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Hypertension Unraveled: From Mechanisms to Modern Management

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Abstract: Hypertension remains the leading preventable risk factor for cardiovascular and renal morbidity worldwide, affecting nearly one-third of adults. Its etiopathogenesis is multifactorial, involving genetic predisposition, neurohormonal dysregulation, renal dysfunction, vascular remodeling, metabolic abnormalities, and environmental influences. Recent advances in diagnostics—including ambulatory blood pressure monitoring, wearable sensors, artificial intelligence, and biomarker discovery—have improved early detection and risk stratification. Pharmacotherapy continues to evolve beyond traditional agents such as thiazides, ACE inhibitors, ARBs, and calcium-channel blockers, with novel drugs including endothelin receptor antagonists, aldosterone synthase inhibitors, RNA interference therapies, and nonsteroidal mineralocorticoid receptor antagonists showing promising results in resistant and high-risk populations. Non-pharmacological strategies, including sodium restriction, weight reduction, physical activity, and the DASH diet, remain the cornerstone of management and prevention. Population-level interventions, precision medicine approaches, and digital health integration further enhance control and adherence. Collectively, these innovations highlight a paradigm shift toward individualized, multi-modal hypertension care, aimed at reducing the persistent global burden of cardiovascular complications.

Keywords: *Hypertension, Endothelin Receptor Antagonists, Lifestyle Modification, DASH Diet.*

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I. INTRODUCTION

Hypertension, commonly referred to as high blood pressure, is a major global health burden and the leading preventable cause of cardiovascular morbidity and mortality, accounting for more than 7 million deaths worldwide each year[1]. It is broadly classified into primary (essential) hypertension, which comprises approximately 90–95% of cases, and secondary hypertension, which arises from identifiable medical conditions such as renal or endocrine disorders[2]. The pathogenesis of primary hypertension is multifactorial, influenced by genetic susceptibility, environmental exposures, lifestyle habits, and social determinants of health[3]. Blood pressure regulation involves a tightly controlled balance among neural, renal, hormonal, and vascular systems[1]. Abnormalities in these systems—particularly excessive activation of the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system stimulation, and endothelial dysfunction—contribute to chronic hypertension[4]. Impaired renal sodium excretion and pressure-natriuresis play a central role in maintaining elevated blood pressure over time[5]. Endothelial injury due to oxidative stress and inflammation accelerates vascular remodeling and increases the risk of cardiovascular complications[6]. Genomic studies have revealed that over 1,000 common loci contribute to blood pressure heritability, although rare monogenic variants are also implicated in a small number of cases[7]. With aging, arterial stiffening and impaired baroreflex sensitivity lead to increased systolic hypertension, especially in older adults[8]. Despite the

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availability of effective pharmacological treatments and lifestyle interventions, control rates remain inadequate globally[3]. As a result, hypertension remains the most significant modifiable risk factor for cardiovascular and renal diseases worldwide[9].

II. ETIOPATHOGENESIS

The development of hypertension is highly multifactorial, involving complex interactions between genetic predisposition, environmental exposures, and social determinants[10]. Overactivation of the renin–angiotensin–aldosterone system (RAAS)—including both circulating and tissue-specific RAAS—promotes vasoconstriction, sodium retention, and vascular remodeling[11]. Increased sympathetic nervous system tone, driven by central and renal mechanisms, elevates peripheral resistance and stimulates renin release[12]. Endothelial dysfunction, marked by reduced nitric oxide and elevated endothelin and oxidative stress, impairs vasodilation and promotes vascular stiffness[13]. Renal microvascular injury, resulting from chronic vasoconstriction and inflammation, shifts the pressure-natriuresis curve and sustains elevated blood pressure[14]. Salt sensitivity—amplified by low dietary potassium—promotes vascular smooth muscle contraction and blood pressure elevation[15]. Obesity and insulin resistance further exacerbate hypertension via RAAS activation, sympathetic overdrive, and adipokine-mediated vascular inflammation[16]. Sleep apnea also contributes to blood pressure elevation through intermittent hypoxia, sympathetic stimulation, and oxidative stress[17]. Immune activation, with renal and vascular infiltration of T-cells and macrophages, fosters local RAAS activity and oxidative injury[18]. Arterial stiffening from aging impairs baroreflex sensitivity and promotes isolated systolic hypertension[19]. Gut microbiota dysbiosis has emerged as a novel contributor, affecting blood pressure via inflammatory and metabolic pathways[20]. Finally, secondary causes such as pheochromocytoma, primary aldosteronism, and renal artery stenosis illustrate how discrete endocrine or renovascular factors can precipitate hypertension[21].

