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THEMED ISSUE REVIEW

Blood pressure effects of SGLT2 inhibitors and GLP-1 receptor agonists: Mechanisms, trial evidence and Real-world data

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Sodium–glucose cotransporter 2 inhibitors (SGLT2is) and glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have transformed the management of type 2 diabetes, obesity and cardiorenal disease. Beyond their established glycaemic and weight-lowering effects, both drug classes consistently lower blood pressure (BP), a benefit that remains relatively underrecognized. This review provides an integrated synthesis of trial evidence, real-world data and meta-analyses examining the antihypertensive effects of SGLT2is and GLP-1 RAs. Across cardiovascular, heart failure, renal and obesity trials, modest but clinically meaningful BP reductions have been observed in diverse populations, including individuals without diabetes. These effects appear largely independent of glycaemic control and offer additive value in high-risk patients with overlapping comorbidities. The totality of evidence supports the strategic incorporation of these agents into future antihypertensive frameworks, warranting further investigation in dedicated blood pressure–focused trials.

KEYWORDS
clinical Pharmacology, evidence-based medicine < clinical Pharmacology, hypertension < cardiology, obesity < nutrition, pharmacotherapy < clinical Pharmacology

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1 | INTRODUCTION

Arterial hypertension (AH) affects more than 1.2 billion people worldwide, and its prevalence continues to rise, particularly in the context of increasing rates of type 2 diabetes mellitus (T2DM) and obesity, which often coexist and have common pathophysiological causes.[1] In people with T2DM or obesity, AH significantly increases the risk of cardiovascular events, stroke, heart failure and chronic kidney disease.[2,3] Nevertheless, it remains one of the most modifiable risk factors in clinical practice.[4]

Patients with T2DM are more likely to have AH than the general population, and hypertensive patients are more likely to have T2DM, with AH occurring in 50% to 80% of patients with T2DM.[2,5,6] When it comes to obesity, 60% to 76% of overweight or obese patients have AH.[7]

The coexistence of AH and cardiometabolic diseases has shown a multiplicative increase in cardiovascular morbidity and all-cause mortality.[8] Also, AH has been shown to be responsible for up to 75% of cardiovascular disease in T2DM.[9] In addition, patients with AH and T2DM have a 66% higher risk of all-cause mortality and more than twice the risk of cardiovascular mortality than patients with either disease alone.[10]

Despite advances in pharmacotherapy and risk factor control, cardiovascular death is the leading cause of death in patients with concomitant metabolic disease and AH.[10,11]

Conventional antihypertensive agents often do not fully address the complex blood pressure patterns and pathophysiological mechanisms seen in patients with metabolic disorders, such as the abnormal nocturnal blood pressure behaviour (non-dipper or riser pattern) that is common in this population.[12]

Sodium-glucose co-transporter-2 inhibitors (SGLT2is),[13] originally developed as antihyperglycaemic agents, also provide cardiovascular and renal benefits, including a blood pressure-lowering effect in patients with and without T2DM, via mechanisms beyond lowering blood glucose levels, including improved tubuloglomerular feedback, improved hemodynamics and decreased sympathetic nervous system activity.[14] These multifactorial effects contribute to fewer hospitalizations, slower progression of kidney disease and lower mortality, making SGLT2is a key therapy in the treatment of heart failure and chronic kidney disease.[15,16]

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs),[17] which are primarily used as antihyperglycaemic agents, have proven to be effective and versatile agents in the treatment of metabolic diseases such as T2DM and obesity. They are also increasingly being used as effective therapeutic options with nephroprotective properties in diabetic kidney disease, demonstrating their cardioprotective capabilities in reducing cardiovascular events, lowering blood pressure and other metabolic effects such as nonalcoholic fatty liver disease.[18,19]

Although the cardiorenal benefits are well described, the antihypertensive effects of GLP-1 RAs and SGLT2is are often underestimated or not comprehensively reviewed. There is a need to summarize the findings from various clinical trials and real-world data. This review aims to provide a comprehensive overview of the antihypertensive effects of SGLT2is and GLP-1 RAs. It is based on mechanistic findings, results from large clinical trials and emerging real-world evidence.

