American Journal of Preventive Cardiology 6 (2021) 100181

Contents lists available at ScienceDirect

American Journal of Preventive Cardiology

journal homepage: www.journals.elsevier.com/the-american-journal-of-preventive-cardiology

State-of-the-Art Review

The Johns Hopkins Ciccarone Center's expanded 'ABC's approach to highlight 2020 updates in cardiovascular disease prevention

David I. Feldman[a,*], Katherine C. Wu[a], Allison G. Hays[a], Francoise A. Marvel[a], Seth S. Martin[a], Roger S. Blumenthal[a], Garima Sharma[a]

[a] The Ciccarone Center for the Prevention of Cardiovascular Disease, The Johns Hopkins University School of Medicine, Baltimore, MD, United States

ARTICLE INFO

Keywords:
Cardiovascular prevention
ASCVD
Risk assessment
Cardiovascular disease risk factors

ABSTRACT

In recent years, improvement in outcomes related to cardiovascular disease is in part due to the prioritization and progress of primary and secondary prevention efforts. The Johns Hopkins Ciccarone Center for the Prevention of Cardiovascular Disease expanded 'ABC's approach is used to highlight key findings in Preventive Cardiology from 2020 and further emphasize the importance of cardiovascular prevention. This simplified approach helps clinicians focus on the most relevant and up to date recommendations for optimizing cardiovascular disease risk through accurate risk assessment and appropriate implementation of lifestyle, behavioral and pharmacologic interventions. While 2020 not only provided practice changing updates by way of clinical guidelines and randomized controlled trials on topics related to antithrombotic and lipid lowering therapy, diabetes management and risk assessment, it also provided promising data on how to improve dietary and exercise adherence and manage genetic risk. By providing clinicians with a systematic approach to cardiovascular prevention and key highlights from the prior year, the goal of significantly reducing the burden of cardiovascular disease worldwide can be achieved.

1. Introduction

The growing prioritization of preventive efforts has been instrumental in helping clinicians confront the challenges of cardiovascular disease (CVD) worldwide. Following an extraordinary 2019 in CVD prevention initiatives [1,2], 2020 built upon the prior year's success with additional progress in managing CVD risk and slowing atherosclerosis development [3]. To further illustrate concepts highlighted by the European Society of Cardiology's (ESC) synopsis of Preventive Cardiology advances from 2020 [3], the Johns Hopkins Ciccarone Center's expanded 'ABC's approach will be used to summarize many of the key findings (Fig. 1).

1.1. Assessment of ASCVD risk

In primary prevention, the American College of Cardiology (ACC)/American Heart Association (AHA) Pooled Cohort Equations risk estimator is used to estimate an individual's 10-year risk for an atherosclerotic cardiovascular disease (ASCVD) event (Class of Recommendation (COR) I, Level of Evidence (LOE) B-NR). In addition to risk enhancing factors, which can be used when treatment decisions are uncertain, the 2018 AHA/ACC Multisociety Guideline recommends a coronary artery calcium (CAC) test to help further stratify risk and determine appropriateness for preventive therapies (COR IIA, LOE B-NR).

In 2020, the National Lipid Association released a scientific statement on CAC scoring to guide preventive strategies for ASCVD risk reduction [4]. It concluded that CAC testing was optimally used in the primary prevention setting among those with a 10-year ASCVD risk <20%, diabetes mellitus (DM) or the metabolic syndrome, and/or severe hypercholesterolemia. In addition, it recommended intervals for repeat CAC testing in adults with CAC=0, which ranged from 5 to 7 years in low-risk adults (<5% 10-year risk) to as frequently as 3 years in high-risk adults (>20% 10-year risk or presence of DM) [5]. Lastly, a CAC scan can still be used for risk prediction in patients on statin therapy and is useful for guiding the allocation of nonstatin therapy, aspirin, as well as antihypertensive therapy [6].

1.2. Antiplatelet/Anticoagulation

The role of aspirin therapy in primary prevention witnessed a complete paradigm shift over the last few years, culminating in the 2019 ACC/AHA CVD Prevention Guideline recommending consideration of its use among only very high-risk individuals (COR IIb, LOE A) [7]. In

* Corresponding author at: The Ciccarone Center for the Prevention of Cardiovascular Disease, 600N. Wolfe Street, Halsted 560, Baltimore, MD 21287, United States.

E-mail addresses: dfeldm11@jhmi.edu (D.I. Feldman), kwu@jhmi.edu (K.C. Wu), ahays2@jhmi.edu (A.G. Hays), fmarvel1@jhmi.edu (F.A. Marvel), smart100@jhmi.edu (S.S. Martin), rblument@jhmi.edu (R.S. Blumenthal), gsharma8@jhmi.edu (G. Sharma).

https://doi.org/10.1016/j.ajpc.2021.100181
Received 8 February 2021; Received in revised form 23 March 2021; Accepted 27 March 2021

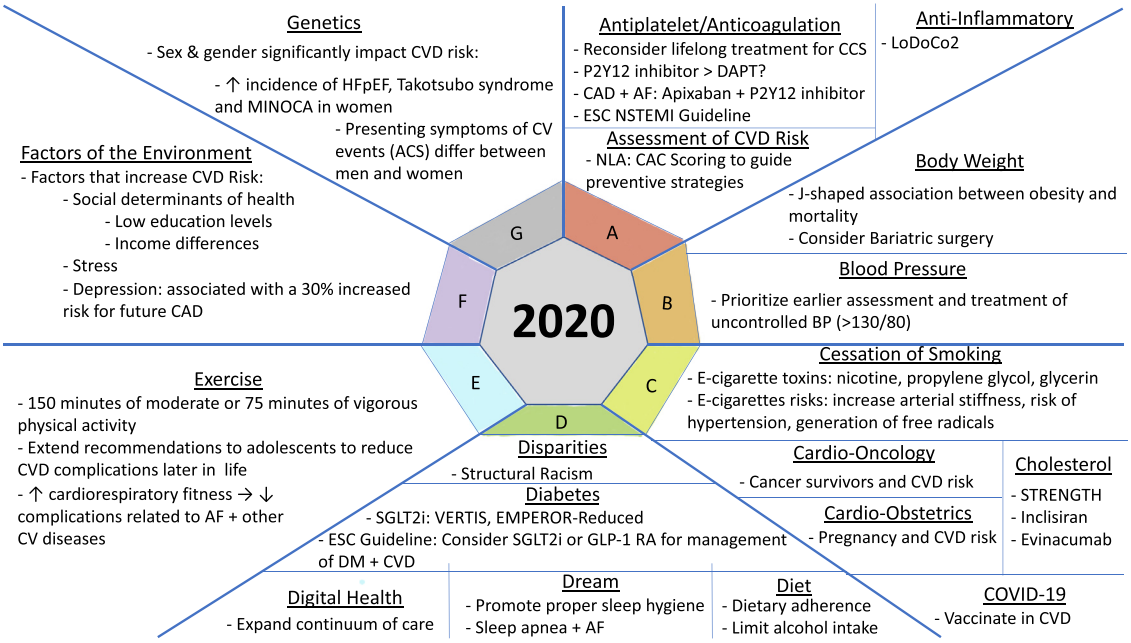

Fig. 1. Central illustration.

2020, the role of long-term aspirin in secondary prevention of ASCVD was also called into question despite a COR I, LOE A recommendation for its use in all patients with coronary artery disease unless contraindicated [8,9].

In certain situations, including immediately following an acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI), the use of aspirin remains incontrovertible. However, despite a current recommendation from the European Guideline for the secondary prevention of chronic coronary syndrome, its lifelong use in all of these patients may not be necessary [10]. This is particularly relevant to those individuals who are concomitantly taking a P2Y12 inhibitor or anticoagulation therapy.

Recent trials of early aspirin discontinuation following PCI or among secondary prevention patients on oral anticoagulation for indications such as atrial fibrillation (AF) provides no evidence for increased ischemic risk as long as a single antiplatelet agent is prescribed. In a secondary analysis from the AUGUSTUS trial, among patients with AF and recent ACS or PCI, the benefit from aspirin as part of dual antiplatelet therapy was lost after 30 days due to increased bleeding without reduction of ischemic events [11].

