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Impact of Lifestyle Interventions on Heart Disease Prevention-Hypertension and Atherosclerotic Cardiovascular Disease.

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Abstract

Background: Cardiovascular disease (CVD), including atherosclerotic cardiovascular disease (ASCVD), represents a major health burden globally. ASCVD involves conditions like coronary artery disease, cerebrovascular disease, and peripheral artery disease, influenced by a range of modifiable risk factors. The American Heart Association's "Life's Essential 8" guidelines address key metrics for reducing ASCVD risk through lifestyle interventions.

Aim: This article aims to review the impact of lifestyle interventions on ASCVD risk and hypertension management, emphasizing dietary patterns, physical activity, and other behavioral modifications.

Methods: A comprehensive review was conducted focusing on the influence of lifestyle changes on ASCVD and hypertension. Key metrics from the AHA's "Life's Essential 8" were evaluated, including dietary habits, physical activity, nicotine exposure, sleep health, body weight, blood lipids, glucose, and blood pressure. The review synthesizes data from epidemiological studies and guidelines to assess the effectiveness of these interventions.

Results: Adhering to the "Life's Essential 8" guidelines significantly reduces ASCVD risk and improves cardiovascular health. Key findings include the effectiveness of healthy dietary patterns (e.g., Mediterranean or DASH diets), regular physical activity, smoking cessation, adequate sleep, and maintaining optimal body weight and blood pressure. Lifestyle modifications are crucial for managing hypertension and preventing its onset, with evidence supporting their benefits both independently and in conjunction with pharmacological treatments.

Conclusion: Lifestyle interventions are essential in mitigating ASCVD and hypertension risks. The "Life's Essential 8" guidelines provide a structured approach to improving cardiovascular health through modifiable behaviors. Adopting these lifestyle changes offers substantial benefits in reducing ASCVD risk and managing hypertension, highlighting the importance of preventive strategies in cardiovascular care.

Keywords: Cardiovascular disease, atherosclerosis, lifestyle interventions, hypertension, "Life's Essential 8", dietary patterns, physical activity, blood pressure.

1. Introduction

Cardiovascular disease (CVD) is a broad term that encompasses conditions affecting the heart and blood vessels, including atherosclerotic CVD (ASCVD) [1]. Atherosclerosis is caused by the accumulation of inflammatory cells, lipids, lipoproteins, extracellular matrix components, and other substances within the arterial walls [2]. ASCVD includes conditions such as coronary artery disease (CAD), also referred to as coronary heart disease (CHD), with clinical manifestations that may present as acute coronary syndrome, myocardial infarction (MI), stable or unstable angina, or require coronary or arterial revascularization procedures. Other associated conditions include cerebrovascular disease (e.g., ischemic stroke, transient ischemic attack, carotid artery stenosis), peripheral artery disease (e.g., intermittent claudication), renal atherosclerotic disease, and aortic atherosclerotic

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disease (e.g., abdominal aortic aneurysm, descending thoracic aneurysm) [3, 4].

Key modifiable risk factors for ASCVD include elevated blood pressure, abnormal lipid profiles, hyperglycemia, and smoking [4,5,6]. The American College of Cardiology/American Heart Association (AHA) Pooled Cohort Equations are used to estimate an individual's 10-year and lifetime risk for ASCVD [4, 7]. This tool incorporates factors such as age, sex, race, total cholesterol, high-density lipoprotein cholesterol (HDL-C), systolic and diastolic blood pressure, use of antihypertensive medication, presence of diabetes, and smoking status [8]. Additional modifiable risk factors for ASCVD include obesity, chronic inflammation, poor dietary habits, excessive alcohol consumption, physical inactivity, and psychosocial factors [4,5,6,7, 9,10,11,12].

Adopting a healthy lifestyle is fundamental to ASCVD prevention [4,5,6,7, 10,11,12,13], as it directly improves major risk factors [6, 7, 10], alongside other contributing factors. Non-pharmacological interventions targeting lifestyle include nutritional modifications, regular physical activity, smoking cessation or avoidance, psychosocial well-being, and sufficient sleep [5,6,7, 12]. Unhealthy behaviors related to diet, physical inactivity, and inadequate sleep can lead to excess adiposity. The AHA's "Life's Essential 8," an update to the "Life's Simple 7," outlines key cardiovascular (CV) health metrics, emphasizing behaviors that influence CV health outcomes. Improvements in these behaviors and CV health metrics are associated with a lower risk of CVD, increased longevity, and enhanced quality of life [12].

Life Essential 8 Rule:

Life's Essential 8 is a comprehensive set of guidelines developed by the American Heart Association (AHA) aimed at promoting optimal cardiovascular health. It represents an updated version of the earlier "Life's Simple 7" and outlines eight key metrics that individuals can target to reduce their risk of cardiovascular disease (CVD) and improve overall health. These metrics are based on the latest research and emphasize both health behaviors and health factors. The eight essential components are:

1. **Dietary habits**: Following a heart-healthy eating pattern, such as the Mediterranean or DASH (Dietary Approaches to Stop Hypertension) diets, which emphasize fruits, vegetables, whole grains, lean proteins, and healthy fats.
2. **Physical activity**: Engaging in at least 150 minutes of moderate-intensity exercise or 75 minutes of vigorous-intensity exercise per week.
3. **Nicotine exposure**: Avoiding tobacco use and minimizing exposure to secondhand smoke. For smokers, cessation support is encouraged.
4. **Sleep health**: Getting 7 to 9 hours of sleep per night to promote overall well-being and cardiovascular health.
5. **Body weight**: Maintaining a healthy body mass index (BMI) of less than 25 kg/m², which is associated with lower risk of CVD.
6. **Blood lipids**: Keeping non-HDL cholesterol levels below 130 mg/dL to reduce the risk of atherosclerotic cardiovascular disease (ASCVD).
7. **Blood glucose**: Maintaining fasting blood glucose levels below 100 mg/dL and HbA1c levels below 5.7% to prevent the onset of diabetes and related CVD risks.
8. **Blood pressure**: Achieving and maintaining a blood pressure below 120/80 mm Hg, which is considered optimal for heart health.

Life's Essential 8 emphasizes the importance of these interrelated factors in promoting long-term heart health and preventing cardiovascular diseases, such as heart attacks, strokes, and atherosclerosis. By focusing on these metrics, individuals can significantly improve their cardiovascular outcomes and overall quality of life.

Lifestyle Interventions and Atherosclerotic Cardiovascular Disease Outcomes

Effective lifestyle interventions are critical in reducing the risk of atherosclerotic cardiovascular disease (ASCVD). A variety of health behaviors have been identified as essential for achieving optimal cardiovascular health outcomes. These behaviors include adhering to a healthy diet, engaging in regular physical activity, maintaining a healthy body weight, managing lipid levels, and ensuring proper glucose control. Collectively, these lifestyle changes contribute to lowering the risk of ASCVD and improving overall health metrics.

Behaviors for Achieving Optimal Scores

To attain optimal cardiovascular health, specific behaviors are recommended. A key element is following a healthy dietary pattern, such as the Mediterranean or DASH diet, both of which are associated with significant cardiovascular benefits. Regular physical activity is also crucial, with a minimum of 150 minutes per week of moderate exercise or 75 minutes per week of vigorous exercise being advised. Additionally, individuals should aim to maintain a body mass index (BMI) below 25 kg/m², as this is associated with reduced cardiovascular risk.

Metrics for Optimal Scores

Several metrics serve as benchmarks for achieving optimal health outcomes. Blood lipid levels, specifically non-HDL cholesterol, should be

maintained below 130 mg/dL to reduce the risk of ASCVD. Nicotine exposure is another critical factor, with individuals who have never smoked reporting the lowest risk; for smokers, cessation support is highly encouraged. Blood glucose and HbA1c levels are also key indicators, with targets of fasting blood glucose below 100 mg/dL or HbA1c below 5.7%, in the absence of diabetes. Adequate sleep, ranging between 7 to 9 hours per night, is important for overall health and ASCVD prevention. Lastly, maintaining a blood pressure below 120/80 mm Hg is essential for optimal cardiovascular outcomes.

