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PRIMARY PREVENTION STRATEGIES IN HEALTHY ADULTS – AN EVIDENCE-BASED RECIPE FOR LONGEVITY

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ABSTRACT

In controlled trials, primary prevention strategies that are often simple and inexpensive have a remarkable power to prevent or delay a large array of diseases. However, a striking discrepancy can be found everywhere between these compelling capacities and the actual performance of physicians in primary care as well as hospital settings. Patient's health behavior is frequently severely flawed and their failure to take advantage of the proven benefits of healthy lifestyles, early diagnosis of risk factors and subclinical disease and preventive interventions, results in premature morbidity and mortality. Changing behavior is notoriously hard, but patient and provider barriers to prevention have been identified, and initial studies indicate potentially effective methods to improve compliance. Starting early is optimal, but a change and adherence at any age significantly improve health outcomes and survival. Evidence-based recommendations regarding healthy lifestyle, lipid-lowering drugs, anti- platelet agents in selected patients, cancer screening, and the problems of screening of other conditions are reviwed, as well as the importance of the provider-patient interface. A much better implementation of existing recommendations is essential and feasible and should be recognized as a major goal by health-policy makers, physicians and patients acting in tandem. This may ensure that many prevalent illnesses are prevented or delayed and that patients may already enjoy improved quality of life and longer and healthier life spans.

KEYWORDS: *Primary prevention; Longevity; Quality of care; Systematic review and meta-analysis.*

INTRODUCTION

"The *quality*, not the quantity, of one's life is what is important," said Martin Luther King Jr. He went on inadvertently to prove his point by remaining a legendary figure, long after he was shot dead in 1968 before reaching the age of forty. Most of us however, would rather enjoy both a long *and* a meaningful life. Fortunately, high-quality evidence on effective health maintenance and the prevention, delay, or early detection of common, life-endangering illnesses is accumulating, and recent insights may make healthy longevity a tangible goal for many in the foreseeable future.

Basically, 2 approaches to increase longevity have long been recognized. The first, so called the "one disorder at a time", is important, but of limited power.[1] The second, undoubtedly the more ambitious of the two, aims to decipher the biological basis of aging.[2,3] and devise genetic-based interventions to extend the human life span. Significant advances achieved by both strategies may already be applied to prevent or delay illness and place longer, healthier life within the realm of possibility.

The potential of prevention

Preventive medicine has had an immense impact on improving public health and increasing life span, but its potential is far from being exploited in full. This deficiency is being documented across *all* major causes of mortality.[4] The remarkable uptake and success of childhood vaccination programs did not repeat itself among the elderly. A very substantial proportion of susceptible patients remain unimmunized against influenza (49.7% ≥19 years) and pneumococcal infections (34% ≥65 years),[5] despite strong evidence of the safety, efficacy and cost-effectiveness of these vaccines, which drastically reduce morbidity and mortality. Cancer screening has the proven potential for early detection and cure of many types of cancer. However, even tumors such as colorectal or cervical cancer that are "accidents waiting to happen" that develop over many years and are very amenable to screening and timely treatment, are still often detected only after the appearance of symptoms, when they are in advanced stages.[6] Chemoprevention – drug or plant products to prevent certain cancers or inhibit atherosclerosis also seems feasible, but remains underused.[7,8] Atherosclerosis starts at an early age,[9]

becomes ubiquitous and progresses relentlessly albeit silently at a variable rate, determined by diverse risk factors (RF). Many are acquired and modifiable, dependent on the patients' own health behavior. However, the burden of obesity, unhealthy diet, sedentary lifestyle, smoking, and alcohol abuse is increasing worldwide, and diabetes and hypertension affect growing portions of the population.[10] The whole spectrum of RF is now much better appreciated and they are additiveand tend to cluster, as in the metabolic syndrome or combined smoking/alcoholism. Most are modifiable.[11] Thus, the harm that they beget is greatly susceptible to primary prevention - timely intervention *before* the appearance of illness, and this was repeatedly demonstrated in many large randomised controlled trials (RCT). We undertook a review of high-quality evidence to underscore the myriad proven benefits of a prevention-driven strategy in myriad aspects of health.

