical syndrome characterized by "diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death."[80] Interventions to prevent frailty are essential for maintaining mobility and functional status and reducing morbidity as people age.

Positive effects of physical activity, particularly muscle strengthening and balance training, on mobility have been observed even among those already experiencing a decline in functional ability.[22]

Frailty greatly increases the risk of falls and related complications. Ninety-five percent of hip fractures, which often result in long-term functional impairment, nursing home admission, and increased mortality, are caused by falls in people aged 65 and above.[96] Key causes of falls among the elderly include gait problems, muscle weakness, dizziness, medication side effects, confusion, visual impairment, postural hypotension, environmental hazards (such as slippery walkways and poor lighting), ill-fitted clothing and footwear, and inappropriate walking aids.[97,98]

> "Research into subjective well-being and health indicates that greater eudemonic well-being, i.e., a sense of purpose and meaning in life, is associated with increased longevity"

	50 - 60 YEARS	60 - 70 YEARS
 PHYSICAL ACTIVITY	Regular moderate-intensity physical activity (at least 150 minutes per week) Regular vigorous physical activity (at least once per week, ideally for more than 300 minutes per week) For those with health conditions impacting the ability to meet recommendations, as much physical activity as their conditions allow	Regular moderate-intensity physical activity (at least 150 minutes per week) Regular vigorous physical activity (at least once per week, ideally for more than 300 minutes per week) For those with health conditions impacting the ability to meet recommendations, as much physical activity as their conditions allow
 DIET	Adherence to Mediterranean or DASH-type diet Optimal caloric intake for healthy weight Salt intake 3-6 grams/day	Adherence to Mediterranean or DASH-type diet Optimal caloric intake for healthy weight Salt intake 3-6 grams/day Adequate calcium and vit D for bone health Emphasis on protein and micronutrient intake to prevent malnutrition
 TOBACCO	Cease tobacco use by any appropriate means, particularly important for those with CHD	Cease tobacco use by any appropriate means, particularly important for those with CHD
 ALCOHOL	Light to moderate intake (less than 1 standard drink/day for women, 1 to 2 standard drinks for men) or abstain from drinking alcohol	Light to moderate intake (less than 1 standard drink/day for women, 1 to 2 standard drinks for men) or abstain from drinking alcohol
 MEDICATION ADHERENCE	Adhere to NCD medications as prescribed, particularly antihypertensive medication	Adhere to NCD medications as prescribed, particularly antihypertensive medication
 SCREENING	Regular screening for colon, breast, and cervical cancer	Regular screening for colon, breast, and cervical (until age 65) cancer
 VACCINES		Influenza yearly from age 65+ Pneumococcal, chickenpox, and shingles once
 MENTAL AND COGNITIVE HEALTH	Screen for and seek treatment for depression as needed	Screen for and seek treatment for depression as needed. Preventive measures for cognitive decline: following a healthful diet, physical activity that incorporates strength training (1-2 times/week) and aerobic activity (2-5 times/week), brain training exercises, and management of risk factors for CVD

	70 - 80 YEARS	80+ YEARS
 PHYSICAL ACTIVITY	Regular moderate-intensity physical activity (at least 150 minutes per week) Vigorous physical activity at least once per week Multi-component exercises at least 3 times per week for 30-45 minutes per session; includes aerobic activity, strength training (at least 10 minutes daily), and balance and flexibility training (at least 10 minutes daily) For those with health conditions impacting the ability to meet recommendations, as much physical activity as their conditions allow	Regular moderate-intensity physical activity (at least 150 minutes per week) Multi-component exercises at least 3 times per week for 30-45 minutes per session; includes aerobic activity, strength training (at least 10 minutes daily), and balance and flexibility training (at least 10 minutes daily) For those with health conditions impacting the ability to meet recommendations, as much physical activity as their conditions allow
 DIET	Adherence to Mediterranean or DASH-type diet Salt intake 3-6 grams/day Emphasis on calcium and vitamin D intake for bone health Emphasis on protein and micronutrient intake to prevent malnutrition	Adherence to Mediterranean or DASH-type diet Emphasis on calcium and vitamin D intake for bone health Emphasis on protein and micronutrient intake to prevent
 TOBACCO	Cease tobacco use by any appropriate means, particularly important for those with CHD	
 ALCOHOL	Light to moderate intake (less than 1 standard drink/ day for women, 1 to 2 standard drinks for men) or abstain from drinking alcohol	
 MEDICATION ADHERENCE	Adhere to NCD medications as prescribed, particularly antihypertensive medication Reduction in polypharmacy use	Reduction in polypharmacy use
 SCREENING	Regular screening for colon and breast cancer, both until age 75, or as per national guidelines	
 VACCINES	Influenza yearly from age 65+	Influenza yearly from age 65+
 MENTAL AND COGNITIVE HEALTH	Screen for and seek treatment for depression as needed Preventive measures for cognitive decline: following a healthful diet, physical activity that incorporates strength training (1-2 times/week) and aerobic activity (2-5 times/week), brain training exercises, and management of risk factors for CVD	Screen for and seek treatment for depression as needed Preventive measures for cognitive decline: following a healthful diet, physical activity that incorporates strength training (1-2 times/week) and aerobic activity (2-5 times/week), brain training exercises, and management of risk factors for CVD