Cardiovascular Diseases (CVD) and Mortality:

Cardiovascular disease (CVD) remains a major threat to global health, ranking as the leading cause of death and morbidity worldwide. This broad spectrum of conditions affects both the heart and blood vessels, including coronary artery disease, stroke, heart failure, and hypertension. Despite advances in medical science and public health initiatives, CVD continues to place a significant burden on individuals and healthcare systems, presenting ongoing challenges for disease prevention and management. One of the defining characteristics of CVD is its gradual progression, often developing silently over many years before manifesting as acute events, such as heart attacks or strokes. This slow development underscores the importance of proactive screening, early detection, and robust management strategies to mitigate its impact. Furthermore, the burden of CVD is unevenly distributed, with certain populations, such as older adults, individuals with a family history of the disease, and those from lower-income groups, being disproportionately affected. Modifiable risk factors, including tobacco use, poor diet, physical inactivity, obesity, and excessive alcohol consumption, significantly contribute to the high incidence of CVD. Managing these risk factors through lifestyle modifications and targeted therapies is a critical component of preventive efforts.

Dietary habits play a crucial role in shaping cardiovascular health, with significant implications for overall well-being. Extensive scientific research has explored the intricate relationship between dietary patterns and the development of cardiovascular diseases, providing compelling evidence that emphasizes the importance of food choices in preventing cardiovascular complications. Dietary patterns encompass not just the intake of individual nutrients, but the overall composition and combination of foods consumed over time. While individual nutrients certainly impact heart health, the cumulative effect of these dietary patterns has emerged as a vital determinant of cardiovascular outcomes. Understanding how different dietary patterns affect cardiovascular health is essential for developing effective preventive strategies to address the growing global burden of CVD. This understanding sets the stage for further exploration into the complex interplay between nutrition and heart health, highlighting the critical role that diet plays in influencing cardiovascular outcomes.

Preventive strategies aimed at promoting overall well-being and longevity place a strong emphasis on nutrition and lifestyle choices. These strategies function as preventive measures, designed to halt the onset or progression of various health conditions, ranging from mental health disorders to chronic diseases. Individuals can significantly reduce their risk of developing conditions such as cardiovascular diseases, diabetes, obesity, and certain cancers by adopting healthy eating habits and making informed lifestyle choices. These strategies not only prevent illness but also enhance energy levels, cognitive function, and emotional resilience. The adoption of preventive measures fosters a culture of self-care and wellness, ultimately contributing to the creation of a healthier society. Through the implementation of these strategies, individuals are empowered to make informed decisions about their diet and daily routines, laying the foundation for a comprehensive investigation into the methods of preventive healthcare.

In the pursuit of optimal health, the combination of physical activity and dietary interventions is essential. While dietary changes focus on managing caloric intake and ensuring nutritional balance, physical activity plays a complementary role in improving overall health outcomes. Scientific evidence supports the synergistic effects of both interventions in weight management, disease prevention, and overall well-being. Physical activity not only accelerates calorie expenditure but also regulates metabolism, promoting sustainable weight loss and maintenance. Additionally, regular exercise supports cardiovascular health, strengthens muscles and bones, and enhances mood and cognitive function. When combined with dietary adjustments, this holistic approach to health management addresses both aspects of the energy balance equation. Acknowledging the interdependent relationship between physical activity and dietary modifications highlights the importance of adopting comprehensive lifestyle strategies for achieving optimal health and vitality.

Lifestyle choices play a crucial role in determining cardiovascular health outcomes. In an era characterized by increasing stress, poor dietary habits, and sedentary lifestyles, understanding how these factors influence cardiovascular health is essential. Numerous studies have demonstrated the clear connection between lifestyle factors—such as nutrition, physical activity, smoking, and stress management—and the prevalence of cardiovascular conditions, including heart attacks, strokes, and hypertension. Beyond traditional risk factors such as age and genetics, lifestyle choices represent modifiable variables that can either significantly reduce or increase the risk of developing CVD. In

response, public health initiatives are placing greater emphasis on interventions and educational programs that promote healthier lifestyles. Encouraging individuals to adopt healthier behaviors holds the potential to drastically reduce the incidence of cardiovascular diseases and improve overall public health.

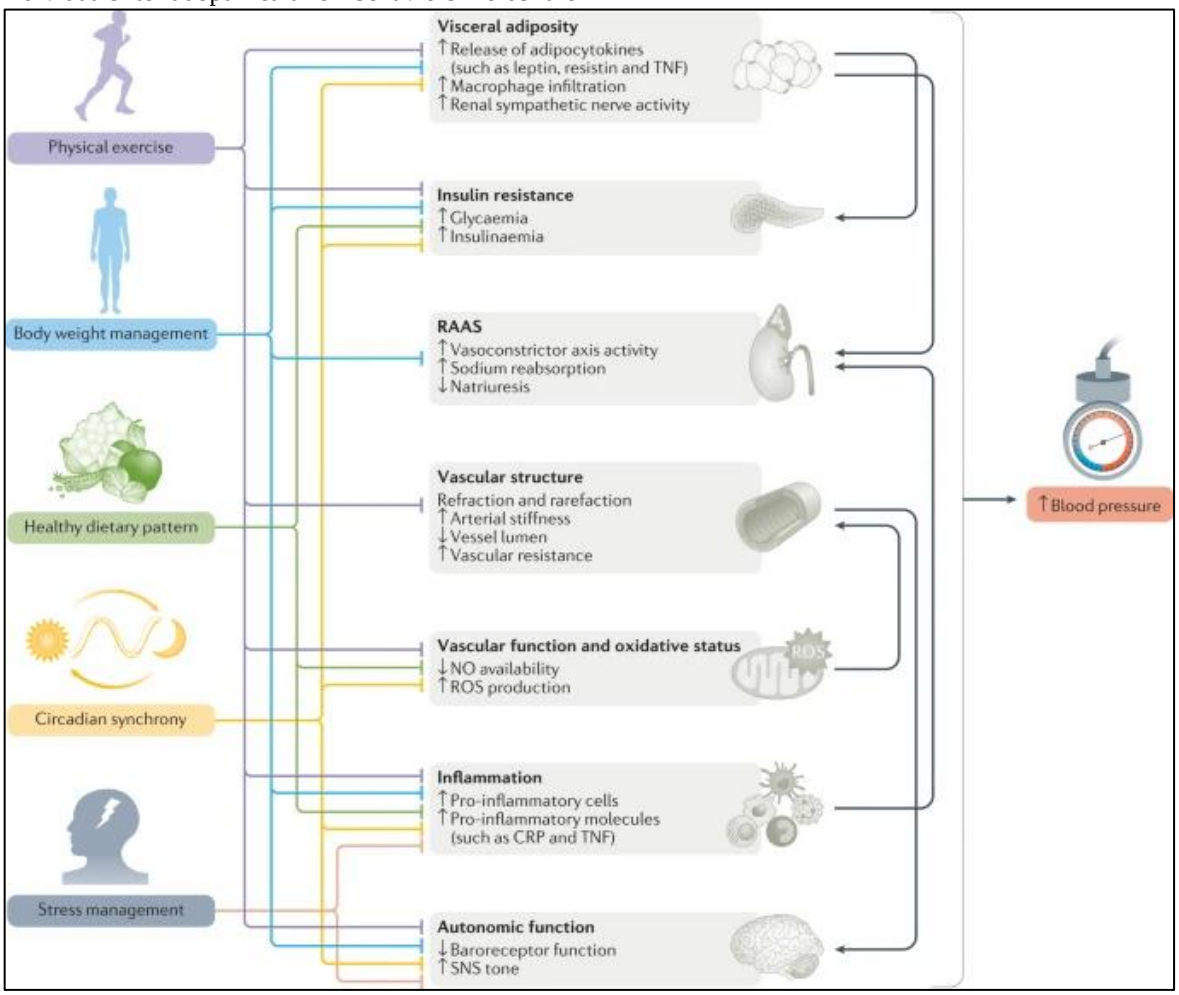

Figure 1: Lifestyle interventions and cardiovascular disorders and Specifically blood pressure.

Life Interventions and Hypertension:

Approximately one-third of the global adult population is affected by arterial hypertension, traditionally defined as a clinic or office blood pressure (BP) of ≥140/90 mmHg [13]. Over the past decade, deaths attributable to high BP have surged by 56.1%, marking hypertension as a major contributor to premature mortality worldwide, despite significant advancements in pharmacological treatments [14]. The direct medical costs related to hypertension management globally are estimated to be US$370 billion annually, with the potential healthcare savings from effective treatment projected at approximately $100 billion per year [15]. Recent changes in international guidelines, however, may lead to an increase in the prevalence of hypertension. The 2017 ACC/AHA guidelines lowered the threshold for defining hypertension to 130/80 mmHg, categorizing stage 1 hypertension as an office systolic BP (SBP) of 130–139 mmHg, and stage 2 as SBP of ≥140 mmHg [16]. In contrast, the 2018 ESC/ESH guidelines classify an SBP of 130–139 mmHg as 'high-normal' [17]. Consequently, many individuals who were not previously considered hypertensive may now be placed on treatment, likely resulting in a rise in those undergoing hypertension management.