METHODS

A PubMed search of the English literature over the last thirty years on adults (19+ years), focusing on systematic reviews and meta-analysis was done, using keywords primary prevention OR preventive health services AND either Health promotion/health maintenance/healthy lifestyle/health education; Cardiovascular disease; Ischemic stroke; Diabetes type 2; cancer; Screening; infection; Barriers; Interventions; Practice guidelines. In addition, the reference lists of retrieved studies was searched, and relevant studies or guidelines providing evidence of high quality were also included. All risk reduction (RR) or hazard ratio (HR) quoted below have been found to be statistically significant. We have selected interventions and recommendations targeting „healthy" adults, defined as individuals at moderate risk who have not been diagnosed with any specific disease, aiming to prolong disease-free period and overall survival.

I. Lifestyle Recommendations

Lifestyle interventions have many singular advantages: they cost nothing, are utterly safe, and can be started immediately, at any age. They are also immensely effective. This is more evident when considering that smoking, obesity and alcohol abuse are the 3 major causes of premature death in the US. Lifestyle recommendations encompass what we eat and drink, how we sleep, the degree of physical activity, our work-life cycle and family and friends, the avoidance of noxious habits (e.g. smoking, drug addiction, high-risk sexual behavior), and occupational hazards.

All have been extensively studied and research has yielded firm recommendations, as follows. The two best" diets associated with improved cardiovascular and other risks are the Mediterranean diet and the DASH diet, which have quite a few elements in common.

The Dietary Approach to Stop Hypertension (DASH) promotes the consumption of fruits, vegetables, and low-fat dairy products; includes whole grains, poultry, fish, and nuts; and attempts to reduce the intakes of red meat, sweets, sugar-containing beverages, total fat, saturated fat and cholesterol. Salt intake is curtailed to 3-6 gr/day. In 20 articles covering 1917 patients it was found to result in with a significant decreases in systolic and diastolic blood pressure and in total and LDL cholesterol potential reduction of ~13 % in the 10-year Framingham risk score for cardiovascular disease (CVD).[12] best achieved in people at higher risk. However, most studies on DASH were conducted in the US, and none lasted >24 weeks, so that evidence on generalizability and adherence is still incomplete.

Mediterranean-style diet is high in monosaturated fats, based on plant foods – vegetables, fruits, herbs, nuts, beans, and whole grains and cereals, with extra virgin olive oil and low/moderate red wine consumption. In 21 large-scale RCTs of low or moderate quality of evidence, mortality was not significantly affected, but cardiovascular risk factors somewhat improved and strokes were significantly reduced HR 0.6,[13] Other studies also showed a 23% reduced risk of developing diabetes mellitus (HR 0.77).[14]

Higher intake of marine polyunsaturated omega-3 fatty acids (PUFA) or plant omega-6 fats led to uncertain conclusions, except for a likely reduced risk of myocardial infarction with 1 g/day marine fatty acids (HR 0.72).[15] Additional notable benefits demonstrated for high" consumers of n-3 PUFA or fish (~250 gr/wk) include a significant decrease in incident chronic kidney disease,[16] lower risk of type 2 diabetes,[17] and even a 30% reduction in the risk of cognitive decline and in particular Alzheimer"s disease.[18,19] A somewhat similar approach, reducing dietary saturated fat also reduced the risk of combined cardiovascular events by 17%, RR 0.83.[20] Caloric restriction is associated with protection against oxidative stress and metabolic disease, and with impressively increased life span in laboratory animals of different species.[21] In humans however, caloric restriction of 10% or more over several months, was studied in relatively few people (334 vs. controls), too few for firm conclusions, and likely hard to adhere to.[22] Supplements such as calcium, vitamin D, or both did not result in lower incidence of cancer or cardiovascular disease and even fragility fractures were not convincingly prevented.[23,24] Moreover, the U.S. Preventive Services Task Force (USPSTF) recently concluded that the evidence is insufficient to recommend for or against the routine use of supplements of vitamins A, C, or E; multivitamins with folic acid; or antioxidant combinations for the prevention of cancer or cardiovascular disease.[25] Beta carotene or vitamin E supplements have even been associated with worse health outcomes.[26,27]