In a 2020 systematic review and meta-analysis, which sought to determine the safety and efficacy of discontinuing aspirin on a background of another antiplatelet agent following PCI, stopping aspirin 1 to 3 months post-PCI and continuing a P2Y12 inhibitor reduced the risk of bleeding without an increased risk of major adverse cardiovascular events (MACE) [12]. With regards to specific anticoagulation regimens, apixaban was associated with fewer ischemic and bleeding events compared to warfarin, for up to 6 months after ACS or PCI.

In the 2020 ESC guideline for the management of patients with ACS, specifically non-ST elevation myocardial infarction (MI), post-treatment antiplatelet therapy and triple antithrombotic therapy were addressed [13]. Recommendations included dual antiplatelet therapy in most cases for up to 12 months following PCI, with special considerations required for individuals based on ischemic and bleeding risk, the occurrence of adverse events, comorbidities, comedications and availability of medications.

For those individuals who require anticoagulation following PCI, triple antithrombotic therapy is recommended for up to 1 week (1 month when ischemic risk outweighs the bleeding risk) followed by a transition to a novel oral anticoagulant plus a single antiplatelet therapy, preferably clopidogrel. While future trials will help answer specifically which secondary prevention patients on optimal preventive treatments can forego long-term aspirin therapy, consideration should be given now to those individuals who are at greater risk for harm from concomitant aspirin therapy.

1.3. Anti-Inflammatory

Following the COLCOT trial, which demonstrated reduction of ischemic cardiovascular events with colchicine in patients following an acute MI, the Low Dose Colchicine 2 (LoDoCo2) trial evaluated the impact of colchicine in patients with stable coronary heart disease (CHD) [14]. The study randomized 5522 patients with chronic CHD to daily colchicine (0.5 mg/day) or placebo. Following a median of 29 months, rates of the primary composite endpoint (cardiovascular death, spontaneous, nonprocedural MI, ischemic stroke, or ischemia-driven coronary revascularization) were significantly lower among those receiving colchicine vs. placebo (6.8% vs. 9.6%, hazard ratios (HR) 0.69, $p<0.001$). Furthermore, the benefits of colchicine occurred early and continued to increase with up to five years of treatment.

However, in LoDoCo2, colchicine therapy was also associated with an increased risk of non-cardiovascular death and higher rates of side effects, including myalgias and gastrointestinal intolerance, leading to medication discontinuation in 15% during the run-in phase. In addition, it is unclear if colchicine had a greater effect in patients with higher levels of systemic inflammation, as inflammatory markers were not reported. Future investigation will need to determine which individuals will receive a net clinical benefit from anti-inflammatory therapy, such as colchicine, for primary and secondary CVD prevention.

1.4. Body weight

With rates of overweight and obesity exceeding two-thirds of the adult population nationwide, strategies to achieve a healthy body weight are imperative (COR I, LOE B-R). Cardiovascular disease accounts for the majority of morbidity and mortality among the obese, with over two-thirds of deaths attributable to high body mass index (BMI) coming mainly from coronary artery disease (CAD). While there is

a clear J-shaped association between obesity and all-cause and CVD mortality, higher BMI is also associated with increased risk of aortic valve stenosis, AF, ischemic stroke and abdominal aortic aneurysms [15,16].

Despite significant efforts to adhere to a heart healthy diet and achieve daily recommendations for physical activity, many obese individuals are unable to significantly lower their risk for CVD morbidity and mortality. Among adults with a BMI ≥40 with obesity-related comorbid conditions refractory to pharmacotherapy and behavioral treatments bariatric surgery can be considered [17]. Based on long-term data from a UK nationwide nested cohort study, obese individuals who underwent bariatric surgery experienced a ~60% reduction in MACE (mainly MI) and new heart failure diagnosis compared to a matched control group [18].

1.5. Blood pressure

Optimal cardiovascular health, which is determined by control of multiple CVD health behaviors and factors, such as diet, BMI, smoking, physical activity, blood pressure, cholesterol, and glucose, is associated with a lower risk of incident hypertension [19]. However, in the United States, many of these factors are poorly or sub-optimally controlled from an early age; this has prompted recommendations to shift and prioritize earlier risk assessment. In adults 40–75 years of age with an estimated 10-year ASCVD Risk <10% and ≥10%, treatment with blood pressure-lowering medications is recommended when blood pressure is ≥140/90 mmHg (COR I, LOE C-LD) and ≥130/80 mmHg (COR I, LOE A), respectively. Because the age of onset of hypertension correlates with subsequent risk for CVD and mortality, early control can help to reduce the risk of CVD development and progression and should be guided by the individuals ASCVD risk and other comorbidities including age, diabetes and chronic kidney disease [20].

In a recent multi-ethnic cohort study, there was a stepwise increase in the presence of coronary artery calcium and the risk of incident ASCVD with an increase in systolic blood pressure beyond 90 mm Hg [21]. Previously, detecting hypertension, especially in young individuals, did not result in treatment because priority is given to lifestyle and behavioral modifications and many are hesitant to start lifelong medications at an early age. This is particularly evident in women, who may develop CVD later but have an earlier onset of hypertension [22]. Now, with more data indicating the importance of early blood pressure control for preventing the development of atherosclerosis and progression to CVD, prevention strategies should start at an early age.

1.6. Cholesterol and other lipids

In 2018 and 2019, the American and European Cholesterol guidelines were published and provided recommendations for managing ASCVD risk via reduction in low-density lipoprotein cholesterol (LDL-C) [COR I, LOE A]. Prior to 2020, statin, ezetimibe and proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitor therapy were the primary treatments used to lower LDL-C and ASCVD risk.

An additional lipid lowering therapy that has recently gained traction for reducing ASCVD risk is icosapent ethyl. Building on the REDUCE-IT trial, data emerged on the significant effect of icosapent ethyl (4 g/day) on both first and total cardiovascular events among individuals at high risk for ASCVD (prior ASCVD or DM plus multiple risk factors) with well-controlled LDL-C but elevated triglycerides [23]. Following this, many clinicians felt the armamentarium for managing residual ASCVD risk should now include icosapent ethyl in those with elevated triglycerides.

Later in 2020, the STRENGTH trial was completed, which sought to determine effects of omega-3 carboxylic acid (4 g/day) on cardiovascular outcomes among individuals on statin therapy with atherogenic dyslipidemia and high cardiovascular risk [24]. Compared to the control group who received corn oil, omega-3 carboxylic acid did not result in a significant difference in a composite outcome of MACE. Consistent with REDUCE-IT, however, patients receiving omega-3 carboxylic acid more commonly experienced investigator-reported AF. Further studies are therefore required to help resolve the discrepancy between STRENGTH and REDUCE-IT. Some of the disparate findings may be due to the lower dose of EPA used, choice of the placebo comparator and/or to the addition of DHA to the high dose EPA in STRENGTH.

Additionally, the results of two other therapies to treat elevated LDL-C were published in 2020. In the first, investigators enrolled patients with ASCVD or an ASCVD risk equivalent from Orion-10 and Orion-11 and randomized them to inclisiran, which inhibits hepatic synthesis of PCSK9, or placebo [25]. Patients who received inclisiran injections every 6 months had a ~50% reduction in LDL-C levels, with a favorable safety profile only notable for injection-site adverse events. Similarly, in individuals with heterozygous familial hypercholesterolemia, inclisiran resulted in significantly lower LDL-C levels compared to placebo (~48% reduction) without an increase in adverse events [26].

The second trial enrolled patients with homozygous familial hypercholesterolemia on stable lipid-lowering therapy to intravenous infusion of evinacumab (15 mg/kg of body weight), a monoclonal antibody against angiopoietin-like 3, every 4 weeks or placebo [27]. At 24 weeks, evinacumab therapy resulted in a 49% reduction in LDL-C compared to placebo with an absolute difference between groups of 132 mg/dL.