➢ *Types*

Hypertension manifests in various forms, each with distinct clinical implications and management strategies[22]. Essential (primary) hypertension, accounting for approximately 85–95% of cases, arises from complex gene–environment interactions without a single identifiable cause[23]. Within primary hypertension, isolated systolic hypertension—marked by elevated systolic but normal diastolic pressure—is particularly prevalent among older adults due to arterial stiffening[22]. White-coat hypertension, where blood pressure is high in clinical settings but normal out of office, affects 10–30% of patients and requires confirmation with home or ambulatory readings[24]. Conversely, masked hypertension—normal office readings but elevated out-of-office measurements—is tied to similar cardiovascular risk as sustained hypertension[24]. Primary aldosteronism represents a common endocrine-mediated secondary hypertension form, accounting for about 5–10% of cases and often amenable to targeted treatment[25]. Renovascular hypertension, due to renal artery stenosis or fibromuscular dysplasia, leads to secondary hypertension through RAAS activation[26]. Obstructive sleep apnea–related hypertension, fueled by intermittent hypoxia and sympathetic overdrive, is now recognized as a significant secondary cause[26]. Additional secondary forms include pheochromocytoma, Cushing's syndrome, thyroid disorders, and coarctation of the aorta, which all distinctly influence blood pressure via hormonal, structural, or metabolic mechanisms[26]. Beyond these, resistant hypertension—blood pressure uncontrolled by three or more antihypertensive agents—requires specialized evaluation and often involves secondary contributors[27]. Although less common, refractory hypertension remains unresponsive even to maximal pharmacotherapy and represents an emerging subtype[27]. Lastly, hypertensive crises, categorized into urgency and emergency based on severity and end-organ impact, demand immediate intervention[22].

➢ *Clinical Presentation*

Hypertension is often silent and asymptomatic, leading many individuals to remain unaware until routine screening or onset of complications[28]. When symptoms occur, patients may report headache, especially in the morning, dizziness, tinnitus, or blurred vision, though these are non-specific[29]. Hypertensive retinopathy may present with visual disturbances and fundoscopic changes such as arteriolar narrowing, A/V nicking, hemorrhages, and cotton-wool spots[30]. Severe, abrupt elevations in blood pressure can cause hypertensive encephalopathy, characterized by headache, confusion, visual changes, and even seizures[31]. Hypertensive emergency may manifest with chest pain, dyspnea, neurological deficits, or acute renal impairment due to end-organ damage[32]. In pregnancy-associated hypertension like pre-eclampsia, clinical signs include headache, visual disturbances, epigastric pain, and edema[33]. Left ventricular hypertrophy may cause exertional dyspnea, palpitations, or chest discomfort in long-standing hypertension[34]. Hypertension-related chronic kidney disease may initially be asymptomatic but progress to reduced urinary output, edema, or azotemia[35]. Patients with masked hypertension may exhibit normal office readings yet have elevated out-of-office pressures and are at increased CVD risk[36]. White-coat hypertension presents with elevated office BP but normal ambulatory measurements and may be accompanied by metabolic risk factors[37]. Hypertensive crises—urgency or emergency—are distinguished by extremely high blood pressure, with only emergencies involving acute end-organ damage[38]. Instances of nocturnal hypertension may contribute to early end-organ dysfunction without evident daytime symptoms[39]. Finally, headache attributed to markedly elevated BP is defined by diffuse, pulsating pain, often worsened by activity and associated with neurological signs[40].