2 | PATHOPHYSIOLOGICAL MECHANISMS OF BLOOD PRESSURE REDUCTION

The blood pressure-lowering effects of SGLT2is and GLP-1 RAs, previously regarded as side effects, have recently garnered growing attention due to their consistent potency in both clinical trials and real-world studies. Most importantly, this potency unfolds well beyond the control of glycaemia, revealing multi-factorial mechanisms that may affect intravascular volume, endothelial function, autonomic activities and inflammatory pathways (Figure 1). Understanding these mechanisms may not only facilitate the application of more clinically optimized principles but also lead to integration when these agents are used in patients with T2DM, obesity and cardiovascular or renal diseases in the treatment of hypertension.[20]

2.1 | Mechanisms of blood pressure reduction with SGLT2 inhibitors

SGLT2is exert antihypertensive effects through an interplay of hemodynamic and vascular mechanisms, several of which manifest early in treatment and remain stable over time.

2.1.1 | Osmotic diuresis and volume contraction

By inhibiting glucose and sodium reabsorption in the proximal renal tubule, SGLT2is induce osmotic diuresis. This mechanism reduces plasma volume and preload, particularly in individuals who are volume-sensitive, such as those with heart failure or diabetic nephropathy. The resultant BP decline is typically observed within days of therapy initiation and contributes to improved cardiac unloading and natriuretic efficiency. These inhibitors induce osmotic diuresis primarily by inhibiting the reabsorption of glucose and sodium in the proximal renal tubules, leading to increased urinary excretion of both glucose and sodium. The resulting glucosuria creates an osmotic gradient that draws water into the tubular lumen, thereby increasing urinary volume (osmotic diuresis) and promoting natriuresis, particularly in the early phase of therapy.[21,22]

Mechanistically, SGLT2is act at the S1 segment of the proximal tubule where the SGLT2 transporter is located and reduces reabsorption of glucose and sodium that has been filtered. This will increase delivery to the distal nephron of both sodium and glucose, thereby enhancing osmotic diuresis, thus causing a transient natriuresis. Therefore, these agents produce an effect different from loop or thiazide diuretics because they act upstream in the nephron and do not create significant loss of potassium; however, all renal conserving mechanisms will eventually make up for any sodium loss in the urine