In another placebo-controlled trial, patients with or without heterozygous familial hypercholesterolemia who had refractory hypercholesterolemia (LDL-$C \geq 70$ mg/dL + atherosclerosis or LDL-$C \geq 100$ mg/dL without atherosclerosis) were randomized to receive subcutaneous or intravenous evinacumab or placebo [28,29]. At 16 weeks, evinacumab resulted in significant reductions of LDL-C, including >50% at the maximum dose. Both therapies will require favorable results with regards to cardiovascular outcomes before considered broadly for LDL-C and ASCVD risk reduction.

While LDL-C remains the primary target for ASCVD risk, lipoprotein(a) [Lp(a)] is a heritable risk factor for the development of ASCVD and to date few therapies are available to reduce Lp(a) concentrations. In a randomized placebo-controlled trial, 286 patients with established ASCVD and screening Lp(a) levels ≥ 60 mg/dL (150 nmol/L) were randomized to hepatocyte directed antisense oligonucleotide AKCEA-APO(a)-L_{Rx} or placebo [30]. Treatment with AKCEA-APO(a)-L_{Rx} resulted in dose-dependent decreases in Lp(a) levels, with mean decreases ranging from 35% at a dose of 20 mg every 4 weeks to 80% at 20 mg every week compared to 6% with placebo. The most common reported side effects included injection-site reactions. While the results are favorable, implementation into clinical practice will depend on additional large trials evaluating its impact on cardiovascular outcomes.

1.7. Cessation of smoking

While the rates of cigarette use have decreased significantly throughout the United States over the last two decades, the introduction of the electronic cigarettes (e-cigarette) has introduced new challenges especially among the younger generation. Originally advertised as a safe alternative and bridge to quitting, e-cigarette use results in significant exposure to toxic compounds including nicotine, propylene glycol and glycerin, and is associated with increased CVD morbidity and mortality [31].

Not only do e-cigarettes negatively affect the cardiovascular system by increasing arterial stiffness and the risk of developing hypertension and generating free radicals [32], but their use is also associated with various forms of pneumonitis, which are more commonly known as vaping-induced lung injury [33]. Therefore, clinicians should advise patients to avoid e-cigarettes for any purpose and if they do use e-cigarettes direct them to cessation interventions immediately [COR I, LOE A] [34].

1.8. COVID-19 and cardiovascular disease

Since the beginning of 2020 in the United States, the rapid spread of the novel coronavirus disease 2019 (COVID-19) has resulted in a dev-

astating pandemic causing upwards of ~25 million cases and ~400k deaths nationwide, and still counting. While it primarily affects the respiratory system, diverse cardiovascular manifestations are not uncommon, particularly in severe hospitalized cases [35,36]. In addition, individuals with pre-existing CVD or CVD-specific risk factors, such as obesity, are frequently more severely affected when infected with COVID-19 [37,38].

As a result, control of CVD risk factors and continuation of CVD-related medications, including renin-angiotensin-aldosterone-system inhibitors, blood thinners and anti-inflammatory therapy, could be beneficial in the management of COVID-19 and minimize infection-related complications [39]. Moreover, patients with increased CVD risk should be encouraged and prioritized for vaccine administration as part of a stepwise approach to reduce COVID-19 associated morbidity and mortality [40].

1.9. Cardio-obstetrics

Cardiovascular disease is the primary cause of pregnancy related mortality in the United States [41]. The field of Cardio-obstetrics is focused on the prevention, early detection and appropriate management of CVD in order to avoid cardiovascular-related complications during pregnancy [42]. By promoting cardiovascular health and appropriately addressing cardiac conditions during pregnancy, including hypertensive disorders, cardiomyopathies, arrhythmias, thromboembolic disease, aortic disease and cerebrovascular diseases, cardio-obstetrics specialist can work to prevent adverse pregnancy outcomes and reduce the rates of maternal morbidity and mortality worldwide.

1.10. Cardio-oncology

Understanding the challenges for managing patients at risk for or with CVD and cancer remains a primary concern for both specialties as they are the number one and two leading causes of death worldwide, respectively. The emergence of Cardio-oncology as a sub-specialty in cardiology has filled a necessary void and has improved the treatment of those individuals who have survived cancer treatment but now face an increased risk of CVD mortality and CVD events such as heart failure, ACS and arrhythmias [43]. Ultimately, if cardiovascular risk factor profiles are optimized through adherence to lifestyle, behavioral and pharmacologic interventions, both cardiovascular and cancer outcomes will improve.

1.11. Diabetes

In 2013, the ACC/AHA recommended treating all individuals with DM with statin therapy given the concomitant increase in CVD risk (COR I, LOE A) [44]. In 2020, the European Society of Cardiology released a guideline on the management of DM/pre-DM and CVD risk [45]. The document recommended classification of patients with DM into three levels of cardiovascular risk—very high, high or moderate risk. Based on the estimated risk and presence or absence of other CVD risk factors, treatment recommendations were provided to improve cardiovascular outcomes in patients with DM.

The backbones of CVD risk-reducing treatment for DM are sodium-glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RA) [COR IIb, LOE B-R]. In 2019, trials such as Canagliflozin and Renal Outcomes in Type 2 Diabetes and Nephropathy (CREDENCE) [46], Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes (DECLARE-TIMI 58) [47], Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction (DAPA-HF) [48], Dulaglutide and Cardiovascular Outcomes in Type 2 Diabetes (REWIND) [49], and Cardiovascular Safety of Oral Semaglutide in Patients with Type 2 Diabetes (PIONEER-6) [50], demonstrated the marked effects of SGLT2 inhibitors and GLP-1 RA in reducing CVD outcomes in individuals with DM.

In 2020, additional data emerged for use of these therapies in patients with diabetes at risk for MACE. The first was the Evaluation of Ertugliflozin Efficacy and Safety Cardiovascular Outcomes (VERTIS) trial, which randomized patients with type 2 DM and ASCVD to ertugliflozin (5 mg or 15 mg daily) or placebo [51]. Ertugliflozin was noninferior to placebo with regards to MACE (incidence rate 11.9% vs. 11.9%, hazard ratio (HR) 0.97; 95 confidence interval (CI) 0.85–1.11, $p<0.001$ for noninferiority).

In the Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure (EMPEROR-Reduced) trial, investigators randomized patients with Class II, III or IV heart failure and an ejection fraction ≤40% to empagliflozin (10 mg daily) or placebo (including recommended heart failure therapy) [52]. Following a median of 16 months, compared to those receiving placebo, those receiving empagliflozin had a lower risk of cardiovascular death or hospitalization for heart failure independent of diabetic status (HR 0.75, 95% CI 0.65–0.86).

In a 2020 meta-analysis, researchers sought to determine the association of SGLT2 inhibitors with cardiovascular and kidney outcomes among patients with type 2 DM [53]. Based on data from six trials (4 different SGLT2 inhibitors) totaling over 46,000 patients, SGLT2 inhibitors were associated with a reduced risk of MACE (HR 0.90, 95% CI 0.85–0.95). Of note, the reduction in risk of hospitalization for heart failure and chronic kidney disease progression was the most notable across the included trials.

Similarly, a meta-analysis based on seven cardiovascular outcome trials including over 56,000 patients sought to determine the efficacy and safety of GLP-1 RA in adults with type 2 DM [54]. A 12% reduction in the three-point MACE endpoint was demonstrated when GLP-1 RA was used for treatment in individuals with type 2 DM (HR 0.88, 95% CI 0.80–0.96). Thus, SGLT2 inhibitors or GLP-1 RA should be prioritized in individuals with type 2 DM and known ASCVD to prevent complications associated with cardiovascular and kidney disease [55].