Other modifiable dietary habits of note are water drinking which is often (and not limited to the lderly) below the recommended 15.5 or 11.5 cups/day for men

and women, respectively. Since ~20% of daily fluid intake comes from food and more from other beverages, about 6±2 cups of water are needed in a day, depending on the climate and level of activity.[28] In addition, coffee consumption appears beneficial for reducing the risk of ischemic stroke (HR 0.83, P<0.001)[29] and cardiovascular risk (RR 0.85 for median 3.5 cups/day)[30] Interestingly, chocolate (2 servings of 30 g/week) was also identified as significantly protective in 14 prospective studies (n=508,705) comparing highest to lowest chocolate consumption (RR 0.9 for heart disease, 0.84 for stroke, 0.82 for diabetes).[31]

In the UK, 10-20% of adults ≥55 years drink alcohol at levels that are harmful to their health and the same problem at different levels is prevalent worldwide. Multi-pronged interventions are likely effective for many.[32] Reducing excessive alcohol consumption or abstaining vs. continued heavy drinking lowers the odds of death by an impressive OR of 0.61 or 0.35, respectively.[33] In contrast, habitual light or moderate alcohol consumption (≤1 drink/day for women and 1-2 for men) is associated with a lower risk for all-cause mortality, coronary artery disease, diabetes, heart failure, and stroke.[34] creating a J-curve. Although based mostly on observational studies, the data seem quite robust, as long as it does not lead to alcohol abuse.

Tobacco use is another prevalent but highly deleterious habit. Quitting smoking before age 50 may eliminate excess associated mortality risk, while later cessation of smoking was found to yield a significantly reduced (HR 0.54) mortality risk.[35]

Finally, physical activity promotes health and longevity. Multiple studies have linked both physical inactivity and excess adiposity to the risk of premature mortality.[36] In contrast, physically active individuals have a lower risk of mortality vs. their physically inactive peers, independent of level of adiposity. These risk factors are closely linked as the risk of being sedentary is higher in obese people, and vice versa. People who are insufficiently physically active have a 20% to 30% increased risk of all- cause mortality compared to those who engage in at least 30 minutes of moderate-intensity physical activity most days of the week (≥150 minutes/week have a well-established protective effect).[37] However, a third of adults were estimated to be insufficiently active and sedentary time was found in prospective studies to associated with all-cause mortality (HR 1.22), cardiovascular disease mortality and incidence (HR 1.15 for each), cancer mortality and incidence (HR 1.13 for each), and type 2 diabetes incidence (HR 1.91)[38] To these substantial benefits must be added the many other positive effects of physical activity on weight; on falls, osteoporosis, and fragility fractures[39] and on anxiety, depression and even cognitive decline and Alzheimer‟s disease in older adults (RR 0.61)[40] Other „Lifestyle‟ routines have also been associated with improved survival and healthy longevity. They include adequate sleep which is neither too short nor too long (7 hrs seems optimal)[41] fulfilling family and friends relationship (as opposed to loneliness and social isolation which increase all-cause mortality)[42] and providing enough leisure time from work. A 10-year follow-up European study of 2339 'healthy' elderly persons dramatically illustrates the impact of „lifestyle‟. Adhering to a Mediterranean diet (HR 0.77), moderate alcohol use (HR 0.78), physical activity (HR 0.63), and non- smoking (HR 0.65) were each associated with a lower all-cause mortality. Similar results were observed for mortality from vascular diseases and cancer. Remarkably, combining all 4 healthy behaviours lowered all-cause mortality to 0.35, whereas lack of adherence was associated with 60% of all deaths in this population.[43]