Prioritizing lifestyle interventions, such as exercise, weight reduction, and healthy dietary practices, is essential for the prevention and management of hypertension, particularly in light of these more stringent thresholds. This approach is especially crucial for individuals with higher cardiovascular risk phenotypes, such as resistant hypertension. Both the ACC/AHA and ESC/ESH guidelines strongly advocate for lifestyle modifications in managing hypertension, emphasizing interventions with proven effectiveness in lowering BP, including regular physical exercise, weight loss, moderation of alcohol intake, and the adoption of low-sodium, high-potassium diets. However, other approaches, such as guided breathing, yoga, transcendental meditation, and

biofeedback, lack robust evidence for long-term BP reduction. This review provides an overview of the epidemiological research supporting the benefits of major lifestyle interventions for preventing and treating hypertension and discusses the key physiological mechanisms that contribute to these benefits.

While both genetic and lifestyle factors contribute to increased BP levels, lifestyle choices can significantly influence BP beyond genetic predisposition. To explore whether lifestyle factors can mitigate the BP effects of an adverse genetic profile, Pazoki et al. developed a genetic risk score for high BP based on 314 known BP loci and applied it to 277,005 individuals from the UK Biobank, aged 40–69 years, with a median follow-up of approximately six years [18]. The researchers also assessed participants based on lifestyle factors such as BMI, diet, sedentary behavior, alcohol consumption, smoking status, and urinary sodium excretion at recruitment, analyzing the relationship between genetic risk, lifestyle scores, and BP levels. The findings revealed that a healthy lifestyle was strongly inversely associated with both SBP and diastolic BP (DBP) across all genetic risk categories. On average, individuals with favorable lifestyles had SBP readings 4–5 mmHg lower than those with unfavorable lifestyles, supporting the notion that population-wide efforts to reduce BP through lifestyle modifications are effective.

Additional evidence from non-westernized populations, where hypertension rates and age-related BP increases are minimal, and CVD prevalence is low despite the lack of pharmacological treatment, further underscores the role of lifestyle factors in preventing hypertension [19-23]. These low rates of hypertension and CVD in non-westernized populations are partly attributable to traditional dietary patterns and lifestyles, which resemble those that characterized most of human evolutionary history. These include non-westernized dietary patterns, regular physical activity, natural sleep–wake cycles, and sun exposure, all of which influence BP levels and hypertension risk. These factors, discussed in detail in the following sections, highlight the importance of lifestyle interventions in managing and preventing hypertension.

Drugs and Lifestyle Interventions:

Lifestyle habits play a crucial role in both the prevention and treatment of hypertension and should be considered alongside antihypertensive medical treatments. In some cases, an optimal lifestyle can serve as a first-line treatment for hypertension. The ESC/ESH guidelines recommend that individuals with mild hypertension follow lifestyle modifications as the sole treatment for the first 3–6 months after diagnosis. If BP is not adequately controlled after this period, pharmacological treatment may then be introduced [17]. Importantly, the benefits of lifestyle interventions should not be disregarded when antihypertensive treatments are used, as these interventions remain a fundamental aspect of hypertension management regardless of medical treatment. For example, physical exercise has been shown to improve BP in individuals whether or not they are undergoing pharmacological treatment [24]. In fact, exercise can significantly lower BP even in those taking multiple medications, including individuals with resistant hypertension [25].

Similarly, dietary changes, such as adopting the Dietary Approaches to Stop Hypertension (DASH) diet, have been found effective in reducing BP in people both with and without hypertension, as well as in those receiving or not receiving antihypertensive medication [26]. A reduction in sodium intake, one of the most common dietary recommendations for hypertension management, is also a powerful strategy for lowering BP, and its effects can complement those of pharmacological treatments [27]. For instance, reducing sodium intake in patients aged 60–80 years who were on one antihypertensive medication resulted in lower BP and reduced the incidence of elevated BP or the need for resuming medication during a 28-month follow-up after stopping the medication [28]. Likewise, weight reduction has been identified as a beneficial strategy for hypertensive patients, regardless of whether they are receiving medication, with particularly strong benefits observed in those undergoing medical treatment [29]. The following sections will examine the lifestyle interventions endorsed by the ACC/AHA [16] and ESC/ESH [17] guidelines for preventing and treating hypertension, which are supported by substantial evidence. These interventions include physical exercise, body weight management, healthy dietary patterns, circadian rhythm alignment, adequate sleep, and stress management. We will review the current evidence on the most impactful lifestyle factors for lowering BP and reducing the risk of hypertension.

Physical Activity:

Physical exercise, although historically receiving less attention in clinical settings compared to drug therapy, is highly recommended by various medical guidelines, including those from the Seventh and Eighth US Joint National Committees, ACC, AHA, ESC, ESH, American College of Sports Medicine, and the Canadian Hypertension Education Program, for both the prevention and management of hypertension [30]. A 2019 umbrella review encompassing 18 meta-analyses and systematic reviews, which included a total of 594,129 adult participants, provided robust evidence supporting the role of physical activity in preventing hypertension in individuals with normal blood pressure and reducing blood pressure in those with pre-hypertension or hypertension [31]. Additionally, a meta-analysis of longitudinal studies indicated that individuals who meet the recommended physical activity levels

outlined in international guidelines have a 6% lower risk of developing hypertension compared to those with sedentary lifestyles [32]. The evidence also suggests an inverse dose-response relationship between physical activity levels and the risk of developing hypertension, with no upper limit to the amount of physical activity that provides benefit [31,32]. Furthermore, a network meta-analysis of 391 randomized controlled trials (RCTs), including 39,742 individuals, found that exercise interventions and antihypertensive drugs were similarly effective in lowering systolic blood pressure (SBP) in individuals with hypertension (SBP ≥140 mmHg) [33].

In patients with resistant hypertension, physical exercise has demonstrated significant benefits, though additional research is necessary to confirm these findings [34]. Higher levels of physical activity have been correlated with a reduced risk of cardiovascular disease (CVD) in individuals with resistant hypertension [35,36], and two RCTs reported that exercise interventions resulted in a 24-hour ambulatory BP reduction, with an average decrease of 20 mmHg in SBP and 10 mmHg in diastolic blood pressure (DBP) in this population [37]. Moreover, meta-analytical evidence indicates that moderate exercise during pregnancy is associated with a significantly lower risk of gestational hypertensive disorders [38,39].

Various exercise modalities have been shown to effectively reduce blood pressure (BP) in individuals with hypertension. Both an umbrella review and a network meta-analysis concluded that the primary forms of exercise—endurance (or aerobic) exercise, resistance (or strength) exercise, and a combination of these—are equally beneficial for lowering BP [33]. While endurance exercise is the most frequently prescribed form of exercise for patients with hypertension, the clinical benefits of resistance exercise, such as weightlifting, or the combination of endurance and resistance exercises remain less explored. However, these modalities have been shown to elicit similar or even greater BP reductions than endurance exercise alone (with reductions of 8.7 mmHg for endurance exercise, 7.2 mmHg for resistance exercise, and 13.5 mmHg for combined exercise) [40,41].

Additionally, emerging evidence suggests that isometric resistance exercises, such as handgrip exercises, may be effective in reducing BP, despite previous associations with acute hypertensive responses. Studies indicate that isometric exercises can lead to decreases in systolic blood pressure (SBP) of 6–8 mmHg and diastolic blood pressure (DBP) of 3–4 mmHg [42,43]. A 2019 meta-analysis demonstrated that isometric resistance exercises result in BP reductions comparable to those seen with endurance or resistance exercises, with a mean decrease of 5.7 mmHg in SBP across individuals with or without hypertension [43]. However, when focusing specifically on individuals with hypertension, the BP reduction (4.9 mmHg) did not reach statistical significance.

Exercise Intensity:

Research indicates that both moderate- and high-intensity exercises have comparable benefits for reducing blood pressure (BP) [43]. However, high-intensity exercise might be more effective in mitigating the pathophysiological mechanisms that contribute to hypertension, such as arterial stiffness [44]. Despite this, a 2019 systematic umbrella review found insufficient evidence to definitively determine the impact of exercise intensity on BP [19].