1.12. Diet

There are ongoing efforts to refine the heart healthy diet to promote ideal cardiovascular health (COR I, LOE B-R). In 2020, priority was also given to identifying why adherence to certain diets, specifically the Mediterranean diet, varies from individual to individual. Using PREDIMED and three United States cohorts, researchers identified 67 metabolites that correlated with the diet's adherence [56]. These metabolites also predicted future CVD risk independent of traditional risk factors. While preliminary, these findings suggest that one day clinicians may be able to individualize dietary recommendations based on the results of metabolomic profiling related to dietary response and adherence as well as disease risk.

Another dietary pattern generating significant interest across the world for its potential health benefits is intermittent fasting. Among 116 overweight and obese participants, a prospective randomized clinical trial was completed to determine the effect of 16:8 hour time-restricted eating (TRE) on weight loss and metabolic health [57]. Time-restricted eating was associated with a modest and statistically insignificant decrease in weight (1.2% vs. 0.8%) without providing cardiometabolic benefits. In another feasibility study, 20 individuals (mean BMI 34.1) were randomized to TRE (8-hour window) versus non-TRE for 12 weeks. Compared to non-TRE individuals, the TRE group had a statistically significant decrease in weight (−3.7%), fat mass (−3.0%) and visceral fat (−11.1%) [58].

In addition to diet, the effect of alcohol intake on CVD risk remains unclear. Using Mendelian randomization, researchers sought to predict the effect of alcohol consumption on eight cardiovascular diseases [59]. They found sufficient evidence for a causal relationship between higher alcohol consumption and increased risk of stroke and peripheral arterial disease.

Another randomized clinical trial evaluated the effect of excessive alcohol intake vs. abstinence on secondary prevention of AF in individuals

with paroxysmal or persistent AF. Compared to individuals who continued drinking 10 or more drinks per week, those who abstained from alcohol had a longer period before recurrence (HR 0.55, 95% CI 0.36–0.84) and a significantly lower burden of AF during 6-month follow-up (% of time in AF: 0.5% vs. 1.2%, $p = 0.01$) [60].

1.13. Digital health & devices

The increasing adoption of mobile health technologies have the potential to expand the continuum of care for patients and improve cardiovascular related outcomes. Two specific areas in CVD prevention that are primed for mobile health integration are physical activity and weight loss. In a 2020 systematic review and meta-analysis, which studied the effect of text messaging interventions on physical activity, text message interventions resulted in higher objectively measured post-intervention physical activity compared to that in the control groups [61].

Similarly, a recent systematic review evaluated the effect of text messaging on behavior change interventions for weight management [62]. According to this analysis, behavior change interventions using text messages resulted in significantly greater weight loss (−2.3 kg) and weight loss maintenance compared to placebo groups.

The COVID-19 pandemic also brought a new direction in CVD prevention and digital health patient engagement in 2020. One example was the approval of telehealth services for the provision of cardiac rehabilitation services as part of COVID-19 Public Health Emergency by the Centers for Medicare and Medicaid Services. This provided an important opportunity to promote secondary CVD prevention using technology enhanced home-based cardiac rehab programs [63].

1.14. Disparities

The COVID-19 pandemic and recent police killings in our nation, which disproportionately affect marginalized communities, have highlighted that simply acknowledging differences in risk based on individual racial and ethnic groups is not enough [64]. Instead, there must be an acknowledgement that the poor health outcomes and disparities in CVD are in part due to the presence of structural racism.

To improve the path forward for these communities, the social determinants of health that have perpetuated these health disparities for generations need to be addressed (COR I, LOE B-NR). The AHA has taken a small, but significant step by starting to identify the social determinants of health that affect a specific subset of patients with heart failure to try and improve not only their outcomes, but also their quality of life [65].

1.15. Dream (sleep)

The evidence to support proper sleep hygiene as a means for achieving optimal cardiovascular health continues to accumulate. In fact, new data from the UK Biobank suggest that a healthy sleep pattern can reduce the risk of CAD and stroke by 34% [66]. Alternatively, sleep disturbances can negatively impact CVD outcomes. Among almost 400k participants, ~10% of CVD events could be attributed to unhealthy sleep patterns and behaviors. One important example is the high prevalence of AF in individuals with sleep apnea [67]. Among 188 individuals with AF, >80% were found to have sleep apnea using a home sleep apnea test.

1.16. Exercise

The benefits of physical activity cannot be overstated and adherence to guideline recommendations, which include at least 150 min of moderate intensity or 75 min of vigorous intensity exercise weekly, is required to optimize cardiovascular health (COR I, LOE B-R/NR). This extends to all ages as low levels of cardiorespiratory fitness and obesity in adolescence is associated with cardiovascular disease later in life [68].

Despite abundant evidence that guideline recommended physical activity and cardiorespiratory fitness levels are inversely related to cardiovascular morbidity and mortality, less is known about the effects of excessive endurance exercise on cardiovascular health. To address this uncertainty, the AHA released a scientific statement to help clinicians advise patients on the benefits and risks of this level of activity [69].

While they warn individuals unaccustomed to exercise about the risks of sudden cardiac death, MI, and cardiac remodeling, they conclude that the benefits associated with long-term exercise training outweigh the risks for the majority of the population. However, as a precaution, they recommend that inactive individuals should start slowly and increase the intensity as able.

In addition to its role in preventing the development of CVD, physical activity also plays a critical role in lowering the complications from various cardiovascular diseases. In patients with AF, physical activity and higher levels of cardiorespiratory fitness were associated with a lower long-term risk of CVD and all-cause mortality [70].

1.17. Factors of the environment

The social determinants of health, including differences in income and education, are known risk factors for CVD. In more than one million Danish employees, low education level was associated with a higher risk of incident CVD and CVD mortality [71]. In the extreme cases, when the stress from these social determinants translates into psychological distress and depression, the detrimental effect on CVD risk is accentuated. A recent European Society of Cardiology work group concluded that depression is associated with a 30% increased risk for future CAD [72].

1.18. Genetics

Both biologic, genetically determined sex as well as gender significantly impact CVD risk. In 2020, we gained further insight into sex and gender differences for various cardiovascular conditions, including a higher incidence of heart failure with preserved ejection fraction, Takotsubo syndrome and myocardial infarction with nonobstructive coronary arteries (MINOCA) in women compared to men [73]. To address an excess of adverse events with conditions like MINOCA, the ESC published new approaches for the diagnosis, risk stratification and management [13]. In addition, presenting symptoms of cardiovascular events such as ACS differ between men and women and therefore personalized treatment protocols to account for these differences may be required [74].

2. Conclusion

Recommendations surrounding CVD prevention are constantly evolving as new practice-changing data are published each year. In 2020, significant advances in the field of CVD prevention were made and are highlighted using the Johns Hopkins Ciccarone Center's expanded 'ABCDEFG' approach. By systematically outlining recommendations, clinicians can more definitively promote lifestyle, behavioral and pharmacologic interventions required to achieve optimal cardiovascular health.

Declaration of Competing Interest

DIF: None; KCW: None, AGH: None, FAM: FAM is the co-founder of and holds equity in Corrie Health, which intends to further develop the platform. This arrangement has been reviewed and approved by the Johns Hopkins University in accordance with its conflict of interest policies; SSM: SSM has current research support from the American Heart Association (20SFRN35380046 and COVID19–811,000), PCORI (ME-2019C1–15,328), NIH (P01 HL108800), the Pollin Digital Innovation Fund, and the David and June Trone Family Foundation. He has served as a consultant in the past 24 months to AstraZeneca, Amgen,

DalCor Pharmaceuticals, Esperion, iHealth, Kaneka, Sanofi, and 89bio. He is a co-inventor on a system to estimate LDL-cholesterol levels, patent application pending. SSM is also the co-founder of and holds equity in Corrie Health, which intends to further develop the platform. This arrangement has been reviewed and approved by the Johns Hopkins University in accordance with its conflict of interest policies; RSB: None; GS: GS has funding from the Blumenthal Scholar Fund and the Johns Hopkins Office of Provost Intramural Grant.

Funding

None.