Pharmacological Lipid-Lowering

Treatment with statins is currently the most effective pharmacologic primary prevention measure available. By inhibiting a key enzyme in the cholesterol biosynthesis pathway, statins lower cholesterol and LDL levels to a high extent, but also stabilize atherosclerotic plaques, independently of their hypolipidemic actions.[44] The latter effect may be important in the protective effects of statins in older people without CVD disease (≥65 and even ≥75 years). Statin therapy in these patients was associated with significantly lower risk of all-cause mortality (HR 0.86), CVD mortality (HR 0.80), myocardial infarction (HR 0.75), and stroke (HR 0.85), based on a recent systematic review and meta- analysis.[45] Similar, even better results have been demonstrated for wider adult populations including myocardial infarction HR 0.62-0.67, stroke HR 0.78-0.83, and composite cardiovascular outcomes HR0.72-0.74, all clearly significant.[46,47] Thus, lipid-lowering therapy in primary prevention was mbraced by both American and European guidelines, and applies to a very high percentage of both men and women.[48] Treatment intensity and targets need to be directly related to the patients‟ risk. Other agents, such as ezetimibe (in combination with statins) or fibrates (alone) are also beneficial in primary prevention.[49,50] However, previous studies have shown that uptake and persistence with statin treatment is rather poor and underuse is very prevalent, poartly because of concerns about side effects, causing millions of eligible people to miss out on life-saving treatment.[51]

II. Anti-platelet Agents

In patients with acute or previous vascular events, 75-150 mg aspirin daily (or clopidogrel) reduces non-fatal myocardial infarction by 33% and ischemic stroke by 25%. Thus, aspirin is definitely indicated for secondary prevention in all subgoups without contraindications.[52] However, primary prevention RCTs (e.g. in healthy older adults, patients with diabetes, or chronic kidney disease) reveala significant increase vs. placebo of major hemorrhage (4%), or gastrointestinal bleeding (2%),

though intracerebral hemorrhage was not increased.[53,55] This significant iatrogenic harm vs. some (HR 0.88) or no benefit in the prevention of major adverse cardiovascular events (MACE).[55,56] led to heightened caution in the use of aspirin for primary cardiovascular prevention. Current guidelines, based on evidence from 13 controlled trials, support its use in some selected cases, *provided* the patient‟s age is 40-59 years *and* the calculated individual risk for 10-year cardiovascular events is ≥10%.[57,58] The guidelines acknowledge the modest beneficial effect of aspirin, the relatively high number-needed-to-treat (NNT) (n=265), and the risk associated with major bleeding which becomes significantly higher in patients aged 60 years and older.[58,59] All aspirin doses are effective, but lower doses appear safer.[60]

III. Cancer Screening

In a remarkable study of 7 million deaths from cancer worldwide, smoking and alcohol use, and low fruit/vegetable intake were identified as the leading risk factors for death from cancer worldwide. In high-income countries, overweight/obesity are additional crucial factors.[61] Thus, recommended Lifestyle‟ measures discussed above (e.g. physical activity, healthy diet, achieving BMI≤25, smoking cessation, reduced alcohol intake) are also effective in reducing cancer incidence.[62] Nevertheless, specific, evidence-based recommendations for cancer screening in people at moderate („average‟) risk (i.e. no predisposing family history or habits or underlying diseases) have been published and will be briefly reviewed. Recommendations are different and more stringent for patients at higher risk (such as patients diagnosed with inflammatory bowel disease, Hashimoto‟s thyroiditis, or liver cirrhosis; those under immunosuppressive medications, etc.) which will not be discussed here. Several of the more revalent cancers are amenable to screening and early detection, as follows:

Men and women

Colonoscopy (currently started at 45 years and repeated every 10 years if normal, up to 75) identifies and treats polyps and early neoplastic lesions and greatly decreases colorectal cancer mortality (HR 0.33).[63] better than other methods that show lesser efficacy (flexible sigmoidoscopy, fecal occult blood tests).[64]