04

Discussion

> Activities that encourage social connectivity and community engagement (such as group exercise classes), as well as technologies (such as wearable fitness devices and smartphone apps) and insights from behavioral economics can encourage adoption of behaviors that promote longevity

These novel recommendations serve as a starting point for the development of age-specific guidelines to improve health throughout adulthood and into old age. There are substantial gaps in the scientific evidence with respect to effective age-specific interventions from 50 and beyond, limiting the development of such guidelines. To refine the recommendations proposed here, these gaps will need to be filled through further research from well-designed, longitudinal population cohort studies.

Nonetheless, if the preventive measures outlined herein are adopted, there are substantial gains to be had in longevity and quality of life. The earlier they are implemented, the better the long-term outcomes. It should be stressed that these recommendations must be considered in a patient-centric manner, accounting for specific comorbidities and changing functional status as individuals age. Cognitive impairment, frailty, and poor mobility affect health behaviors and an individual's ability to manage conditions.

Readiness for and acceptance of lifestyle changes among older people pose different challenges than among younger people. Older individuals may be less likely to adopt new behaviors because of heavily ingrained habits or lack of motivation to engage in behaviors that take years to show benefits. Those of more advanced age may experience functional or cognitive impairments that make it difficult to change habits. Thus, it is important to consider methods to help the older population adopt change. Activities that encourage social connectivity and community engagement (such as group exercise classes), as well as technologies (such as wearable fitness devices and smartphone apps) and insights from behavioral economics can encourage adoption of behaviors that promote longevity. For example, the HealthyFood program by Vitality, which provides a 25% cash rebate for healthful food purchases, results in improved healthy-purchasing habits.[99] The Experience Corps approach is a novel strategy to drive engagement of the older population.[100] This social model promotes health through an appeal to older adults to participate in national and community services. Older adults volunteer in public schools to boost students' academic performance; at the same time they increase their own physical, cognitive, and social activity. Such interventions have the potential to engage older adults who might not respond to traditional advice on adopting behaviors to improve their health.

Strategies to promote functioning in old age need to be embraced across all sectors of society. Fall-prevention programs, sensors, personal alarms, and other emerging technologies (such as robotic walkers), meal delivery services for those unable to cook, and medication management systems (such as text message reminder systems, smartphone applications, pill packs, and "smart" pill bottles) will

become increasingly important, particularly with the increasing prevalence of dementia.

Currently, more than 35 million people worldwide are living with dementia, and this is expected to nearly double by 2030 and triple by 2050.[101]

Ongoing research into genetic determinants of illness and longevity has the potential to yield individualized recommendations for healthy aging. Promising data from the New England Centenarian Study[102] and the Okinawa Centenarian Study[103] demonstrate a number of genetic modifiers that, combined, can extend survival to more than 100 years of age. Research into the effects of calorie restriction and periods of fasting on longevity among humans is in its infancy. Among animals, calorie restriction can extend life, likely as a result of decreased oxidative stress, reduced metabolic rate, altered nervous system function, and improved insulin sensitivity. Whether this occurs in humans is unknown, and there is a lack of well-designed studies to test this association.[104] Observationally, among adults in Okinawa, Japan, there is an association between reduced energy intake (adults consuming 20% fewer calories than the national average) and reduced mortality from CVD. However, the association is likely genetic, and environmental factors are also at play.[104] The practicality of calorie restriction for longevity while ensuring a nutritionally adequate diet overall is also questionable.