Contributions

DIF: DIF, RSB participated in the conception and design of the review, DIF drafted the manuscript. DIF, GS prepared the figure. DIF, KCW, AGH, FAM, SSM, RSB and GS participated in the interpretation of the data, drafting of the manuscript, and revised subsequent drafts critically for important intellectual content. All authors approved the final version.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ajpc.2021.100181.

References

[1] Ray KK, Laufs U, Cosentino F, Lobo MD, Landmesser U. The year in cardiology, cardiovascular prevention: the year in cardiology 2019. Eur Heart J 2019;41(11):1157–63.

[2] Feldman DI, Dudum R, Alfaddagh A, Marvel FA, Michos ED, Blumenthal RS, Martin SS. Summarizing 2019 in cardiovascular prevention using the Johns Hopkins ciccarone center for the prevention of cardiovascular disease's 'ABC's approach. Am J Prev Cardiol 2020;2:100027. doi:10.1016/j.ajpc.2020.100027.

[3] Estruch R, Ruilope LM, Cosentino F. The year in cardiovascular medicine 2020: epidemiology and prevention. Eur Heart J 2021;00:1–9. doi:10.1093/eurheartj/ehaa1062.

[4] Orringer CE, Blaha MJ, Blankstein R, Budoff MJ, Goldberg RB, Gill EA, Maki KC, Mehta L, Jacobson TA. The national lipid association scientific statement on coronary artery calcium scoring to guide preventive strategies for ASCVD risk reduction. J Clin Lipidol 2020 Dec 11:S1933-2874(20)30342-1. doi: 10.1016/j.jacl.2020.12.005. Epub ahead of print.

[5] Dzaye O, Dardari ZA, Cainzos-Achirica M, Blankstein R, Szklo M, Budoff MJ, Lima JAC, Blumenthal RS, Nasir K, Blaha MJ. Incidence of new coronary calcification: time to conversion from CAC = 0. J Am Coll Cardiol 2020;75(13):1610–13 Apr 7doi: 10.1016/j.jacc.2020.01.047.

[6] Cainzos-Achirica M, Miedema MD, McEvoy JW, Al Rifai M, Greenland P, Dardari Z, Budoff M, Blumenthal RS, Yeboah J, Duprez DA, Mortensen MB, Dzaye O, Hong J, Nasir K, Blaha MJ. Coronary artery calcium for personalized allocation of aspirin in primary prevention of cardiovascular disease in 2019: the mesa study (multi-ethnic study of atherosclerosis). Circulation 2020;141(19):1541–53 May 12. doi:10.1161/CIRCULATIONAHA.119.045010.

[7] Arnett DK, Blumenthal RS, Albert MA, Buroker AB, Goldberger ZD, Hahn EJ, Himmelfarb CD, Khera A, Lloyd-Jones D, McEvoy JW, Michos ED, Miedema MD, Muñoz D, Smith SC Jr, Virani SS, Williams KA Sr, Yeboah J, Ziaeian B. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American college of cardiology/American heart association task force on clinical practice guidelines. Circulation 2019;140(11) Sep 10e596-e646. doi:10.1161/CIR.0000000000000678.

[8] Jacobsen AP, Raber I, McCarthy CP, Blumenthal RS, Bhatt DL, Cusack RW, Serruys PWJC, Wijns W, McEvoy JW. Lifelong aspirin for all in the secondary prevention of chronic coronary syndrome: still sacrosanct or is reappraisal warranted? Circulation 2020;142(16):1579–90 Oct 20. doi:10.1161/CIRCULATIONAHA.120.045695.

[9] Smith SC Jr, Benjamin EJ, Bonow RO, Braun LT, Creager MA, Franklin BA, Gibbons RJ, Grundy SM, Hiratzka LF, Jones DW, Lloyd-Jones DM, Minissian M, Mosca L, Peterson ED, Sacco RL, Spertus J, Stein JH, Taubert KAWorld Heart Federation and the Preventive Cardiovascular Nurses Association. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American heart association and American college of cardiology foundation. Circulation 2011;124(22):2458–73 Nov 29. doi:10.1161/CIR.0b013e318235eb4d.

[10] Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Valgimigli M, Achenbach S, Bax JJESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 2020;41(3):407–77 Jan 14. doi:10.1093/eurheartj/ehz425.

[11] Alexander JH, Wojdyla D, Vora AN, Thomas L, Granger CB, Goodman SG, Aronson R, Windecker S, Mehran R, Lopes RD. Risk/benefit tradeoff of antithrombotic therapy in patients with atrial fibrillation early and late after an acute coronary syndrome or percutaneous coronary intervention: insights from AUGUSTUS. Circulation 2020;141(20):1618–27 May 19. doi:10.1161/CIRCULATIONAHA.120.046534.

[12] O'Donoghue ML, Murphy SA, Sabatine MS. The safety and efficacy of aspirin discontinuation on a background of a $P2Y_{12}$ inhibitor in patients after percutaneous coronary intervention: a systematic review and meta-analysis. Circulation 2020;142(6):538–45 Aug 11. doi:10.1161/CIRCULATIONAHA.120.046251.

[13] Collet JP, Thiele H, Barbato E, Barthélémy O, Bauersachs J, Bhatt DL, Dendale P, Dorobantu M, Edvardsen T, Folliguet T, Gale CP, Gilard M, Jobs A, Jüni P, Lambrinou E, Lewis BS, Mehilli J, Meliga E, Merkely B, Mueller C, Roffi M, Rutten FH, Sibbing D, Siontis GCM. ESC scientific document group. 2020 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. Eur Heart J 2020;29:ehaa575 Aug. doi:10.1093/eurheartj/ehaa575.

[14] Nidorf SM, Fiolet ATL, Mosterd A, Eikelboom JW, Schut A, Opstal TSJ, The SHK, Xu XF, Ireland MA, Lenderink T, Latchem D, Hoogslag P, Jerzewski A, Nierop P, Whelan A, Hendriks R, Swart H, Schaap J, Kuijper AFM, van Hessen MWJ, Saklani P, Tan I, Thompson AG, Morton A, Judkins C, Bax WA, Dirksen M, Alings M, Hankey GJ, Budgeon CA, Tijssen JGP, Cornel JH, Thompson PL. LoDoCo2 trial investigators. Colchicine in patients with chronic coronary disease. N Engl J Med 2020;383(19):1838–47 Nov 5. doi:10.1056/NEJMoa2021372.

[15] Estruch R, Ros E. The role of the Mediterranean diet on weight loss and obesity-related diseases. Rev Endocr Metab Disord 2020;21(3):315–27 Sep. doi:10.1007/s11154-020-09579-0.

[16] Larsson SC, Bäck M, Rees JMB, Mason AM, Burgess S. Body mass index and body composition in relation to 14 cardiovascular conditions in UK Biobank: a Mendelian randomization study. Eur Heart J 2020;41(2):221–6 Jan 7. doi:10.1093/eurheartj/ehz388.

[17] Jensen MD, Ryan DH, Apovian CM, Ard JD, Comuzzie AG, Donato KA, Hu FB, Hubbard VS, Jakicic JM, Kushner RF, Loria CM, Millen BE, Nonas CA, Pi-Sunyer FX, Stevens J, Stevens VJ, Wadden TA, Wolfe BM, Yanovski SZ, Jordan HS, Kendall KA, Lux LJ, Mentor-Marcel R, Morgan LC, Trisolini MG, Wnek J, Anderson JL, Halperin JL, Albert NM, Bozkurt B, Brindis RG, Curtis LH, DeMets D, Hochman JS, Kovacs RJ, Ohman EM, Pressler SJ, Sellke FW, Shen WK, Smith SC Jr, Tomaselli GF. American college of cardiology/American heart association task force on practice guidelines; obesity society. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American college of cardiology/American heart association task force on practice guidelines and the obesity society. Circulation 2014;129 Jun 24(25 Suppl 2):S102-38. doi:10.1161/01.cir.0000437739.71477.ee.

[18] Moussa O, Ardissino M, Heaton T, Tang A, Khan O, Ziprin P, Darzi A, Collins P, Purkayastha S. Effect of bariatric surgery on long-term cardiovascular outcomes: a nationwide nested cohort study. Eur Heart J 2020;41(28):2660–7 Jul 21. doi:10.1093/eurheartj/ehaa069.