➢ *Diagnosis*

The diagnosis of hypertension requires accurate blood pressure measurement, ideally with validated devices and standardized procedures to minimize variability[41]. According to international guidelines, hypertension is defined as office blood pressure ≥140/90 mmHg, confirmed on at least two different occasions[42]. Out-of-office blood

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pressure monitoring, including home blood pressure monitoring (HBPM) and 24-hour ambulatory blood pressure monitoring (ABPM), is strongly recommended to improve diagnostic accuracy[43]. ABPM provides additional prognostic value by assessing nocturnal dipping patterns and morning surges in blood pressure[39]. HBPM is useful for identifying white-coat hypertension and masked hypertension, both of which carry distinct cardiovascular risks[44]. Clinical evaluation also involves a detailed history and physical examination to identify risk factors, comorbidities, and secondary causes[45]. Laboratory investigations, including serum creatinine, electrolytes, fasting glucose, and lipid profile, help assess cardiovascular and renal risk[46]. Electrocardiography and echocardiography are recommended for evaluating target-organ damage such as left ventricular hypertrophy[47]. Fundoscopic examination may reveal hypertensive retinopathy, which provides clues about chronicity and severity[30]. Renal ultrasound or imaging studies are warranted when renovascular hypertension is suspected[26]. Screening for secondary hypertension—such as primary aldosteronism, pheochromocytoma, or thyroid dysfunction—is recommended in resistant or early-onset cases[48]. Risk stratification using tools such as the SCORE or Framingham model helps guide treatment intensity[49]. Ultimately, a diagnosis of hypertension integrates repeated blood pressure measurements with clinical, laboratory, and imaging assessments to determine cardiovascular risk and identify underlying causes[42].

➢ *Recent Advances in Diagnosis*

Recent advances have expanded diagnostic approaches for hypertension beyond conventional office blood pressure measurement, aiming for greater precision and early detection[50]. Ambulatory blood pressure monitoring (ABPM) remains the gold standard, providing valuable data on circadian variation, nocturnal dipping, and morning surges[39]. Home blood pressure monitoring (HBPM) is increasingly integrated with telemedicine platforms, enabling remote assessment and improving patient adherence[44]. The use of wearable devices and cuffless sensors employing photoplethysmography (PPG) and tonometry allows continuous blood pressure tracking in real-life conditions[51]. Emerging smartphone-based oscillometric applications offer low-cost, portable screening tools with acceptable accuracy[52]. Central blood pressure (CBP) measurement, derived from applanation tonometry or oscillometric devices, provides superior prognostic information compared to brachial pressure[42]. Pulse wave velocity (PWV), a marker of arterial stiffness, is now recognized as a diagnostic adjunct to identify subclinical hypertension-related vascular damage[53]. Twenty-four-hour urinary sodium and potassium monitoring, integrated with digital health tools, refines diagnosis of salt-sensitive hypertension[54]. Artificial intelligence–based algorithms applied to ABPM and HBPM datasets improve classification of white-coat and masked hypertension[55]. Machine learning techniques using electrocardiography-derived signals have shown potential in predicting hypertension even before persistent elevation is established[56]. Novel biomarkers, such as circulating microRNAs, are being investigated as early diagnostic indicators of hypertensive vascular changes[57]. Additionally, integration of digital health ecosystems—including mobile health apps, cloud platforms, and AI-driven decision support—offers a transformative approach to hypertension diagnosis and management[58].

III. MANAGEMENT

➢ *Pharmacological Therapy*

Pharmacotherapy for hypertension starts with four preferred first-line classes—thiazide/thiazide-like diuretics, ACE inhibitors, ARBs, and calcium-channel blockers—selected and combined based on comorbidities and blood-pressure (BP) targets.[59] Combination therapy at initiation is recommended for most patients, and single-pill combinations (SPCs) are favored to improve adherence and speed BP control.[60] Thiazide-like diuretics such as chlorthalidone or indapamide have longer action and stronger outcome data than hydrochlorothiazide and are often preferred as the diuretic component.[60] Large pragmatic analyses suggest first-line thiazides are at least as effective and often superior to ACE inhibitors for preventing cardiovascular events in routine practice.[61] ACE inhibitors reduce BP and provide vascular and renal protection but may cause cough or, rarely, angioedema, necessitating a switch to an ARB when intolerance occurs.[59] ARBs offer similar cardioprotective benefits with lower cough risk and are preferred when ACE inhibitor intolerance is present.[60] Dihydropyridine calcium-channel blockers (e.g., amlodipine) are potent BP-lowering agents across diverse populations and are core components of most effective combination regimens.[59]