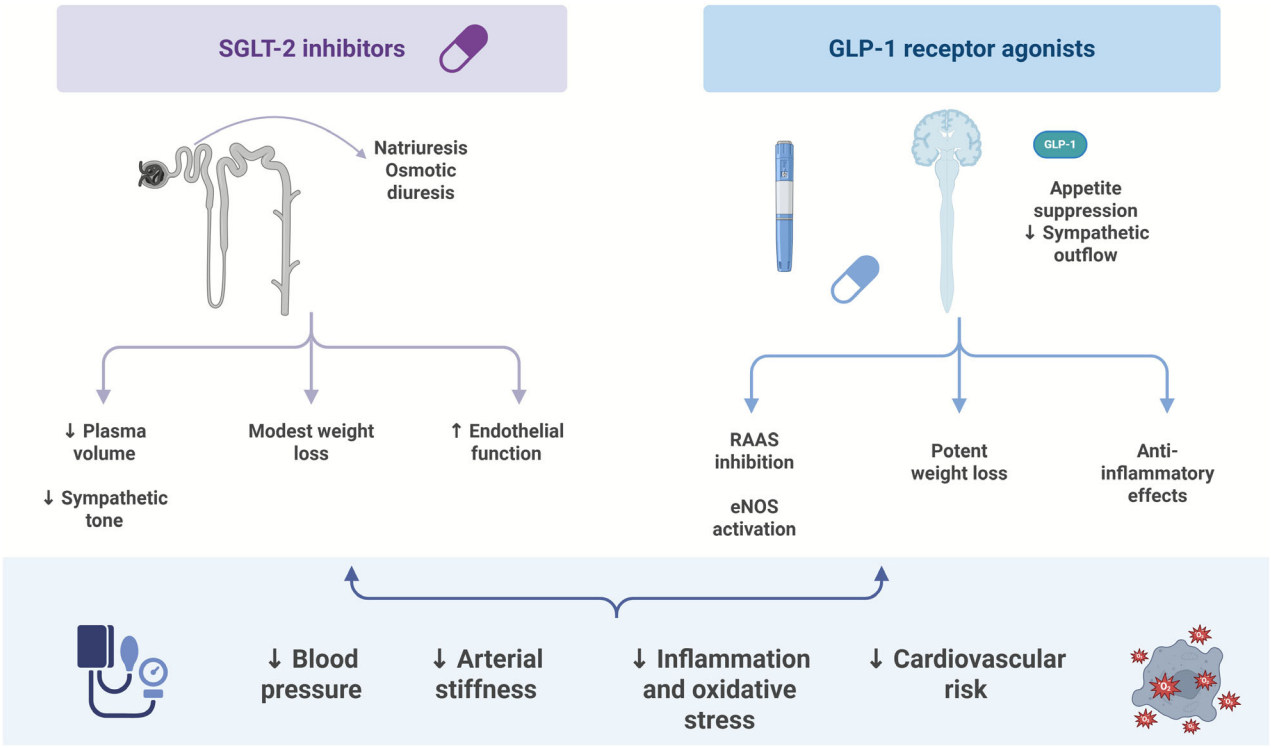

FIGURE 1 Complementary mechanistic pathways of SGLT2 inhibitors and GLP-1 receptor agonists in blood pressure reduction. Abbreviations: RAAS, Renin angiotensin aldosterone system; eNOS, endothelial nitric oxide synthase.

by enhancing absorption elsewhere in the nephron.[23,24] The natriuretic effect is typically transient, as compensatory mechanisms in the distal nephron eventually increase sodium reabsorption, but the osmotic diuresis from persistent glucosuria continues.[25,26]

2.1.2 | Natriuresis and restoration of Tubuloglomerular feedback

SGLT2is potentiate natriuresis independently of glycaemia. Concomitant inhibition of sodium-hydrogen exchanger 3 (NHE3) also promotes natriuresis, allowing tubuloglomerular feedback to reduce glomerular hyperfiltration and intrarenal renin-angiotensin-aldosterone system (RAAS) activation, factors that may lead to stable blood pressure control therapy.[22]

SGLT2 inhibition decreases sodium reabsorption at the proximal tubule, therefore increasing distal delivery of sodium to the nephron. Increased delivery of downstream nephron segments activates tubuloglomerular feedback, resulting in afferent arteriolar vasoconstriction, decreasing intraglomerular pressure, believed to be not only a site of kidney damage but also instrumental in eliciting protective effects from these drugs.[23,24] The natriuresis seen with SGLT2is is quite different from any traditional diuretic; SGLT2is act before the loop of Henle, and their diuresis manifests as a mixture of natriuresis with osmotic diuresis caused by glucosuria.[27]

The initial natriuresis and osmotic diuresis result in a slight decrease in plasma volume and blood pressure. It is assumed that this accounts for part of the cardiovascular benefits seen in large outcome trials. When administered with loop diuretics, SGLT2is exhibit a synergistic natriuretic effect that can be clinically significant in treating volume overload associated with heart failure. The long-term natriuretic impact of SGLT2is is not sustained because compensatory sodium reabsorption in the distal nephron limits continued sodium loss.[28]

SGLT2is also transiently activated by the RAAS as a likely physiological response to natriuresis and volume contraction; however, they do not appear to chronically activate the intrarenal RAAS. Other mechanistic insights include reduced sympathetic nervous system activity and increased energy metabolism within the kidney, which may further explain the cardiorenal benefits of SGLT2is.[29]

2.1.3 | Reduction in arterial stiffness

SGLT2is are proven to decrease arterial stiffness, a major pathway of cardiovascular risk by way of combined direct effects on the vasculature and indirect systemic changes through several mechanistic pathways that extend beyond glycaemic control. These improvements in arterial compliance complement the early hemodynamic effects driven by natriuresis and volume contraction.