[19] Plante TB, Koh I, Judd SE, Howard G, Howard VJ, Zakai NA, Boothll JN, Safford MM, Muntner P, Cushman M. Life's simple 7 and incident hypertension: the regards study. J Am Heart Assoc 2020;9(19) Oct 20e016482. doi:10.1161/JAHA.120.016482.

[20] Wang C, Yuan Y, Zheng M, Pan A, Wang M, Zhao M, Li Y, Yao S, Chen S, Wu S, Xue H. Association of age of onset of hypertension with cardiovascular diseases and mortality. J Am Coll Cardiol 2020;75(23):2921–30 Jun 16. doi:10.1016/j.jacc.2020.04.038.

[21] Whelton SP, McEvoy JW, Shaw L, Psaty BM, Lima JAC, Budoff M, Nasir K, Szklo M, Blumenthal RS, Blaha MJ. Association of normal systolic blood pressure level with cardiovascular disease in the absence of risk factors. JAMA Cardiol 2020;5(9):1011–18 Sep 1doi: 10.1001/jamacardio.2020.1731.

[22] Ji H, Kim A, Ebinger JE, Niiranen TJ, Claggett BL, Bairey Merz CN, Cheng S. Sex differences in blood pressure trajectories over the life course. JAMA Cardiol 2020;5(3):19–26 Mar 1. doi:10.1001/jamacardio.2019.5306.

[23] Boden WE, Bhatt DL, Toth PP, Ray KK, Chapman MJ, Lüscher TF. Profound reductions in first and total cardiovascular events with icosapent ethyl in the REDUCE-IT trial: why these results usher in a new era in dyslipidaemia therapeutics. Eur Heart J 2020;41(24):2304–12 Jun 21. doi:10.1093/eurheartj/ehz778.

[24] Nicholls SJ, Lincoff AM, Garcia M, Bash D, Ballantyne CM, Barter PJ, Davidson MH, Kastelein JJP, Koenig W, McGuire DK, Mozaffarian D, Ridker PM, Ray KK, Katona BG, Himmelmann A, Loss LE, Rensfeldt M, Lundström T, Agrawal R, Menon V, Wolski K, Nissen SE. Effect of high-dose omega-3 fatty acids vs corn oil on major adverse cardiovascular events in patients at high cardiovascular risk: the strength randomized clinical trial. JAMA 2020;324(22):2268–80 Dec 8doi: 10.1001/jama.2020.22258.

[25] Ray KK, Wright RS, Kallend D, Koenig W, Leiter LA, Raal FJ, Bisch JA, Richardson T, Jaros M, Wijngaard PLJ, Kastelein JJP. ORION-10 and ORION-11 investigators. Two phase 3 trials of inclisiran in patients with elevated LDL cholesterol. N Engl J Med 2020;382(16):1507–19 Apr 16. doi:10.1056/NEJMoa1912387.

[26] Raal FJ, Kallend D, Ray KK, Turner T, Koenig W, Wright RS, Wijngaard PLJ, Curcio D, Jaros MJ, Leiter LA, Kastelein JJP. ORION-9 investigators. Inclisiran for the treatment of heterozygous familial hypercholesterolemia. N Engl J Med 2020;382(16):1520–30 Apr 16. doi:10.1056/NEJMoa1913805.

[27] Raal FJ, Rosenson RS, Reeskamp LF, Hovingh GK, Kastelein JJP, Rubba P, Ali S, Banerjee P, Chan KC, Gipe DA, Khilla N, Pordy R, Weinreich DM, Yancopoulos GD, Zhang Y, Gaudet D. ELIPSE HoFH investigators. evinacumab for homozygous familial hypercholesterolemia. N Engl J Med 2020;383(8):711–20 Aug 20. doi:10.1056/NEJMoa2004215.

[28] Rosenson RS, Burgess LJ, Ebenbichler CF, Baum SJ, Stroes ESG, Ali S, Khilla N, Ham-