The ALLHAT trial established that chlorthalidone was at least as effective as amlodipine or lisinopril for major coronary outcomes, with advantages for heart failure prevention, supporting thiazide-based therapy.[62] In ASCOT-BPLA, an amlodipine-perindopril strategy reduced stroke and all-cause mortality versus an atenolol-thiazide regimen, highlighting benefits of CCB-RAAS blockade combinations.[63] The LIFE study showed losartan-based therapy reduced stroke and new-onset diabetes more than atenolol-based therapy in hypertension with left-ventricular hypertrophy, supporting ARB use when LVH is present.[64] ACCOMPLISH demonstrated that benazepril-amlodipine lowered cardiovascular events more than benazepril-hydrochlorothiazide in high-risk hypertensive patients, emphasizing the superiority of ACEi+CCB over ACEi+HCTZ in this setting.[65] For most adults, initial dual therapy combining a RAAS blocker with either a thiazide-like diuretic or a dihydropyridine CCB achieves greater and faster BP reduction than monotherapy.[60] SPCs consistently improve adherence and persistence versus free-equivalent combinations, translating into better BP control in real-world and trial settings.[66] A growing body of evidence supports polypill or fixed-dose combination strategies for primary prevention, which reduce major cardiovascular events compared with usual care.[67] In secondary prevention populations, a cardiovascular polypill including ramipril achieved lower recurrent events than usual care, underscoring the adherence and risk-reduction advantages of fixed combinations.[68]

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Intensive BP lowering with multi-drug regimens reduces major cardiovascular outcomes, as shown in SPRINT where a systolic target <120 mmHg lowered events versus <140 mmHg, albeit with more adverse events requiring careful selection and monitoring.[69] In very elderly patients, indapamide (± perindopril) significantly reduced stroke and heart failure in HYVET, supporting treatment benefits even after age 80 when tolerated.[70] Beta-blockers are reserved for compelling indications such as coronary disease, arrhythmia, or heart failure, as comparative data show less stroke protection when used as routine first-line therapy.[59] Dihydropyridine-related ankle edema can be mitigated by pairing with an ACE inhibitor or ARB, which reduces CCB-associated edema rates.[71] In resistant hypertension, adding spironolactone is the most effective fourth-line option, outperforming alternative add-ons in PATHWAY-2.[72] For resistant hypertension with advanced chronic kidney disease, low-dose chlorthalidone improved BP control in the CLICK trial but requires monitoring for hypokalemia and creatinine rise.[73] Hyperkalemia limits spironolactone in CKD, but concurrent patiromer enabled sustained use and better BP lowering in AMBER.[74] Direct renin inhibition lowers BP, but dual RAAS blockade increased adverse events without added benefit in ALTITUDE, arguing against combinations like aliskiren plus ACEi/ARB in diabetes with CKD.[75] As monotherapy, aliskiren is antihypertensive, but outcome advantages over established classes are unproven, so it is not first-line.[76]

In patients with hypertension and LVH, ARB-based regimens have favorable effects on regression of hypertrophy and stroke prevention relative to beta-blockers, supporting ARB selection in this phenotype.[64] For individuals at high stroke risk, CCB-inclusive regimens confer robust stroke reduction, consistent with ASCOT-BPLA and guideline endorsements.[63] Among thiazides, evidence and guidelines increasingly favor chlorthalidone or indapamide due to longer half-life and outcome data, while hydrochlorothiazide may be less potent over 24 hours.[60] In Black adults without compelling indications, CCBs and thiazide-type diuretics are generally more effective at BP lowering than RAAS blockers as initial choices.[59] When diabetes or albuminuric CKD coexists, ACE inhibitors or ARBs are prioritized for renal protection while achieving BP control.[59] Choice among ACE inhibitors and ARBs should be individualized, but class effects for BP lowering are generally similar at equivalent doses, so tolerability and comorbidities guide selection.[60] For patients with gout or hyperuricemia risk, losartan and CCBs are associated with lower gout incidence, whereas diuretics, beta-blockers, ACE inhibitors, and non-losartan ARBs increase risk.[77] Clinicians should watch for thiazide-related metabolic effects (hyponatremia, hypokalemia) and adjust accompanying RAAS blockade or add potassium-sparing agents as needed.[59] ACE inhibitor cough occurs in a minority but can limit use; switching to an ARB typically resolves symptoms while maintaining RAAS blockade benefits.[59]