Smokers ≥20 pack/years over the age of 40 who are followed by low-radiation chest CT survive longer vs. no imaging, due to earlier detection and treatment of occult lung cancer.[65]

Skin cancer visual screening by clinician cannot be recommended at present due to insufficient evidence.[66]

Women# Mammography (from age 40 to 75, biennially) significantly decreases mortality from breast cancer, especially when combined with breast ultrasound.[67,68] The risk reduction is age-dependent: RR 0.98 for women aged 39-49; 0.86 for ages 50-59; and 0.67 for those aged 60-69.[69] # Papanicolaou (Pap) smear (from age 21 to 65, every 3-5 years) decreases mortality from cervical cancer by up to 80%,[71] though a negative human papillomavirus (HPV) test is more reassuring than a negative cytological test.[71] # In the Ashkenazi Jewish population, BRCA testing is both effective and cost-effective in the prevention of breast and ovarian cancer.

Men

Prostate cancer screening with repeated prostate-specific antigen (PSA) testing alone may have a small benefit in decreasing prostate cancer mortality.[72] Despite the grade D recommendation against it by the USPSTF, Its adoption remains to be decided by shared decision-making, best done at the age of 50 years and on, and coupled with MRI imaging in equivocal cases.[73]

However, to be viable, screening must conform to several principles set by the WHO.[74] And screening of asymptomatic populations harbors a potential of harm. A considerable risk of false- positive results exists, estimated at 5% per mammography or Pap smear, 10% per PSA test, and ~20% for low-dose lung CT scan advocated annually for adults 50-80 years old who are at risk of lung cancer due to smoking ≥20 pack-year. With the combined, multiple screening policy advised, this risk accrues and often begets further testing (some of it invasive), cost, and much anxiety.[74] Moreover, patients‟ adherence to ongoing screening over years may be far lower in real life than that reported in RCTs.[76] Thus, adoption of screening recommendations is a complex result, affected by multiple patient, provider, and system-related barriers.[77] Nevertheless, interventions to increase uptake of evidence- based screening procedures seem to be effective and likely cost effective too.[78]

IV. Screening for Other Conditions

Certain diseases and risk factors are so prevalent, impactful, treatable, and cost-effective to diagnose that they satisfy the strict WHO criteria,[74] and warrant a preemptive approach. Heading the list is screening for modifiable cardiovascular risk factors that can be undertaken in each encounter with providers (physicians and nurses) in primary care settings, and combined with advice and intervention.[79] Varied interventions were shown to increase the uptake of screening for cardiovascular disease risk factors.[80] and although studies of systematic vs. opportunistic screening failed to demonstrate statistically significant effects of systematic risk assessment on clinical end points,[81] there is no doubt that lifestyle issues (such as overweight, unhealthy diet, excessive alcohol consumption, smoking cessation, sedentary behavior) should be clarified, discussed, and modified if possible. This is essential since cardiovascular risk is inversely proportional to the number of healthy lifestyle factors.[82] and heart disease, stroke, and diabetes are prominent among the ten most