Mechanisms:

Obesity, independent of other cardiometabolic conditions, is linked to an increased risk of hypertension. This association is primarily due to the compression of kidneys by visceral, perirenal, and renal sinus fat, as well as heightened renal sympathetic nerve activity leading to activation of the renin–angiotensin–aldosterone system (RAAS) [45]. Additionally, excess adipose tissue, particularly visceral fat, produces and secretes adipocytokines such as tumor necrosis factor (TNF), resistin, and leptin, which contribute to inflammation and increased hypertension risk [47]. Leptin further exacerbates hypertension by stimulating renal sympathetic nerve activity via the melanocortin 4 receptor (MC4R) pathway [46]. Research has shown that individuals with MC4R loss-of-function mutations experience reduced adrenergic activity and a lower likelihood of developing hypertension [48]. Exercise interventions can effectively reduce visceral fat, which is more likely to induce insulin resistance and inflammation compared to subcutaneous fat [50-52].

Insulin resistance and subsequent hyperinsulinemia are traditionally associated with elevated hypertension risk. Population studies have shown correlations between these metabolic disturbances and increased BP in individuals with obesity and metabolic syndrome [54]. For instance, in a Japanese cohort, worsening glucose metabolism stages were linked to higher hypertension prevalence, with hyperglycemia and hyperinsulinemia contributing significantly to hypertension risk [55]. However, in the absence of obesity, the association between insulin resistance and hypertension is weaker, suggesting that obesity, particularly excess visceral fat, is a significant confounder [56-57]. While hyperinsulinemia can acutely increase renal tubular sodium reabsorption and sympathetic nervous system (SNS) activity, these effects do not consistently translate into increased BP in non-obese individuals or in non-rodent animal models [54]. Nonetheless, insulin resistance's metabolic effects, including hyperglycemia and dyslipidemia, can

exacerbate pre-existing hypertension [54]. Exercise has been shown to improve insulin sensitivity, glucose control, and overall metabolic health [58-60]. The RAAS plays a central role in BP regulation and is a critical target for hypertension treatment [61]. The RAAS comprises two main axes: the classic vasoconstrictive axis (renin–angiotensin-converting enzyme (ACE)–angiotensin II (Ang II)–type 1 Ang II receptor) and the opposing vasorelaxant axis (ACE2–Ang 1–7–Mas receptor) [50]. Imbalances between these axes can contribute to hypertension. However, evidence from a meta-analysis does not support a significant role for physical exercise in targeting the RAAS [63]. While exercise interventions (≥4 weeks) have been shown to reduce plasma renin activity and BP, no significant relationship was observed between improvements in these markers and plasma levels of Ang II or aldosterone. Structural changes in microcirculatory beds contribute to increased vascular resistance in hypertension, primarily through vessel remodeling and rarefaction [64-65]. Hypertension also leads to reduced diameter and increased wall thickness of large peripheral arteries [66]. Regular exercise has been shown to counteract these effects, resulting in increased luminal diameter of conduit and resistance arteries, as well as enhanced capillary density in skeletal muscles [67]. Exercise training can also reduce carotid intima–media thickness in hypertensive patients [68].

Vascular endothelial dysfunction (VED) is a reversible condition marked by impaired endothelium-dependent vasodilation and inflammatory activation [69-70]. VED may contribute to hypertension, although its influence is less clear compared to its role in atherosclerosis [70]. Reduced nitric oxide (NO) bioavailability is a key feature of VED in hypertension and may diminish NO's inhibitory effects on endothelin 1, a potent vasoconstrictor [71]. Increased production of reactive oxygen species and heightened inflammation also play a role in VED [72]. Oxidative stress can inactivate NO and oxidize LDL particles, leading to endothelial cell toxicity and leukocyte migration [73-74]. Meta-analytical evidence shows that exercise improves endothelial function, typically assessed by flow-mediated dilation of the brachial artery, and arterial stiffness, measured by pulse wave velocity and augmentation index [75-76]. The benefits of exercise on endothelial function and arterial stiffness have been confirmed in individuals with pre-hypertension and hypertension [77-79]. However, aerobic exercise alone for 8 months did not significantly reduce arterial stiffness in children with excess body weight, suggesting that longer interventions or additional body weight reduction may be necessary [80]. Exercise enhances NO bioavailability, potentially due to improved redox homeostasis and reduced inflammation, mediated by downregulation of nuclear factor-κB (NF-κB) signaling [82]. It also stimulates the production of vasodilatory and angiogenic agents through increased shear stress [83]. Exercise training has been shown to improve redox status across various populations, including hypertensive women aged 60–75 years [84-85].

Chronic systemic inflammation plays a significant role in the pathophysiology of hypertension. Elevated levels of inflammatory biomarkers, such as C-reactive protein (CRP), high-sensitivity CRP (hsCRP), and interleukin-6 (IL-6), are associated with an increased risk of developing hypertension [86-87]. Inflammation can also increase activity in the renin–angiotensin–aldosterone system (RAAS) vasoconstrictor axis, with IL-6 being particularly implicated in Ang II-mediated hypertension [88]. Mechanistic evidence further supports a causal link between inflammation and hypertension. Activation of the innate immune system following arterial wall injury can trigger an inflammatory response, involving Toll-like receptors (TLRs) such as TLR4 in endothelial cells and leukocytes. This response leads to increased production of inflammatory cytokines and reactive oxygen species [89]. Physical inactivity is a known cause of chronic systemic inflammation [90], while regular exercise has anti-inflammatory effects. A meta-analysis indicates that exercise training is associated with reduced circulating levels of CRP, regardless of age or sex [91]. The anti-inflammatory effects of exercise are largely mediated by myokines.

Muscle tissues act as endocrine organs, secreting peptides known as myokines, which can have beneficial effects on cardiovascular health and BP [92]. For example, exercise-induced IL-6 has anti-inflammatory properties by promoting production of anti-inflammatory cytokines and reducing pro-inflammatory factors [93-94]. Other myokines, such as irisin, have been shown to reduce BP through mechanisms not directly related to anti-inflammatory effects. Irisin, for instance, can stimulate vasorelaxation and reduce BP in hypertensive rats by activating the AMP-activated protein kinase (AMPK)–AKT–endothelial NO synthase (eNOS)–NO pathway and ATP-sensitive potassium channels in smooth muscle [95-96]. However, findings regarding the relationship between irisin and BP are mixed, with some studies showing positive associations in specific populations, while others report no significant association [97-100]. Regular exercise also reduces levels of leptin and pro-inflammatory adipokines like omentin and resistin, even without major body weight reductions [102-103]. These effects contribute to the overall benefits of exercise in individuals with hypertension and other chronic diseases [104-106]. Nevertheless, more research is needed to fully understand these effects.

The autonomic nervous system plays a crucial role in modulating BP through SNS and parasympathetic nervous system (vagal) activity.

Chronic SNS activation is common in individuals with hypertension, and impaired carotid baroreceptor function may contribute to this neurogenic component of hypertension [107-108]. Exercise training has been shown to counteract autonomic dysfunction by increasing vagal tone and decreasing SNS tone [109]. It also improves arterial baroreflex control, which helps to reduce BP in both healthy individuals and those with hypertension [110-111]. These benefits are attributed to both mechanical mechanisms (e.g., reduced vascular stiffness) and neural adaptations (e.g., improved baroreflex control) [112].

Body Weight and Obesity:

Overweight and obesity are significant risk factors for hypertension. A meta-analysis of prospective studies involving 173,828 participants found that individuals with overweight had a 52% higher risk (RR 1.52, 95% CI 1.37–1.67) and those with obesity had a 117% higher risk (RR 2.17, 95% CI 1.84–2.50) of developing hypertension compared to individuals with normal body weight [112]. Reducing body weight to normal levels can substantially lower the risk of hypertension: by 24–40% for overweight individuals and 40–54% for those with obesity [100]. Similarly, a meta-analysis of 25 randomized controlled trials (RCTs) demonstrated that each kilogram of body weight lost was associated with a reduction of approximately 1 mmHg in both systolic blood pressure (SBP) and diastolic blood pressure (DBP) [17]. A prospective study of around 14,000 individuals found that weight loss reduced the risk of uncontrolled hypertension among those with hypertension and overweight or obesity [113].

Strategies for body weight management, including energy-restricted diets and physical exercise, are crucial for hypertension prevention and management. A meta-analysis found that weight loss interventions, including energy-restrictive diets, resulted in greater reductions in SBP (5 mmHg) and DBP (4 mmHg) compared to exercise interventions alone (2 mmHg) [17]. However, when results were adjusted for the amount of body weight lost, the impact of diet and exercise on BP reduction was similar, especially for DBP [17]. A Cochrane review and meta-analysis involving eight studies and 2,100 participants with high BP found moderate-quality evidence that hypocaloric dietary interventions led to a significant reduction in body weight (mean difference of −4.0 kg) and BP (SBP reduction of 4.5 mmHg and DBP reduction of 3.2 mmHg) compared to no dietary intervention [114]. Despite these findings, the evidence regarding BP reduction from body weight-reducing diets was of low quality due to the small number of participants and studies included. The review concluded that while body weight-reducing diets are effective in reducing both body weight and BP in people with primary hypertension, the magnitude of these effects remains uncertain [114].