In pregnancy, labetalol, nifedipine, and methyldopa are preferred choices, while ACE inhibitors, ARBs, and direct renin inhibitors are contraindicated due to fetotoxicity.[78] For heart failure with reduced ejection fraction and hypertension, guideline-directed beta-blockers, ACEi/ARB (or ARNI), and MRAs are prioritized, tailoring add-ons for BP and outcomes.[59] In chronic coronary syndromes, beta-blockers and ACEi/ARBs provide anti-ischemic and prognostic benefit while contributing to BP control; CCBs assist when angina persists or beta-blockers are not tolerated.[59] For atrial fibrillation with hypertension, beta-blockers or non-DHP CCBs manage rate while the foundational antihypertensives are adjusted to maintain BP targets.[60] In patients with prior stroke or TIA, robust BP reduction with combinations—often including a diuretic and an ACEi/ARB—prevents recurrence.[59] Amlodipine-induced edema is dose related and less frequent when combined with an ACEi/ARB, supporting the rationale for SPCs pairing these classes.[71]

When three drugs at optimal doses fail (including a diuretic), adding spironolactone is generally the most effective step, provided potassium and renal function are monitored.[72] If spironolactone is limited by hyperkalemia in CKD, patiromer co-administration can enable continued MRA therapy and greater BP reductions.[74] For stage-4 CKD, thiazide-like diuretics remain useful at low GFR; chlorthalidone reduced ambulatory BP in CLICK but requires electrolyte vigilance.[73] Intensive targets often necessitate three or more agents, and benefits must be balanced with risks of hypotension, syncope, and electrolyte disturbances.[69] ACEi/ARB combinations should be avoided due to increased adverse events without added cardiovascular benefit.[59] Evidence supports titrating to maximally tolerated doses before class switching, but earlier combination therapy generally achieves control more reliably than dose escalation alone.[60] In patients at high global risk, SPC-based strategies and polypills reduce pill burden and improve long-term risk factor control, facilitating sustained BP achievement.[66] A quadruple low-dose single pill achieved greater BP lowering than standard-dose monotherapy, supporting early multi-mechanism blockade with low-dose components.[79]

Thiazide-like diuretics remain central in elderly patients, with HYVET showing event reduction even with modest BP goals when therapy is well-tolerated.[70] For hypertensive patients with LVH, ARB-based regimens like losartan reduce stroke and new-onset diabetes compared with beta-blockers, guiding class choice.[64] In high-risk patients, ACEi+CCB combinations outperform ACEi+HCTZ for hard outcomes, favoring CCB-RAAS SPCs in many scenarios.[65] Diuretic choice matters: outcome and pharmacokinetic profiles favor chlorthalidone or indapamide over hydrochlorothiazide for sustained 24-hour BP control.[60] When gout risk is a concern, losartan and CCBs are urate-friendly options, whereas thiazides raise gout risk and may warrant alternatives or urate management.[77] In diabetes with hypertension, RAAS blockade is foundational for kidney protection and BP control, with addition of CCBs or thiazide-like diuretics as needed to reach targets.[59] For patients with ischemic heart disease, beta-blockers and ACEi/ARBs are prioritized for prognosis, while CCBs and nitrates assist symptom relief

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and BP lowering.[59] In atrial fibrillation, rate-controlling beta-blockers integrate well with standard antihypertensives to achieve BP targets without excess hypotension.[60]