frequent causes of death in the US today.[4] By the same token, office blood pressure should be monitored in all adults (Grade A recommendation)[83] since asymptomatic hypertension is almost ubiquitous with advancing age (especially isolated systolic hypertension) yet an estimated ~third of the cases remain undiagnosed and adolescence, needs to be another ~third undertreated.[84] Lipid profile, ideally first obtained once in monitored starting age 35 for men and 45 for women. Simple to perform, accurate, cost-effective, and successfully modifiable, predominantly by statin treatment, this is a grade A USPSTF recommendation.[85] Screening for diabetes and prediabetes (fasting plasma glucose 100-125 mg/dL) needs to start at the age of 45 for all people (35 years when obese or overweight) and continued at 3-year intervals, although mortality benefit could not be demonstrated.[86] Progression of prediabetes to diabetes is common, occurring in 74% over 10-15 years, but can be prevented. Treatment with metformin showed a RR of 0.50, whereas high-intensity lifestyle intervention was more effective.[87,88] Their combined use seems optimal.[89] and adding semaglutide in overweight/obese patients improves results.[90] Patients with obesity or metabolic syndrome are at increased risk of nonalcoholic fatty liver disease (NAFLD) which may progress to steatohepatitis, advanced fibrosis, cirrhosis, and liver cancer. Some guidelines support screening such patients with liver enzymes and/or ultrasound, but others recommend against screening.[91] Unfortunately, a recent study of over 6,000 non-pregnant eligible US adults without diagnosed diabetes revealed that ~25% did not have a glucose test in the past 3 years.[92] Moreover, >20% of Americans with diabetes do not know they have it, and >80% of Americans with prediabetes are not aware of their risk for type 2 diabetes. This gap in awareness needs to be addressed by health care providers, since the earlier the intervention – the better the health outcomes and the fewer the complications.

Nevertheless, population-based screening of established but unrecognized cardiovascular disease (e.g coronary artery disease, peripheral artery disease, etc.) is not currently recommended. However, early, pre-symptomatic recognition alters treatment and treatment-intensity and likely to prevent many future adverse events,[79] Recent data may support this strategy: a scrutiny of such a trial in a large population of elderly men (n=46,611), many with prior diseases, reveals that the grossly „negative" conclusion can be interpreted differently. When looking at subgroups, particularly those younger than 70 years and those who have no known disease, cardiovascular screening significantly reduced death from any cause (RR 0.85 to 0.90) when started early enough.[93]

Paroxysmal atrial fibrillation (PAF) is often asymptomatic, but accounts for up to a third of ischemic (cardioembolic) strokes, and severe stroke can well be its presenting manifestation. Evidence is lacking to support large scale screening.[94] However, repeated opportunistic evaluation (palpation of pulse, auscultation, ECG) of people at risk (e.g. old age, hypertension, diabetes, obesity, reduced ejection fraction, mitral valve disease) is very desirable since documentation of PAF and starting anticoagulant treatment will greatly improve health outcomes. CT-derived coronary calcium score (CACS) may reclassify some low-risk patients to higher-risk categories, but the vast majority of reclassified patients do not experience an adverse cardiovascular event over 5-10 years.[95] and thus, this incremental important cardiovascular risk factors are non-modifiable, information remains of limited value. Other yet they should be ascertained and included in the estimation of cardiovascular risk and in treatment decisions. They include age (the higher, the greater the risk); gender (men have a higher prevalence of cardiovascular disease than women); ethnicity (black persons have the highest prevalence of cardiovascular disease); and family history (in particular, a first-degree male relative with coronary disease <55 years).

Screening for many other conditions such as chronic obstructive pulmonary disease (COPD) – a leading cause of morbidity and mortality,[96] thyroid dysfunction in asymptomatic persons.[97] impaired visual acuity and glaucoma; age-related hearing loss; oral health (especially periodontal disease which is a cardiovascular risk factor by ongoing inflammatory activity,[98] are all important components of health maintenance, but there is insufficient evidence at present to support their endorsement in screening of asymptomatic adults (e.g. Grade D for COPD). Obstructive sleep apnea (OSA) is one good example of the complexity of the problems associated with screening. On one hand, OSA constitutes a major health burden with an estimated one billion people affected worldwide, a rising prevalence with the ongoing obesity epidemic, and myriad associated adverse outcomes. On the other hand however, Potential harms of routine screening include overdiagnosis and overtreatment and costs vs. insufficient current evidence of benefits.[99]