Mechanisms of Body Weight Management in Hypertension:

Excessive adiposity, particularly visceral fat, is a major risk factor for hypertension. A high Body Mass Index (BMI) with excessive visceral fat correlates strongly with hypertension [115-116]. Intentional body weight reduction has beneficial effects on hypertension through various mechanisms. Insulin resistance is closely linked to adiposity and obesity, with visceral fat being the strongest correlate [117]. Moderate body weight reductions (average 9%) significantly decrease insulin resistance (26% reduction in HOMA-IR) and both systolic (7 mmHg) and diastolic blood pressure (6 mmHg) [118]. In obese individuals with diabetes, a 10% reduction in BMI improves insulin sensitivity and reduces circulating levels of leptin and resistin [119]. Long-term weight reduction alters cytokine gene expression in peripheral immune cells, enhancing insulin sensitivity, though its impact on BP needs further investigation [120-121].

Moderate weight loss (<10%) reduces RAAS activity and BP in individuals with obesity. For instance, a 5% reduction in body weight decreases plasma angiotensinogen (27%), renin (43%), and aldosterone (31%), and reduces angiotensin-converting enzyme (ACE) activity by 12% [122-123]. Bariatric surgery-induced weight loss also reduces RAAS components but does not always correlate with BP reductions [124]. Obesity is associated with impaired endothelial function, whereas weight loss improves it. Each 10-kg weight decrease correlates with a 1.1% increase in flow-mediated dilatation [125-126]. However, the translation of these improvements into BP reductions needs further study. Body weight loss also reduces oxidative stress, but its impact on BP requires more research [127]. Obesity leads to higher levels of pro-inflammatory adipokines and systemic inflammation. Adipokines such as leptin and resistin, and dysfunction of perivascular adipose tissue (PVAT) contribute to inflammation and vascular dysfunction [128-131]. Weight reduction decreases pro-inflammatory factors and increases anti-inflammatory molecules, with even modest reductions in body weight reducing plasma inflammatory markers [132-133]. Long-term weight loss maintains these benefits, improving inflammation and BP [134-136]. Preclinical studies suggest weight loss reverses PVAT damage, enhancing nitric oxide synthase activity [137]. Increased sympathetic nervous system (SNS) activity plays a role in obesity-related hypertension. Body weight reduction, with or without exercise, reduces SNS activity and improves baroreflex sensitivity [138-144]. Obstructive sleep

apnea (OSA), common in obesity, exacerbates hypertension through chronic hypoxia and SNS activation [145]. Weight loss benefits include reduced SNS activity and improved baroreflex sensitivity, though some effects on BP may be independent of SNS changes [146-148].

Healthy Dietary Patterns for Hypertension Management:

Sodium and Potassium Intake:

Sodium restriction is a well-established recommendation for preventing and managing hypertension. A 2020 meta-analysis revealed that sodium reduction leads to a significant decrease in blood pressure (BP), with a dose-response relationship observed. The reduction in systolic BP (SBP) and diastolic BP (DBP) correlates with the amount of sodium reduced, with greater effects in older populations, non-white populations, and those with higher BP [150-151]. However, for individuals with lower baseline BP, the benefits may be less pronounced due to compensatory increases in circulating aldosterone, renin, and noradrenaline [152]. Some studies suggest a U-shaped or J-shaped curve relationship between sodium intake and mortality, indicating potential adverse effects of very low sodium intake [153-154]. Despite these findings, the evidence generally supports sodium reduction as beneficial for cardiovascular health [15]. The effects of sodium intake on BP also depend on concomitant water intake, with salt-induced BP increases potentially mitigated by adequate water consumption [155].

Potassium is essential for maintaining fluid balance and normal cell function. Historically, potassium intake was much higher, but modern diets, often high in processed foods, are lower in potassium [158]. Current intake levels in many countries are below recommended values [159-161]. Potassium supplementation has been shown to lower BP, especially in hypertensive individuals, with average reductions of 6.8 mmHg in SBP and 4.6 mmHg in DBP [162]. A meta-regression analysis confirmed that increased potassium excretion and a lower sodium-to-potassium ratio are associated with BP reduction [162]. The implementation of potassium-enriched salt substitutes has also demonstrated BP-lowering effects and reduced hypertension incidence [163-164]. A diet with a sodium-to-potassium molar ratio of approximately one-to-one is considered beneficial for health [147].

Dietary Approaches:

The Dietary Approaches to Stop Hypertension (DASH) diet, introduced in 1997, has been shown to effectively manage hypertension. The PREMIER trial demonstrated that the DASH diet leads to significant BP reductions compared to lifestyle advice alone [166-167]. The ENCORE trial also found that the DASH diet significantly decreased BP in individuals with pre-hypertension or stage 1 hypertension [168]. A meta-analysis of 30 randomized controlled trials (RCTs) confirmed that the DASH diet is effective in lowering BP [14]. Long-term benefits include sustained reductions in SBP even after the intervention period [169-170].

The Mediterranean diet, rich in fruits, vegetables, olive oil, and nuts, has been associated with reduced hypertension risk. A study of Spanish individuals found that high adherence to this diet was linked to decreases in mean SBP and DBP [171-172]. The PREDIMED RCT showed that Mediterranean diets enriched with extra-virgin olive oil or nuts resulted in BP reductions compared to a low-fat control diet [173-174]. Additional studies have reported modest BP reductions and improved endothelial function among older adults following the Mediterranean diet [175-176]. However, more research is needed to quantify its effects and establish its efficacy in diverse populations [159].

Vegan diets, which exclude all animal products, have gained popularity and are associated with several health benefits, including improved glycaemia and blood lipid profiles. The evidence regarding their effect on blood pressure (BP) is less conclusive. A meta-analysis of 983 individuals found that a vegan diet without calorie restrictions did not significantly change systolic BP (SBP) or diastolic BP (DBP) compared to less restrictive diets [177]. However, in a subgroup analysis of studies involving participants with a baseline SBP of ≥130 mmHg, vegan diets were found to significantly reduce both SBP (by 4.1 mmHg) and DBP (by 4.0 mmHg) [177]. This suggests that while the overall effect of vegan diets on BP might be modest, they could be beneficial for individuals with higher baseline BP.

Numerous dietary approaches have demonstrated BP-lowering effects compared to control interventions. A network meta-analysis found that both low-fat diets (e.g., Ornish diet) and low-carbohydrate diets (e.g., Atkins, South Beach, Zone diets) were effective in reducing SBP (5.1 mmHg for both low-fat and low-carbohydrate diets) and DBP (3.2 mmHg and 2.9 mmHg, respectively) in the medium term (6 months) [178]. The effects of these diets tended to diminish over the long term (12 months). Among individual diets, the Palaeolithic diet was particularly effective in decreasing SBP (14.6 mmHg) and DBP (3.3 mmHg), while the Atkins diet also showed significant reductions in BP [178]. The DASH diet, which emphasizes low sodium and high potassium intake, was also highly effective, with reductions of 4.7 mmHg in SBP and 2.8 mmHg in DBP [178].

A systematic review and meta-analysis involving 23,858 participants found that various dietary interventions resulted in overall decreases of 3.1 mmHg in SBP and 1.8 mmHg in DBP [179]. The DASH diet was the most effective, showing reductions of 7.6 mmHg in SBP and 4.2 mmHg in DBP. Other effective diets included low-sodium,

low-sodium–high-potassium, low-sodium–low-calorie, and low-calorie diets. The Mediterranean diet, while showing significant reductions in DBP, did not significantly lower SBP in this review [179]. Another network meta-analysis reviewed 67 trials comparing 13 dietary approaches (including DASH, low-fat, Mediterranean, Palaeolithic, and others) with 17,230 participants [180]. This analysis ranked the DASH diet as the most effective for reducing both SBP and DBP, followed by the Palaeolithic, low-carbohydrate, and Mediterranean diets. Overall, the DASH diet remains the most effective dietary approach for managing BP in individuals with pre-hypertension or hypertension [180].