Personalized approaches to health promotion must be complemented with population-wide approaches. At the community level, opportunities for social engagement and lifelong learning can foster a sense of purpose and mental well-being. Changes to the physical environment through urban design focused on healthy aging can aid mobility among older adults, particularly those with a degree of physical or cognitive impairment. Key areas to address include access to transport, outdoor recreation, and safe street design.

Partnerships are needed across public and private sectors to promote NCD prevention and healthy aging. Organizations must work together to address the challenges of an aging population, including how to keep people engaged in the workforce, how to restructure pension systems and retirement plans, and how to ensure financial security with advancing age (particularly for those suffering from cognitive impairment).

Technology and software companies, as well as pharmaceuticals and medical device manufacturers, are uniquely positioned to invest in research to drive healthy aging. Health and life insurers, by promoting health within their insured population, have the mutual benefit of cost-savings for both business and policyholders. In South Africa, Discovery Health Insurance members highly engaged in the Vitality health promotion program have lower health care costs and less frequent hospital admissions than do less-engaged members.[105] Further, the Vitality program is uniquely placed to influence morbidity and mortality of aging members, particularly if recommendations described here are incorporated into the offering and age-specific disease risks are considered in the calculation of 'Vitality Age,' a risk-adjusted age indicating a member's health status.

> Strategies to promote functioning in old age need to be embraced across all sectors of society

Conclusion

The environmental conditions and individual health behaviors that result in NCDs operate throughout a person's lifespan, from gestation through childhood, adolescence, adulthood, and old age. The cumulative effect of healthier choices across the lifespan will therefore improve the quality and length of the aging process. This fact must remain central to the planning and implementation of health policies and interventions.

Though aging is inevitable, the diseases that afflict old age do not need to be. Projections of the future costs of an aging population fail to take into account the impact of disease prevention measures being widely in place. Advances in the science of prevention, personalized health technologies, behavioral economics, and genomic predictions are changing the way we approach disease prevention throughout each decade of adulthood. Building partnerships across sectors to drive these advances and promote longevity can realize the opportunities, rather than the burden, of an aging population.

“The cumulative effect of healthier choices across the lifespan will therefore improve the quality and length of the aging process”

05

Appendix

Methods

Online databases including PubMed, Cochrane, and Google Scholar were searched. Articles relating to NCD risk factors, NCD prevention, and behavioral interventions were collected. Search terms included a combination of <risk factor> and "intervention," "mortality," "reduction," "improvement," "death," and "morbidity."

The search parameters for the literature review were as follows:

- Primary research or meta-analysis
- Adult population (ideally mean age >40 years old)
- Long term (ideally >1 year)
- Prospective
- Intervention based (NOT observational)
- Randomized
- Outcome includes all-cause and/or disease-specific mortality

Explicit outreach to experts in the field was simultaneously undertaken to obtain input on existing age-specific guidelines and unpublished literature. Evidence of intervention effects apparent at age 50 or above and that measured changes in life expectancy or health outcomes over time was sought.

In formulating our recommendations, we prioritized evidence from long-term, prospective, randomized, controlled trials in adult populations over that from observational or associational studies or studies of shorter duration, as per the Centre for Evidence-Based Medicine Level of Evidence framework for therapy, prevention, etiology, or harm (http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/).

> Health and life insurers, by promoting health within their insured population, have the mutual benefit of cost-savings for both business and policyholders

Acknowledgements

We would like to thank the following people who were consulted for their expertise in issues of aging and provided valuable insights throughout the development of this paper:

Jane Barratt (International Federation on Ageing), John Beard (Department of Ageing and Life Course World Health Organization), Arnaud Bernaert (World Economic Forum Global Agenda Council on Ageing), Harry Burns (Center for Health Policy, University of Strathclyde), Linda Fried (Mailman School of Public Health, Columbia University), Ali Hassan (Vitality UK), Vicki Lambert (Department of Human Biology, University of Cape Town), Naomi Levitt (Department of Medicine, University of Cape Town), and Krisela Steyn (Department of Medicine, University of Cape Town).

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