lin R, Pordy R, Dong Y, Son V, Gaudet D. Evinacumab in patients with refractory hypercholesterolemia. N Engl J Med 2020;383(24):2307–19 Dec 10. doi:10.1056/NEJMoa2031049.
[29] Martin SS. Factoring in ANGPTL3 when LDL is refractory. N Engl J Med 2020;383(24):2385–6 Dec 10. doi:10.1056/NEJMe2032798.
[30] Tsimikas S, Karwatowska-Prokopczuk E, Gouni-Berthold I, Tardif JC, Baum SJ, Steinhagen-Thiessen E, Shapiro MD, Stroes ES, Moriarty PM, Nordestgaard BG, Xia S, Guerriero J, Viney NJ, O'Dea L, Witztum JL. AKCEA-APO(a)-LRx study investigators. Lipoprotein(a) reduction in persons with cardiovascular disease. N Engl J Med 2020;382(3):244–55 Jan 1610.1056/NEJMoa1905239. Epub 2020 Jan 1.
[31] Münzel T, Hahad O, Kuntic M, Keaney JF, Deanfield JE, Daiber A. Effects of tobacco cigarettes, e-cigarettes, and waterpipe smoking on endothelial function and clinical outcomes. Eur Heart J 2020;41(41):4057–70 Nov 1. doi:10.1093/eurheartj/ehaa460.
[32] Kuntic M, Oelze M, Steven S, Kröller-Schön S, Stamm P, Kalinovic S, Frenis K, Vujacic-Mirski K, Bayo Jimenez MT, Kvandova M, Filippou K, Al Zuabi A, Brückl V, Hahad O, Daub S, Varveri F, Gori T, Huesmann R, Hoffmann T, Schmidt FP, Keaney JF, Daiber A, Münzel T. Short-term e-cigarette vapour exposure causes vascular oxidative stress and dysfunction: evidence for a close connection to brain damage and a key role of the phagocytic NADPH oxidase (NOX-2). Eur Heart J 2020;41(26):2472–83 Jul 7. doi:10.1093/eurheartj/ehz772.
[33] Stanbrook MB, Drazen JM. Vaping-induced lung disease - a look forward by looking back. N Engl J Med 2020;382(17):1649–50 Apr 23. doi:10.1056/NEJMe2004876.
[34] Siedlinski M, Harrison DG, Guzik TJ. E-vaporating benefits of e-vaping. Eur Heart J 2020;41(26):2484–6 Jul 7. doi:10.1093/eurheartj/ehz875.
[35] Libby P, Lüscher T. COVID-19 is, in the end, an endothelial disease. Eur Heart J 2020;41(32):3038–44 Sep 1. doi:10.1093/eurheartj/ehaa623.
[36] Nishiga M, Wang DW, Han Y, Lewis DB, Wu JC. COVID-19 and cardiovascular disease: from basic mechanisms to clinical perspectives. Nat Rev Cardiol 2020;17(9):543–58 Sep. doi:10.1038/s41569-020-0413-9.
[37] Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, Madhur MS, Tomaszewski M, Maffia P, D'Acquisto F, Nicklin SA, Marian AJ, Nosalski R, Murray EC, Guzik B, Berry C, Touyz RM, Kreutz R, Wang DW, Bhella D, Sagliocco O, Crea F, Thomson EC, McInnes IB. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res 2020;116(10):1666–87 Aug 1. doi:10.1093/cvr/cvaa106.
[38] Bae S, Kim SR, Kim MN, Shim WJ, Park SM. Impact of cardiovascular disease and risk factors on fatal outcomes in patients with COVID-19 according to age: a systematic review and meta-analysis. Heart 2020 Dec 17:heartjnl-2020-317901. doi:10.1136/heartjnl-2020-317901.
[39] Ruilope LM, Tamargo J, Ruiz-Hurtado G. Renin-angiotensin system inhibitors in the COVID-19 pandemic: consequences of antihypertensive drugs. Eur Heart J 2020;41(22):2067–9 Jun 7. doi:10.1093/eurheartj/ehaa487.
[40] Griffith DM, Sharma G, Holliday CS, Enyia OK, Valliere M, Semlow AR, Stewart EC, Blumenthal RS. Men and COVID-19: a biopsychosocial approach to understanding sex differences in mortality and recommendations for practice and policy interventions. Prev Chronic Dis 2020;17 Jul 16E63. doi:10.5888/pcd17.200247.
[41] Mehta LS, Warnes CA, Bradley E, Burton T, Economy K, Mehran R, Safdar B, Sharma G, Wood M, Valente AM, Volgman ASAmerican Heart Association Council on Clinical Cardiology. Council on arteriosclerosis, thrombosis and vascular biology; council on cardiovascular and stroke nursing; and stroke council. cardiovascular considerations in caring for pregnant patients: a scientific statement from the american heart association. Circulation 2020;141(23) Jun 9e884-e903. doi:10.1161/CIR.0000000000000772.
[42] Sharma G, Lindley K, Grodzinsky A. Cardio-obstetrics: developing a niche in maternal cardiovascular health. J Am Coll Cardiol 2020;75(11):1355–9 Mar 24doi:10.1016/j.jacc.2020.02.019.
[43] Alvarez-Cardona JA, Ray J, Carver J, Zaha V, Cheng R, Yang E, Mitchell JD, Stockerl-Goldstein K, Kondapalli L, Dent S, Arnold A, Brown SA, Leja M, Barac A, Lenihan DJ, Herrmann J. Cardio-oncology leadership council. Cardio-oncology education and training: JACC council perspectives. J Am Coll Cardiol 2020;76(19):2267–81 Nov 10. doi:10.1016/j.jacc.2020.08.079.
[44] Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, Goldberg AC, Gordon D, Levy D, Lloyd-Jones DM, McBride P, Schwartz JS, Shero ST, Smith SC Jr, Watson K, Wilson PWAmerican College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American college of cardiology/American heart association task force on practice guidelines. J Am Coll Cardiol 2014;63 Jul 1(25 Pt B): 2889-934. doi:10.1016/j.jacc.2013.11.002.
[45] Cosentino F, Grant PJ, Aboyans V, Bailey CJ, Ceriello A, Delgado V, Federici M, Filippatos G, Grobbee DE, Hansen TB, Huikuri HV, Johansson I, Jüni P, Lettino M, Marx N, Mellbin LG, Östgren CJ, Rocca B, Roffi M, Sattar N, Seferović PM, Sousa-Uva M, Valensi P, Wheeler DCESC Scientific Document Group. 2019 ESC guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J 2020;41(2):255–323 Jan 7. doi:10.1093/eurheartj/ehz486.
[46] Perkovic V, Jardine MJ, Neal B, Bompoint S, Heerspink HJL, Charytan DM, Edwards R, Agarwal R, Bakris G, Bull S, Cannon CP, Capuano G, Chu PL, de Zeeuw D, Greene T, Levin A, Pollock C, Wheeler DC, Yavin Y, Zhang H, Zinman B, Meininger G, Brenner BM, Mahaffey KW. CREDENCE trial investigators. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med 2019;380(24):2295–306 Jun 13. doi:10.1056/NEJMoa1811744.
[47] Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH, Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS. DECLARE–TIMI 58 investigators. dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2019;380(4):347–57 Jan 24. doi:10.1056/NEJMoa1812389.
[48] McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, Ponikowski P, Sabatine MS, Anand IS, Bělohlávek J, Böhm M, Chiang CE, Chopra VK, de Boer RA, Desai AS, Diez M, Drozdz J, Dukát A, Ge J, Howlett JG, Katova T, Kitakaze M, Ljungman CEA, Merkely B, Nicolau JC, O'Meara E, Petrie MC, Vinh PN, Schou M, Tereshchenko S, Verma S, Held C, DeMets DL, Docherty KF, Jhund PS, Bengtsson O, Sjöstrand M, Langkilde AM. DAPA-HF trial committees and investigators. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019;381(21):1995–2008 Nov 21. doi:10.1056/NEJMoa1911303.
[49] Gerstein HC, Colhoun HM, Dagenais GR, Diaz R, Lakshmanan M, Pais P, Probstfield J, Riesmeyer JS, Riddle MC, Rydén L, Xavier D, Atisso CM, Dyal L, Hall S, Rao-Melacini P, Wong G, Avezum A, Basile J, Chung N, Conget I, Cushman WC, Franek E, Hancu N, Hanefeld M, Holt S, Jansky P, Keltai M, Lanas F, Leiter LA, Lopez-Jaramillo P, Cardona Munoz EG, Pirags V, Pogosova N, Raubenheimer PJ, Shaw JE, Sheu WH, Temelkova-Kurktschiev T. REWIND investigators. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. Lancet 2019;394(10193):121–30 Jul 13. doi:10.1016/S0140-6736(19)31149-3.
[50] Bain SC, Mosenzon O, Arechavaleta R, Bogdański P, Comlekci A, Consoli A, Deerochanawong C, Dungan K, Faingold MC, Farkouh ME, Franco DR, Gram J, Guja C, Joshi P, Malek R, Merino-Torres JF, Nauck MA, Pedersen SD, Sheu WH, Silver RJ, Tack CJ, Tandon N, Jeppesen OK, Strange M, Thomsen M, Husain M. Cardiovascular safety of oral semaglutide in patients with type 2 diabetes: rationale, design and patient baseline characteristics for the PIONEER 6 trial. Diabetes Obes Metab 2019;21(3):499–508 Mar. doi:10.1111/dom.13553.
[51] Cannon CP, Pratley R, Dagogo-Jack S, Mancuso J, Huyck S, Masiukiewicz U, Charbonnel B, Frederich R, Gallo S, Cosentino F, Shih WJ, Gantz I, Terra SG, Cherney DZI, McGuire DK. VERTIS CV investigators. cardiovascular outcomes with ertugliflozin in type 2 diabetes. N Engl J Med 2020;383(15):1425–35 Oct 8. doi:10.1056/NEJMoa2004967.
[52] Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, Januzzi J, Verma S, Tsutsui H, Brueckmann M, Jamal W, Kimura K, Schnee J, Zeller C, Cotton D, Bocchi E, Böhm M, Choi DJ, Chopra V, Chuquiure E, Giannetti N, Janssens S, Zhang J, Gonzalez Juanatey JR, Kaul S, Brunner-La Rocca HP, Merkely B, Nicholls SJ, Perrone S, Pina I, Ponikowski P, Sattar N, Senni M, Seronde MF, Spinar J, Squire I, Taddei S, Wanner C, Zannad F. EMPEROR-reduced trial investigators. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med 2020;383(15):1413–24 Oct 8. doi:10.1056/NEJMoa2022190.
[53] McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZI, Dagogo-Jack S, Pratley R, Greenberg M, Wang S, Huyck S, Gantz I, Terra SG, Masiukiewicz U, Cannon CP. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. JAMA Cardiol 2020 Oct 7:e204511. doi: 10.1001/jamacardio.2020.4511. Epub ahead of print.
[54] Marsico F, Paolillo S, Gargiulo P, Bruzzese D, Dell'Aversana S, Esposito I, Renga F, Esposito L, Marciano C, Dellegrottaglie S, Iesu I, Perrone Filardi P. Effects of glucagon-like peptide-1 receptor agonists on major cardiovascular events in patients with Type 2 diabetes mellitus with or without established cardiovascular disease: a meta-analysis of randomized controlled trials. Eur Heart J 2020;41(35):3346–58 Sep 14. doi:10.1093/eurheartj/ehaa082.
[55] McMurray JJV, Wheeler DC, Stefánsson BV, Jongs N, Postmus D, Correa-Rotter R, Chertow GM, Greene T, Held C, Hou FF, Mann JFE, Rossing P, Sjöström CD, Toto RD, Langkilde AM, Heerspink HJL. DAPA-CKD trial committees and investigators. effect of dapagliflozin on clinical outcomes in patients with chronic kidney disease, with and without cardiovascular disease. Circulation 2020 Nov 13. doi:10.1161/CIRCULATIONAHA.120.051675.
[56] Li J, Guasch-Ferré M, Chung W, Ruiz-Canela M, Toledo E, Corella D, Bhupathiraju SN, Tobias DK, Tabung FK, Hu J, Zhao T, Turman C, Feng YA, Clish CB, Mucci L, Eliassen AH, Costenbader KH, Karlson EW, Wolpin BM, Ascherio A, Rimm EB, Manson JE, Qi L, Martínez-González MÁ, Salas-Salvadó J, Hu FB, Liang L. The Mediterranean diet, plasma metabolome, and cardiovascular disease risk. Eur Heart J 2020;41(28):2645–56 Jul 21. doi:10.1093/eurheartj/ehaa209.
[57] Lowe DA, Wu N, Rohdin-Bibby L, Moore AH, Kelly N, Liu YE, Philip E, Vittinghoff E, Heymsfield SB, Olgin JE, Shepherd JA, Weiss EJ. Effects of time-restricted eating on weight loss and other metabolic parameters in women and men with overweight and obesity: the treat randomized clinical trial. JAMA Intern Med 2020;180(11):1–9 Sep 28doi: 10.1001/jamainternmed.2020.4153. Epub ahead of print.
[58] Chow LS, Manoogian ENC, Alvear A, Fleischer JG, Thor H, Dietsche K, Wang Q, Hodges JS, Esch N, Malaeb S, Harindhanavudhi T, Nair KS, Panda S, Mashek DG. Time-restricted eating effects on body composition and metabolic measures in humans who are overweight: a feasibility study. Obesity 2020;28(5):860–9 (Silver Spring)May. doi:10.1002/oby.22756.
[59] Larsson SC, Burgess S, Mason AM, Michaëlsson K. Alcohol consumption and cardiovascular disease: a mendelian randomization study. Circ Genom Precis Med 2020;13(3) June002814. doi:10.1161/CIRCGEN.119.002814.
[60] Voskoboinik A, Kalman JM, De Silva A, Nicholls T, Costello B, Nanayakkara S, Prabhu S, Stub D, Azzopardi S, Vizi D, Wong G, Nalliah C, Sugumar H, Wong M, Kotschet E, Kaye D, Taylor AJ, Kistler PM. Alcohol abstinence in drinkers with atrial fibrillation. N Engl J Med 2020;382(1):20–8 Jan 2. doi:10.1056/NEJMoa1817591.
[61] Smith DM, Duque L, Huffman JC, Healy BC, Celano CM. Text message interventions for physical activity: a systematic review and meta-analysis. Am J Prev Med 2020;58(1):142–51 Jan. doi:10.1016/j.amepre.2019.08.014.
[62] Skinner R, Gonet V, Currie S, Hoddinott P, Dombrowski SU. A systematic review with meta-analyses of text message-delivered behaviour change interventions