Dietary Compounds and Hypertension:

Current dietary guidelines emphasize the intake of certain food groups to prevent hypertension, including whole grains, fresh fruits, vegetables, nuts, and legumes. Conversely, high intakes of red and processed meats and sugar-sweetened beverages (SSBs) are discouraged [4, 5]. Evidence supports these guidelines:

- **Whole Grains, Fruits, Nuts, and Dairy Products:** A meta-analysis indicated an inverse association between hypertension risk and the intake of 30 g of whole grains, 100 g of fruit, 28 g of nuts, and 200 g of dairy products daily [181].
- **Red and Processed Meats, SSBs:** Conversely, higher intake of 100 g of red meat, 50 g of processed meat, and 250 ml of SSBs per day is positively associated with increased hypertension risk [181]. However, the quality of this evidence is often low.
- **Eggs and Meat Consumption:** A large meta-analysis found that red meat (both processed and unprocessed) and poultry are linked to a higher risk of hypertension, whereas egg consumption is associated with a lower risk [182]. Despite this, a meta-analysis of eight RCTs found no significant difference in BP effects between consuming more than four whole eggs per week versus fewer [183]. Similarly, a meta-analysis of 14 RCTs found that substituting a high-carbohydrate diet with one high in monounsaturated fatty acids did not significantly impact BP [184].

Sugar Intake

Increased sugar intake, particularly over periods longer than 8 weeks, is associated with elevated BP [185]. High fructose consumption may enhance sodium absorption and activate renal sympathetic nerve activity and the RAAS [186]. Evidence links SSB consumption with hypertension, with each additional serving per day increasing the risk by 8% [187-188]. Reducing SSB consumption is associated with lower BP (1.8 mmHg for SBP and 1.1 mmHg for DBP per daily serving) [189-191]. Additionally, artificially sweetened beverages have been linked to a 9% increase in hypertension risk per additional serving per day [188].

Alcohol

There is strong evidence that excessive alcohol intake adversely affects BP. A meta-analysis of longitudinal studies involving 361,254 participants concluded that intake beyond two drinks per day (12 g of pure ethanol per drink) is consistently linked to increased hypertension incidence in both men and women [192]. Even low alcohol intake (around one drink per day) is associated with a higher prevalence of cardiovascular disease, including hypertension [193]. Reducing alcohol intake is recommended by both ACC/AHA and ESC/ESH guidelines for hypertension management. A meta-analysis of 36 trials found that alcohol reduction was not associated with BP reductions in individuals with moderate consumption (two or fewer drinks per day) but led to significant BP reductions in those with higher consumption (1.2 mmHg decrease in SBP and 1.1 mmHg in DBP for three drinks per day, and 5.5 mmHg and 4.0 mmHg for more than six drinks per day) [194].

Mechanisms

1. **Adiposity:** Westernized diets, high in processed foods, fats, sugars, and salts, contribute to obesity, which is a known risk factor for hypertension [195].
2. **Insulin Resistance:** Western diets high in energy but low in essential micronutrients like magnesium may contribute to insulin resistance [196-197]. Magnesium supplementation has been shown to reduce BP, with a median dose of 368 mg per day lowering SBP by 2.0 mmHg and DBP by 1.8 mmHg [190]. AGEs, prevalent in western diets, can impair insulin sensitivity, though diets low in AGEs might improve insulin sensitivity without significant BP effects [198-207].
3. **Renin–Angiotensin–Aldosterone System (RAAS):** Extreme sodium reduction activates the RAAS, but a modest reduction in salt intake (≥4 weeks) has been shown to significantly lower BP in both hypertensive and normotensive individuals [208-210]. Combining moderate salt restriction with RAAS blockers enhances BP control [211].
4. **Potassium:** Low potassium intake, common in western diets, leads to increased sodium retention and elevated BP. Conversely, high potassium intake from fruits and vegetables helps suppress sodium retention and benefit BP control [212-216].
5. **Vascular Function and Oxidative Status:** High salt intake impairs vascular endothelial

function, potentially through oxidative stress [217-218]. Dietary AGEs and trans fats can also trigger endothelial dysfunction. Conversely, certain dietary components like nitrates (from vegetables) can improve endothelial function and reduce BP [219-223]. Chronic alcohol consumption may promote oxidative stress and endothelial dysfunction [223-237].

Overall, dietary choices significantly impact BP, with specific patterns and nutrients contributing to both positive and negative outcomes.

Inflammation and Hypertension:

Certain dietary patterns and food components can contribute to inflammation, which is linked to hypertension:

- **High-Glycemic Foods:** Foods with high glycemic indices, such as those containing added sugars and refined grains, can elevate inflammation by increasing NF-κB activation in blood mononuclear cells [238].
- **Saturated and Trans-Fats:** Diets high in saturated fatty acids [239] and trans-fatty acids [240] have been associated with pro-inflammatory effects. Additionally, dietary advanced glycation end-products (AGEs) can activate receptors on various cells, including leukocytes, contributing to inflammation [241]. More research, particularly high-quality RCTs, is needed to establish dietary AGE restriction as a definitive strategy for reducing inflammation [210].

Sodium and Inflammation

Westernized diets are often high in sodium, which can disrupt gut microbiota composition and promote a pro-inflammatory phenotype in immune cells, such as CD4+ T cells and macrophages [242]. In cases of resistant hypertension, sodium accumulation combined with endothelial glycocalyx dysfunction leads to microcirculation impairment, macrophage infiltration, and vascular inflammation [243]. Western diets also tend to be low in nutrients and bioactive compounds that help regulate inflammation, such as zinc [244], magnesium [245, 246], potassium [247], and omega-3 fatty acids [248].

Dietary Interventions

Certain dietary changes may help reduce inflammation:

- **Fruits and Vegetables:** Diets high in fruits and vegetables have been shown to inhibit or decrease inflammation [249].
- **Low Glycemic Load:** Reducing glycemic load may also help mitigate inflammation [250].
- **Micronutrient Intake:** Adequate intake of micronutrients like zinc, magnesium, and potassium can support inflammation regulation. For example, potassium supplementation may counteract the pro-inflammatory effects of sodium on T cells by inhibiting the p38–MAPK–SGK1 pathway [247].

Autonomic Function

Alcohol consumption can diminish baroreflex sensitivity and is associated with increased sympathetic nervous system (SNS) tone [251-253], which may contribute to elevated BP.

Gut Microbiota

The gut microbiota plays a crucial role in maintaining host physiology, including nutritional regulation, pathogen protection, and metabolite production [254]. Dysbiosis of the gut microbiota is linked to inflammation and cardiovascular disease (CVD). For instance, the metabolite trimethylamine N-oxide (TMAO), derived from gut microbiota, has been associated with increased hypertension risk [255]. High salt intake may lead to gut microbiota dysbiosis [256, 257]. Probiotics have shown modest effects in reducing BP in patients with type 2 diabetes, as well as in healthy individuals and those with hypertension or metabolic syndrome [258, 259].

Xenobiotics

Westernized diets often expose individuals to xenobiotics such as bisphenol A (BPA), which is associated with increased BP and higher hypertension risk [260-264]. Observational studies and RCTs indicate that high BPA exposure (e.g., from canned beverages) can elevate SBP by approximately 4.5 mmHg [265]. BPA may induce hypertension through mechanisms such as decreased NO bioavailability, increased oxidative stress, and activation of the aryl hydrocarbon receptor signaling pathway [266]. Other potential mechanisms include endocrine disruption, inflammation, epigenetic changes, and impaired endothelial function [267]. BPA exposure also affects autonomic function, though this effect is not directly linked to increased BP [262].

Circadian Rhythm and Sleep:

Circadian Entrainment Many bodily functions and physiological responses, including blood pressure (BP), exhibit diurnal variations [269]. The rhythmicity of biological activities is essential for survival, with the circadian rhythm being the most dominant. In mammals, including humans, the circadian rhythm is regulated by the central biological clock within the suprachiasmatic nucleus (SCN) of the hypothalamus, along with peripheral clocks found in various cells throughout the body. The SCN has evolved to align activities such as rest, energy consumption, and autonomic rhythms to both circadian and circannual cycles through the autonomic nervous system. To synchronize these autonomic rhythms with external environmental cues, the SCN relies on regular stimuli such as light exposure, sleep, physical activity, and nutrient intake at specific times.