SPCs not only improve adherence but are increasingly associated with better clinical outcomes versus multipill regimens in observational cohorts and meta-analyses.[66] Polypill strategies combining antihypertensives with statins (± aspirin) significantly reduce major cardiovascular events in primary prevention, supporting their use where appropriate.[67] Secondary prevention polypills enhance implementation of proven therapies and reduce recurrent events, complementing individualized BP targets.[68] Clinicians should avoid routine alpha-blocker monotherapy due to inferior outcome data and reserve them for men with concomitant symptomatic BPH when needed for BP.[59] For patients prone to edema on CCBs, pairing with an ACEi/ARB in an SPC both improves adherence and reduces edema incidence.[71] Resistant hypertension management should confirm adherence and diuretic optimization, then add spironolactone as the preferred fourth agent, consistent with randomized evidence.[72] In CKD or hyperkalemia-prone patients, potassium binders like patiromer can broaden use of MRAs to achieve BP control while maintaining safety.[74] Thiazide-like diuretics retain efficacy even at lower eGFR than traditionally assumed, supporting their inclusion alongside loop diuretics when needed.[73] Across risk strata, earlier use of two-drug therapy in an SPC shortens time to control and reduces therapeutic inertia compared with sequential monotherapy.[60] Intensive BP targets confer event reduction but require vigilant monitoring for hypotension, electrolyte disorders, and renal function changes when using multidrug regimens.[69] Diuretic-centric regimens remain effective foundations, as shown by ALLHAT, with add-on RAAS and CCB agents layered to meet individualized targets.[62] CCB-RAAS combinations have repeatedly outperformed β-blocker–thiazide regimens for stroke and metabolic outcomes in large trials, shaping modern combination preferences.[63] When edema limits CCB dosing, shifting to or adding a thiazide-like diuretic or adjusting to an ACEi/ARB-based SPC can restore tolerability while maintaining BP control.[71] Real-world and trial evidence converge that SPC-based care improves adherence, persistence, BP control, and—emerging data suggest—cardiovascular outcomes versus multipill therapy.[66] Guideline-concordant pharmacotherapy emphasizes patient-specific comorbidities (diabetes, CKD, CAD, HF, pregnancy) when choosing classes and combinations to maximize benefit and minimize harm.[59] Contemporary European guidance similarly centers on RAAS blockers, CCBs, and thiazide-like diuretics in SPCs as default first-line treatment, escalating to triple therapy before labeling hypertension as resistant.[60] Low-dose multi-component strategies (e.g., QUARTET) achieve larger BP reductions with favorable tolerability, providing a modern path to rapid control.[79] Ultimately, sustained BP control that reduces cardiovascular, cerebrovascular, and renal events is most reliably achieved with guideline-based class selection, early combination therapy—preferably as SPCs—and vigilant safety monitoring.[59]

➢ *Recent Advances in Pharmacotherapy*

Recent pharmacotherapeutic advances in hypertension now include SGLT2 inhibitors, which have demonstrated consistent, modest reductions in both systolic and diastolic blood pressure through mechanisms like osmotic diuresis and improved vascular function[80]. In 2023–2024, these agents earned Class I, Level-A recommendations for hypertensive patients with coexisting chronic kidney disease, diabetes, or heart failure[81]. A major leap came with the FDA approval of aprocitentan, the first endothelin receptor antagonist (ERA) specifically for resistant hypertension, offering a novel vascular target[82]. Lorundrostat, an aldosterone synthase inhibitor, showed promising BP reductions in patients inadequately controlled despite multiple drugs[83]. Neuroscience-inspired advances include firibastat, an innovative aminopeptidase A inhibitor targeting brain RAAS to lower BP—particularly in overweight or African ancestry populations[84]. Cutting-edge RNA interference (RNAi) therapies like zilebesiran, which suppress angiotensinogen synthesis via siRNA, have shown sustained BP lowering with dosing only twice yearly[85].

In non-steroidal mineralocorticoid receptor antagonists (nsMRAs) such as finerenone and esaxerenone, researchers report enhanced safety profiles over spironolactone and eplerenone, reducing hyperkalemia risk[86]. The experimental nonsteroidal agent ocedurenone (KBP-5074) is undergoing Phase III trials for hypertension in advanced CKD populations, showing promise with lower hyperkalemia risk[87]. Another novel candidate, MT-1207, is a multitarget inhibitor discovered in 2024 with potent antihypertensive efficacy in preclinical models[88]. Phosphodiesterase-5 inhibitors (e.g., sildenafil) and soluble guanylate cyclase stimulators are being reassessed for hypertension due to their vasodilatory enhancement via NO–cGMP pathways[89].

A revolution in drug delivery includes transdermal nanosystems delivering antihypertensive agents with controlled release and improved patient convenience[90]. Simultaneously, early trials of hypertension vaccines—targeting Ang II or α1D-AR—show BP reduction and organ protection in animal models, pointing toward long-acting immunotherapies[91]. Polypill strategies such as the GMRx2 “super-pill” combine low-dose agents in single formulation, achieving rapid BP control in over 70% of trial patients[92]. At ACC 2025, a low-dose triple-pill meta-analysis confirmed enhanced efficacy with no increased adverse events[93]. Novel precision medicine approaches use genomic and AI-supported dynamic treatment regimes to tailor pharmacotherapy and monitoring frequency[94]. Finally, targeted thermal therapy (TTT)—an ablation method for primary aldosteronism—has demonstrated near-curative BP normalization in early trials, potentially reducing lifelong medication needs[95].