for weight loss and weight loss maintenance. Obes Rev 2020;21(6) June12999. doi:10.1111/obr.12999.

[63] Yeo TJ, Wang YL, Low TT. Have a heart during the COVID-19 crisis: making the case for cardiac rehabilitation in the face of an ongoing pandemic. Eur J Prev Cardiol 2020;27(9):903–5 Jun. doi:10.1177/2047487320915665.

[64] Churchwell K, Elkind MSV, Benjamin RM, Carson AP, Chang EK, Lawrence W, Mills A, Odom TM, Rodriguez CJ, Rodriguez F, Sanchez E, Sharrief AZ, Sims M, Williams OAmerican Heart Association. Call to action: structural racism as a fundamental driver of health disparities: a presidential advisory from the american heart association. Circulation 2020;142(24) Dec 15e454-e468. doi:10.1161/CIR.0000000000000936.

[65] White-Williams C, Rossi LP, Bittner VA, Driscoll A, Durant RW, Granger BB, Graven LJ, Kitko L, Newlin K, Shirey M. American heart association council on cardiovascular and stroke nursing; council on clinical cardiology; and council on epidemiology and prevention. addressing social determinants of health in the care of patients with heart failure: a scientific statement from the american heart association. Circulation 2020;141(22) Jun 2e841-e863. doi:10.1161/CIR.0000000000000767.

[66] Fan M, Sun D, Zhou T, Heianza Y, Lv J, Li L, Qi L. Sleep patterns, genetic susceptibility, and incident cardiovascular disease: a prospective study of 385 292 UK biobank participants. Eur Heart J 2020;41(11):1182–9 Mar 14. doi:10.1093/eurheartj/ehz849.

[67] Shapira-Daniels A, Mohanty S, Contreras-Valdes FM, Tieu H, Thomas RJ, Natale A, Anter E. Prevalence of undiagnosed sleep apnea in patients with atrial fibrillation and its impact on therapy. JACC Clin Electrophysiol 2020;6(12):1499–506 Novdoi: 10.1016/j.jacep.2020.05.030.

[68] Henriksson H, Henriksson P, Tynelius P, Ekstedt M, Berglind D, Labayen I, Ruiz JR, Lavie CJ, Ortega FB. Cardiorespiratory fitness, muscular strength, and obesity in adolescence and later chronic disability due to cardiovascular disease: a cohort study of 1 million men. Eur Heart J 2020;41(15):1503–10 Apr 14. doi:10.1093/eurheartj/ehz774.

[69] Franklin BA, Thompson PD, Al-Zaiti SS, Albert CM, Hivert MF, Levine BD, Lobelo F, Madan K, Sharrief AZ, Eijsvogels TMH. American heart association physical activity committee of the council on lifestyle and cardiometabolic health; council on cardiovascular and stroke nursing; council on clinical cardiology; and stroke council. exercise-related acute cardiovascular events and potential deleterious adaptations following long-term exercise training: placing the risks into perspective-an update: a scientific statement from the american heart association. Circulation 2020;141(13) Mar 31e705-e736. doi:10.1161/CIR.0000000000000749.

[70] Garnvik LE, Malmo V, Janszky I, Ellekjær H, Wisløff U, Loennechen JP, Nes BM. Physical activity, cardiorespiratory fitness, and cardiovascular outcomes in individuals with atrial fibrillation: the HUNT study. Eur Heart J 2020;41(15):1467–75 Apr 14. doi:10.1093/eurheartj/ehaa032.

[71] Framke E, Sørensen JK, Andersen PK, Svane-Petersen AC, Alexanderson K, Bonde JP, Farrants K, Flachs EM, Hanson LLM, Nyberg ST, Villadsen E, Kivimäki M, Rugulies R, Madsen IEH. Contribution of income and job strain to the association between education and cardiovascular disease in 1.6 million Danish employees. Eur Heart J 2020;41(11):1164–78 Mar 14. doi:10.1093/eurheartj/ehz870.

[72] Vaccarino V, Badimon L, Bremner JD, Cenko E, Cubedo J, Dorobantu M, Duncker DJ, Koller A, Manfrini O, Milicic D, Padro T, Pries AR, Quyyumi AA, Tousoulis D, Trifunovic D, Vasiljevic Z, de Wit C, Bugiardini R. ESC scientific document group reviewers. Depression and coronary heart disease: 2018 position paper of the ESC working group on coronary pathophysiology and microcirculation. Eur Heart J 2020;41(17):1687–96 May 1. doi:10.1093/eurheartj/ehy913.

[73] Lüscher TF. Sex and gender and cardiovascular medicine: impact in diabetes, acute coronary syndromes, and heart failure. Eur Heart J 2020;41(13):1311–14 Apr 1. doi:10.1093/eurheartj/ehaa217.

[74] Haider A, Bengs S, Luu J, Osto E, Siller-Matula JM, Muka T, Gebhard C. Sex and gender in cardiovascular medicine: presentation and outcomes of acute coronary syndrome. Eur Heart J 2020;41(13):1328–36 Apr 1. doi:10.1093/eurheartj/ehz898.