Circadian rhythms have significant implications for cardiovascular function. BP, cardiac

output, and heart rate all follow a distinct circadian pattern, with dysregulation of this rhythm, particularly in BP, being linked to an increased risk of cardiovascular disease (CVD) [269]. In this regard, 24-hour ambulatory BP monitoring offers valuable clinical insights and has been identified as a more accurate predictor of CVD and mortality than clinic-based BP measurements [270-273]. The effect of circadian entrainment on hypertension risk is especially significant when considering the clinical relevance of nocturnal BP, which has been recognized as a better predictor of adverse cardiovascular events compared to daytime ambulatory BP [274]. In individuals with well-controlled BP, a typical drop of more than 10% is observed from daytime to night-time, known as the 'dipping pattern' [275]. However, abnormal BP patterns such as 'extreme dipping' (a >25% drop), 'non-dipping' (a <10% drop), and the 'riser' pattern (an increase in BP from day to night) are associated with higher risks of CVD [276-277]. Consequently, elevated nocturnal BP, regardless of the pattern, alongside an increased 24-hour BP, correlates with heightened risks of CVD morbidity and mortality [278].

Disruption of circadian rhythms, commonly seen in shift workers, results from misalignment between behavioral and environmental cycles. A meta-analysis suggests a link between shift work, particularly rotational shifts, and hypertension risk [279]. Non-dipper BP patterns are typically seen after the first night of shift work, with recovery occurring after four consecutive night shifts [280]. Misalignment of circadian rhythms over three days can increase 24-hour BP, primarily due to elevated nocturnal BP (5.6 mmHg for systolic BP [SBP] and 1.9 mmHg for diastolic BP [DBP]) [281]. Additionally, factors such as exercise and meal timing influence circadian rhythms. Aligning food intake with circadian rhythms by limiting meals to earlier hours can reduce BP and improve cardiometabolic health in individuals with metabolic syndrome or prediabetes [282-284].

Early humans likely experienced daily sleep durations exceeding 8 hours for most of the year [285]. Those residing further from the equator were subjected to seasonal variations in photoperiod, resulting in shorter sleep during summer and longer sleep during winter [286]. BP typically drops by 10-20% during sleep [287], meaning that shorter summer sleep durations led to higher 24-hour BP and extended exposure to heightened sympathetic nervous system (SNS) activity, as well as physical and psychological stressors. For early humans, the BP effects of seasonally shortened sleep were temporary. However, in modern times, shorter sleep durations and sleep disturbances are common year-round. For instance, more than 57% of participants in a 2013 study reported getting insufficient sleep on workdays [288]. Humans today face constant exposure to potential sleep disruptors, such as shift work, multiple jobs, 24-hour access to shopping, the Internet, television, smartphones, and travel across time zones, all of which interfere with sleep schedules. Furthermore, exposure to artificial light, particularly blue light, at night degrades sleep quality and disrupts sleep patterns [289]. These disturbances can lead to insomnia and circadian misalignment. Although some individuals may compensate for nighttime awakenings by sleeping during the day, chronic insomnia is linked to elevated nocturnal SBP and a diminished day-to-night SBP reduction [290].

Other sleep-related factors can also elevate BP. Evidence from longitudinal and cross-sectional studies across various ethnic groups indicates a correlation between sleep duration and hypertension and/or increased BP. A meta-analysis of 1,074,207 participants showed that both short (≤5 hours) and long (≥9 hours) sleep durations were associated with elevated BP [291]. Another large meta-analysis involving 5,172,710 adults identified a significant association between short sleep and hypertension risk [292], with similar findings observed in adolescents [293]. Sleep quality also plays a critical role in hypertension risk. A meta-analysis found that self-reported poor sleep quality is significantly associated with a higher risk of hypertension (OR 1.48, 95% CI 1.13–1.95) [294]. Changes in sleep architecture, such as reduced slow-wave sleep and decreased non-rapid eye movement sleep, have been linked to a higher risk of hypertension in older men [295] and middle-aged women [296]. The relationship between sleep and hypertension risk is particularly relevant given the importance of nocturnal ambulatory BP as a predictor of adverse cardiovascular events [274]. The presence of obstructive sleep apnea (OSA) or insomnia, coupled with short sleep durations, can hinder the control of nocturnal BP in hypertensive patients, thereby raising the risk of CVD [297-299].

The link between sleep duration and hypertension has led to the hypothesis that extending sleep duration and improving sleep quality could serve as effective interventions for hypertension prevention [286]. Treatment of OSA and the use of sleep aids can enhance the control of nocturnal BP [300]. A randomized controlled trial (RCT) involving patients with prehypertension or stage 1 hypertension and habitual sleep durations of ≤7 hours demonstrated that a 6-week sleep extension intervention (yielding an average extension of 35 minutes) significantly reduced SBP by 14 mmHg and DBP by 8 mmHg over a 24-hour period compared to maintaining habitual sleep patterns [301]. However, a more recent RCT in individuals with mild sleep impairments found no significant effect of a sleep intervention on BP, despite improvements in sleep

quality [302]. Enhanced sleep may also positively influence other hypertension-related markers. Sleep deprivation has been associated with obesity, a major risk factor for hypertension [303], as well as with disrupted fasting leptin levels and increased hunger [304]. Adequate sleep may therefore support dietary interventions, weight management, and provide the energy necessary for regular physical activity [304]. Shift work, combined with circadian misalignment and short sleep durations, has been identified as a risk factor for hypertension [305]. Therefore, promoting sufficient sleep should go hand in hand with strategies to synchronize circadian rhythms, such as maintaining regular sleep-wake times, adhering to time-restricted eating, and regulating light exposure throughout the day and night.

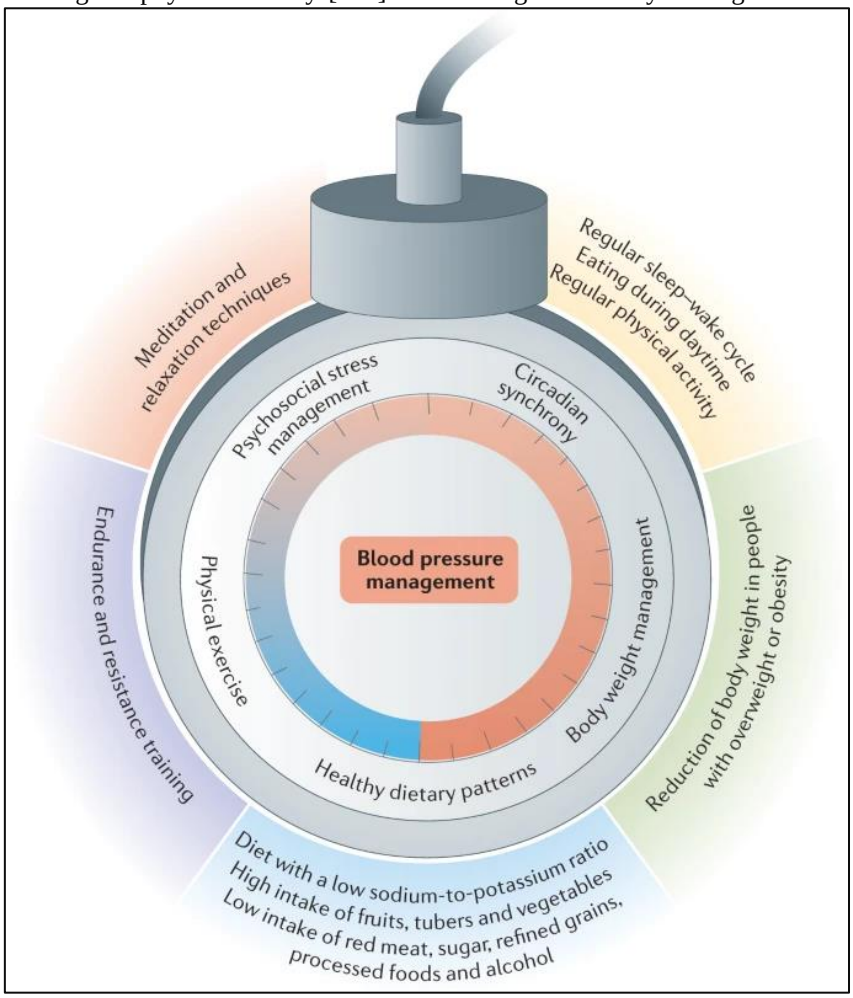

Figure 2: Diets and Lifestyle interventions for management of Hypertension.