➢ *Non-Pharmacological Interventions*

Non-pharmacological interventions form the cornerstone of hypertension management and are recommended for all patients regardless of drug therapy[96]. Dietary Approaches to Stop Hypertension (DASH diet), rich in fruits, vegetables, and low-fat dairy with reduced

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saturated fat, significantly lowers blood pressure and cardiovascular risk[97]. Sodium restriction, ideally limiting intake to <2 g/day, is associated with a dose-dependent reduction in blood pressure[98]. Increasing dietary potassium, through fruits and vegetables, counteracts sodium's effects and supports vascular function[99]. Weight reduction, even as modest as 5–10% of body weight, leads to clinically meaningful improvements in blood pressure[100]. Regular aerobic and resistance exercise has been shown to lower systolic and diastolic blood pressure by 5–8 mmHg[101]. Limiting alcohol consumption to no more than 1–2 drinks per day reduces hypertension risk[102]. Smoking cessation is strongly advised as tobacco use increases arterial stiffness and cardiovascular risk[103]. Stress reduction strategies, including mindfulness, yoga, and meditation, have shown beneficial effects on autonomic regulation and blood pressure[104]. Adequate sleep hygiene and treatment of sleep apnea also contribute to better hypertension control[105]. When applied consistently, these lifestyle modifications can prevent the onset of hypertension and reduce the need for pharmacotherapy in early stages[106].

- *Prevention*

Lifestyle modification is the cornerstone of hypertension prevention and should be promoted at both individual and population levels[107]. Modest and sustained weight loss substantially lowers incident hypertension and blood pressure, so weight management is recommended for prevention in overweight and obese adults[108]. Adoption of the DASH dietary pattern—rich in fruits, vegetables, whole grains, low-fat dairy and low in saturated fat and red meat—produces clinically meaningful systolic and diastolic blood pressure reductions and reduces progression from prehypertension to hypertension[109]. Population and individual sodium reduction reduce systolic blood pressure in a dose–response fashion and are among the most effective dietary strategies to prevent hypertension at scale[110]. Increasing dietary potassium through fruit and vegetable intake also lowers blood pressure and mitigates sodium's adverse effects, making potassium promotion a complementary prevention strategy[111]. Regular aerobic and resistance physical activity show a clear inverse relationship with incident hypertension and lower resting blood pressure across risk groups, so activity promotion is a first-line preventive measure[112]. Sustained weight-loss programs and dietary interventions produce longer-term blood pressure benefits, although the magnitude and durability depend on adherence and program design[113]. Reduction of excessive alcohol intake lowers blood pressure in heavy drinkers and should be part of targeted prevention counseling for those who exceed recommended limits[114]. Smoking cessation programs, besides preventing many other diseases, have been shown in recent trials to reduce arterial blood pressure in hypertensive smokers and should be integrated into prevention services[115]. Limiting sugar-sweetened beverages and processed foods, and increasing whole grains and dietary fiber, are associated with lower hypertension risk and improved cardiometabolic profiles[116]. Addressing sleep quality, stress reduction and circadian health is an emerging preventive target because short sleep and chronic stress are linked to higher incident hypertension in cohort and mechanistic studies[117]. Policy-level interventions—such as mandatory reformulation to lower salt in processed foods, front-of-pack labeling, and health-promoting fiscal measures—have repeatedly been modeled or trialed to shift population blood pressure distributions and prevent new cases of hypertension[118]. Finally, embedding prevention into primary care with opportunistic screening, brief lifestyle counseling, digital supports (apps, remote monitoring) and community programs from early life onward amplifies individual measures and helps reduce the population burden of hypertension[119].

IV. CONCLUSION

Hypertension continues to impose a substantial health and economic burden globally, yet advances in diagnostics, therapeutics, and preventive strategies offer new opportunities for improved outcomes. Early detection through digital health tools, biomarkers, and ambulatory monitoring ensures timely intervention, while novel pharmacotherapies expand options for resistant and comorbid cases. Despite pharmacological innovations, lifestyle modification—including diet, exercise, weight management, and risk factor control—remains fundamental. Integrating population-level prevention policies with individualized, precision-based care represents the most effective path to controlling hypertension and reducing its cardiovascular consequences. Moving forward, collaborative implementation of clinical, technological, and policy-based strategies will be critical to bridging the gap between scientific progress and real-world hypertension control.

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