In contrast, all adults need to be screened once by serology for chronic hepatitis B and hepatitis C infection.[100,101] Other fields of consensus are the benefits of screening of post-menopausal women over 65for osteoporosis, started earlier when they have certain risk factors.[102] Osteoporosis is common, clinically silent until a fracture occurs, and treatable, for example, bisphosphonates which can stop and possibly reverse decreased bone mineral density (BMD)[103] However, hormone replacement therapy (HRT) with combined estrogen and progestin has no proven value in prevention[104] Emotions arehighly important in peoples" quality of life, productivity, and „hard" outcomes. In one primaryprevention study an appalling 24.5% of the population evaluated were found to be depressed[105] often with a marked effects. Thus, USPSTF grade B recommendation supports screening for depression of all adults[106] many of whom suffer from unrecognized

depression and are untreated. The role of screening for anxiety is somewhat less clear[107] however, primary care physicians need to remain vigilant about their patients‟ emotional status in encounters of all sorts[108] This is essential since emotional factors have a substantial impact not only the quality of patients‟ lives and their daily functioning but on cardiovascular morbidity and mortality as well[109] Screening instruments for both conditions have acceptable accuracy, and once identified, effective treatment exists, that can transform peoples‟ lives.

V. Vaccinations

According to the Advisory Committee on Immunization Practices (ACIP)/ Centers for Disease Control and Prevention (CDC), immunizations recommendations are updated yearly, apply worldwide, and all immunocompetent adults need to be vaccinated.[110] Patient who are immunocompromized by disease, treatment, or both are even more needy, but special considerations apply. Immunizations are a safe procedure with only minor local side effects for the vast majority of people.[111,112] and their impact on the substantial morbidity and mortality caused by the more prevalent infectious diseases is enormous, both in personal and public health terms.

Inactivated parenteral influenza vaccines vs. no vaccine in healthy adults not only reduce influenza (RR 0.41) and influenza-like illness (RR 0.84),[113] but significantly decrease the risk of vascular events, in particular acute myocardial infarction which is markedly increased in the first week of influenza (RR 4.52-5.79),[114] These effects are more pronounced in elderly patients whose a-priori risk of influenza-associated morbidity and mortality is significantly higher, with as many as 90% of influenza-related deaths occurring among senior citizens.[115,116] Covid-19 infections were the third most frequent cause of death in the US in 2020,[4] and now that effective vaccines/boosters are available,[117] people should be regularly immunized.

Community-acquired pneumonia (CAP) continues to be associated with a significant risk of mortality. The burden of pneumococcal pneumonia alone, the major cause of CAP and pneumonia mortality, causes approximately 150,000 hospitalizations in the US each year, killing about 5-7%. The death rate is much higher among adults aged ≥65 years and people with comorbidities, going up to ~20% of hospitalized patients.[118] In addition, pneumonia is an independent risk factor for acute myocardial infarction and stroke: a three-fourfold increased risk had been reported in several studies.[119] Available vaccines for the two most common organisms causing CAP (pneumococci and haemophilus influenza) effectively decrease all these risks and are to be given universally with special attention to persons ≥65 years.[110] More recently, respiratory syncytial virus (RSV) vaccines have been recommended by the CDC to protect adults over 60 from severe RSV infection (also to be given from week 32-36 of pregnancy).

Other important preventive recommendations include vaccinations against hepatitis A virus (HAV), hepatitis B virus (HBV), meningococcus, human papilloma virus (HPV) in sexually-active younger women, and against herpes zoster (VZV) in older adults.[110]

The major problem involved is not vaccine efficacy or safety, but rather their very partial rates of uptake in populations at risk.[120] Common misbeliefs about vaccines abound – including the belief that the disease is inconsequential; that vaccines are unsafe; and that they are ineffective. Awareness and affordability are additional problems, causing unfortunate disparities in health care delivery. All result in compromised uptake of many vaccines (different for different populations), and hence, personal and public health adverse outcomes thatcan be prevented and remain a major challenge.