Diets and Atherosclerosis:

The overall quality of dietary patterns can significantly impact their relationship with health outcomes. The term "dietary pattern quality" refers to the general healthfulness of a diet, evaluated based on the variety of foods, nutrients, and bioactive compounds it contains, suggesting that the cumulative effect of a dietary pattern is more substantial than that of individual components [306]. Typically, tools for assessing dietary patterns reward higher consumption of whole grains, fruits, vegetables, seafood, plant proteins, nuts, MUFAs, and PUFAs while penalizing high intakes of processed meats, refined grains, SFAs, animal fats, sodium, and added sugars [306]. Although there are no randomized controlled trials (RCTs) specifically examining the direct effect of dietary pattern quality on ASCVD outcomes, numerous observational studies have explored the link between dietary quality and outcomes such as cardiovascular disease (CVD) incidence, mortality, and overall mortality. These studies employ various tools, including the Healthy Eating Index (HEI), Alternative Healthy Eating Index (AHEI), the alternate Mediterranean diet (aMedDiet) score, DASH score, and the Healthful Plant-Based Diet Index (HPDI) [29,30,31,32]. Evidence from multiple studies on large cohort datasets reveals that higher scores in HEI-2015, AHEI-2010, aMedDiet, DASH, and HPDI are correlated with a 14-21% reduction in CVD incidence, a 21-34% reduction in CVD mortality, and a 12-24% reduction in all-cause mortality [307-309].

In the Prospective Urban Rural Epidemiology (PURE) study, Mente et al. developed a healthy diet score focused on dietary components linked to health outcomes to evaluate the association

between this score and major cardiovascular (CV) events (CVD, myocardial infarction, stroke) and overall mortality [310]. Results showed that higher PURE Healthy Diet Scores were associated with significant reductions in CVD (18%), myocardial infarction (14%), stroke (19%), and all-cause mortality (30%). Compared to other indices, such as the HEI, Mediterranean, DASH, and Planetary Health diet scores, the PURE Healthy Diet Score had slightly stronger associations with mortality and CVD outcomes. Despite its simplicity, this score adds to the growing body of evidence suggesting that diets rich in fruits, vegetables, nuts, legumes, fish, and dairy can lower ASCVD risks. Similar results were found when alternative scoring methods were used, incorporating consumption of whole grains and unprocessed meats.

Although both RCT and observational evidence support the favorable effects of recommended dietary patterns for ASCVD prevention and risk reduction, further RCTs with cardiovascular event endpoints are necessary to enhance the evidence quality for dietary guidelines. Additionally, the observed beneficial associations between dietary patterns and ASCVD outcomes appear larger than can be explained by traditional risk factors alone. This suggests that the underlying mechanisms are not fully understood, or that high dietary quality may be indicative of other health-promoting behaviors and characteristics. Despite these uncertainties, the overall evidence supports the recommendation of scientifically backed dietary patterns—such as the Mediterranean, DASH, Healthy U.S.-Style, and healthy plant-based diets—as effective strategies for reducing ASCVD risk. Healthcare providers should confidently recommend these dietary patterns to promote cardiovascular health and lower ASCVD risk.

Dietary Fatty Acids and ASCVD Outcomes:

There is widespread agreement among professional and scientific bodies that replacing SFAs with MUFAs and PUFAs can reduce ASCVD risk. Both RCT and observational evidence support this recommendation. Hooper et al. conducted a meta-analysis of 15 RCTs that compared the effects of reducing SFA intake to usual intake on CV events [34]. The findings indicated that lowering SFA intake led to a 17% reduction in combined CV events, though individual components of CV events (CVD, CHD events, and all-cause mortality) showed favorable but non-significant trends. Criticism of the Hooper et al. study arises from the use of an unconventional definition of combined CV events, which included events not directly resulting from ASCVD, such as heart failure and atrial fibrillation. Therefore, the results should be interpreted cautiously [311].

As part of an AHA Presidential Advisory on dietary fats and CVD, Sacks and colleagues conducted a meta-analysis of four RCTs examining the effect of replacing SFAs with PUFAs on CHD, which found a 29% reduction in CHD risk [312]. Similarly, a subgroup analysis in Hooper et al.'s meta-analysis revealed a significant 21% reduction in CV events when SFAs were replaced with PUFAs, though no significant effect on CVD mortality was observed [34]. It is important to recognize the limitations of RCTs investigating SFAs and ASCVD outcomes. Many of these studies had small sample sizes and short intervention durations, limiting their statistical power. Additionally, dietary interventions aimed at reducing SFAs likely impacted other dietary aspects, such as lowering total fat and salt intake or increasing the consumption of fruits, vegetables, and unsaturated fatty acids. Thus, some of the cardiovascular benefits observed may be attributed to these secondary dietary changes [312].

Observational studies further support the benefits of replacing SFAs with unsaturated fats, particularly PUFAs. Modeling analyses using data from large cohorts suggest that replacing 5% of energy from SFAs with PUFAs leads to a significant 25% reduction in CHD risk, a 9% reduction in CHD events, and a 13% reduction in CHD mortality [313-315]. Furthermore, Li et al. found that replacing SFAs with whole-grain carbohydrates was associated with a significant 9% reduction in CHD risk, while replacement with refined starches and added sugars showed a non-significant increase in CHD risk [314]. The AHA Presidential Advisory concluded that replacing SFAs with PUFAs (mainly omega-6 PUFA, linoleic acid) reduces CHD risk more effectively than replacing SFAs with MUFAs (mainly oleic acid), while substituting SFAs with unspecified carbohydrates does not reduce CHD risk [313].

There is no direct evidence from randomized controlled trials (RCTs) linking high intake of added sugars to increased ASCVD risk, though meta-analyses suggest that high added sugar intake can increase triglyceride (TG) levels, especially when excess calories are consumed [316-318]. A notable association between added sugars and ASCVD outcomes has been observed with sugar-sweetened beverages (SSBs), as meta-analyses have shown that higher SSB consumption is associated with a significantly increased risk of myocardial infarction (MI) and cardiovascular disease (CVD) outcomes [319-323]. However, RCTs that have examined the impact of added sugars on cardiometabolic risk factors were considered low-quality evidence using the GRADE framework, especially regarding stroke, CVD, and mortality [323]. It is suggested that limiting added sugar, particularly from SSBs, may be beneficial for ASCVD prevention. The AHA and 2020 Dietary Guidelines support limiting added sugar

intake to less than 10% of daily energy to enhance dietary quality and cardiovascular (CV) health [324-325].

Regarding alcohol consumption, observational studies suggest that moderate alcohol intake is linked with favorable ASCVD biomarkers such as increased HDL-C and reduced fibrinogen levels [326-327]. However, results on LDL-C and inflammatory markers like interleukin-6 (IL-6) have been inconsistent [328-329]. The J-shaped association between alcohol consumption and ASCVD or all-cause mortality has been confirmed in cohort studies, where moderate drinkers have lower risks compared to non-drinkers and heavy drinkers [330-333]. Current guidelines recommend ≤2 drinks/day for men and ≤1 drink/day for women in the U.S., while European guidelines suggest ≤10 g/day or 100 g/week. It is emphasized that non-drinkers should not be encouraged to start drinking, and those who do should limit consumption to balance potential ASCVD benefits with other health risks [334].

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Conclusion:

Cardiovascular disease (CVD) remains the leading cause of death globally, encompassing various conditions such as coronary artery disease, stroke, and peripheral artery disease. Atherosclerotic cardiovascular disease (ASCVD) is a significant component of CVD, characterized by the buildup of inflammatory and lipid deposits in the arterial walls. The primary modifiable risk factors for ASCVD include elevated blood pressure, abnormal lipid levels, hyperglycemia, and smoking. Addressing these risk factors through lifestyle changes is critical in preventing and managing ASCVD. The American Heart Association's "Life’s Essential 8" guidelines offer a comprehensive approach to improving cardiovascular health by focusing on eight key metrics: dietary habits, physical activity, nicotine exposure, sleep health, body weight, blood lipids, glucose levels, and blood pressure. Adherence to these guidelines has been shown to significantly lower ASCVD risk and enhance overall cardiovascular outcomes. Dietary modifications, such as adopting the Mediterranean or DASH diets, and engaging in regular physical activity are among the most effective strategies. Additionally, achieving optimal body weight, managing blood lipids and glucose levels, and maintaining healthy blood pressure are crucial components of cardiovascular health. Hypertension, a common and serious condition, also benefits from lifestyle interventions. The global increase in hypertension rates, driven by lower diagnostic thresholds and lifestyle factors, underscores the need for effective prevention and management strategies. Lifestyle modifications, including exercise, weight management, and dietary changes, play a vital role in controlling blood pressure and reducing hypertension-related complications. These interventions complement pharmacological treatments and can be effective even in individuals with resistant hypertension. In summary, implementing lifestyle changes based on the "Life’s Essential 8" guidelines offers a robust strategy for reducing ASCVD risk and managing hypertension. Emphasizing preventive measures through diet, physical activity, and other behavioral modifications not only enhances cardiovascular health but also contributes to overall well-being. Public health initiatives and individual efforts to adopt these lifestyle practices are crucial in addressing the global burden of cardiovascular diseases and improving long-term health outcomes.

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