VI. Patient-physician Interface

While routine „health checks‟ lack evidence of efficacy.[121] a good, preferably continuous, patient-physician relationship has many advantages including improved hard‟ health outcomes.[122,123] Each encounter constitutes an opportunity, not only to address the patient‟s acute problem (“chief complaint”), but also to reflexively briefly screen lifestyle risk factors and provide counseling, enhance the patient‟s health literacy, and encourage self-efficacy. All these strategies have important long-standing benefits, not least, strengthening the physician-patient relationship and bonding, which was demonstrated to be associated with patient trust, and significantly improved adherence.[124-126] Since optimal guideline-based screening and vaccination status are important for the patient‟s healthy survival, the patient-provider encounter should be used as a window of opportunity to check and complete patient-tailored recommendations.[108] This applies primarily to primary care, but hospital admissions could also be used to survey primary prevention status and intervene as needed. Time constraints are a notorious barrier in all settings.[127] but it takes mostly attention and very little time to review a patient‟s status. Providing an attentive timely simple advice on prevention can substantially prolong the patient‟s healthy lifespan.

Barriers and Directions

Despite distinct improvement, many opportunities for prevention are still being missed, and this applies to hospital settings as well as to primary care. Physicians very often omit to suggest preventive measures to their patients. Even when they do, they frequently fail to recommend essential behavior- changing strategies. Older patients or women may get even less counseling than others, and evidence- based risk-factor screening, cancer screening, and vaccinations are often not discussed. Just recently, about a third of all deaths in the US were attributed to smoking and obesity. According to CDC data, in 2021 the estimated prevalence of smoking

in the US was still 11.5% (though much better than the 2000‟ figure of 21%) and that of obesity 42.4%, approximately quadruple the figure for 1991. More than 30% of US adults are now overweight and >75% do not meet recommendations for physical activity or diet.[7,128,131]

Lack of focus on prevention during training, time constraints and absence of reimbursement are major physicians‟ barriers to prevention.[132,133] Medical schools‟ curriculum and continuing medical education (CME) activities need to highlight the high impact of preventive measures on patients‟ healthy lifespan, their cost-effectiveness, and prevalent underuse common to all settings. This is a crucial step in the achievement of prevention-oriented practice. However, physicians‟ practice habits are not easily changed.[134] Adopting a value-based care model that prioritizes and reimburses positive health outcomes may increase physicians‟ awareness and motivation to provide preventive care.[135] The recently defined cardiovascular-kidney-metabolic syndrome construct (CKM) will also likely lead to increased intensity of preventive interventions by primary care providers.[136] Changing patients‟ behavior is an even harder undertaking. Health education beginning in elementary school and continued through graduation is needed, together with broader outreach programs by HMOs and as a national effort. As the escalating prevalence of unhealthy eating and lifestyle reveal, this is an urgent undertaking.[137,138] However, this major public health undertaking must be approached individually as well. Patients‟ barriers are even more challenging as the obesity/sedentary epidemic demonstrates. Concerns of the time required, cost, skepticism about the possibility of changing ingrained habits, the effort of giving up things they like and are accustomed to do, and real difficulties in starting and persevering are identified patients‟ barriers to the adoption of a healthy lifestyle. Here, explaining the 5A‟s model, actively encouraging and supporting patients‟ health literacy and enablement, and shared decision-making are time-tested methods.[139] Behavioral interventions can improve patients‟ compliance with healthier lifestyle habits.[140] Nevertheless, it is notoriously hard to persuade younger, well persons to undertake tests, use medications or change their common disregard for high- risk health behavior. A single intervention is less likely to succeed.[80] but together with multipronged actions, changes in health policy and funding, and targeted public campaigns are imperative.[141]

Unfortunately, most health care expenditures in the US go to the treatment of advanced diseases and a meager 3% are devoted to prevention.

CONCLUSIONS

The time is ripe for society, healthcare policy makers, medical schools, physicians and patients to take advantage of the impressive body of evidence accumulated, and preach and practise evidence-proven and effective prevention measures earlier and to a much greater extent than done today.

Prevention is a 'neutral' word, and we advocate substituting Longevity for prevention to make "Longevity counseling" more catchy and alluring to the patients. With our current level of knowledge, steadily enriched by research, patients can be confident that their chances of a healthy and active longevity will be very considerable and it is never too late to start.

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