Mechanistically, SGLT2is enhanced endothelial function by increasing nitric oxide (NO) bioavailability, thereby restoring endothelium-dependent vasodilation, which has been impaired due to any pathological condition. This occurs through reduced oxidative stress in response to lowered NADPH oxidase activity and the

expression of pro-inflammatory signalling pathways such as NF-κB. Collectively, these effects reduce endothelial dysfunction and improve vascular tone.[30,31]

Apart from their positive effects on endothelial function, SGLT2is also exert direct actions on vascular smooth muscle cell contraction, proliferation and migration. This is involved in preventing maladaptive remodelling and stiffening of the arterial wall. Preclinical studies also indicate attenuation of fibrosis and extracellular matrix accumulation, which would lead to improved elasticity of the vasculature.[32]

Changes in systemic hemodynamics with SGLT2 inhibition result in a modest reduction in plasma volume, afterload and blood pressure, which contribute to reduced arterial wall stress and improved arterial compliance. Other ancillary effects that may further advantage the vasculature include weight loss and reduced serum uric acid levels.[33]

Recent evidence suggests that SGLT2is also improve cell metabolism and ionic homeostasis. These include the modulation of sodium-hydrogen exchanger activity and mitochondrial function, which further facilitate vascular resilience against arterial stiffening.[30]

Clinical evidence also supports a modest but measurable reduction in arterial stiffness with SGLT2 inhibition. A systematic review and meta-analysis confirmed a modest, but statistically significant reduction in pulse wave velocity in patients with type 2 diabetes.[34] Furthermore, mechanistic and preclinical studies demonstrate improvements in endothelial function, suppression of oxidative stress and inflammation and direct vascular smooth muscle remodelling with SGLT2 inhibition.[31,35,36] Importantly, experimental models show that SGLT2 inhibitors can blunt arterial stiffening even in the absence of measurable blood pressure changes.[37] These additions clarify the evidence base for BP-independent effects of SGLT2 inhibitors.

2.1.4 | Modest weight loss and metabolic modulation

Weight loss with SGLT2is is mainly mediated through the induction of glycosuria, which leads to a net caloric loss. By inhibiting SGLT2 in the proximal renal tubules, these agents prevent the reabsorption of filtered glucose, resulting in urinary glucose excretion and a daily caloric deficit of approximately 200–300 kcal/day in patients with T2DM. The loss of these calories is the primary mechanism for weight reduction.[38]

However, the weight loss has always been less than what would be predicted based on the total caloric deficit from glycosuria. Quantitative modelling and clinical studies demonstrate that compensatory mechanisms, particularly an increase in energy intake — hyperphagia — attenuate the expected weight loss. For example, Ferrannini et al. found that only about 29% of the predicted weight loss was realized; the rest was made up for by an adaptive increase in calories consumed. This compensatory hyperphagia is most probably mediated by central mechanisms, which are typically activated in response to a negative energy balance.[39]

With SGLT2is treatment, significant metabolic changes extend far beyond mere loss of calories. With glycosuria accompanying reduced plasmatic levels of glucose and insulin, conditions favour lipolysis and more efficiently support fatty acid oxidation. Available data suggest that SGLT2 inhibition initiates a shift in substrate utilization from carbohydrates to lipids, thereby enhancing both ketogenesis and gluconeogenesis. This change in metabolism is associated with decreases in fat mass, particularly visceral adiposity, as demonstrated in both clinical and mechanistic studies.[40]

Emerging data also suggest an important role for neurohormonal pathways. Preclinical evidence suggests that the hepatic glycogen depletion induced by SGLT2is activates a specific neurocircuitry pathway involving the liver, brain and adipose tissue. This then results in sympathetic outflow to adipose tissue, increasing lipolysis via protein kinase A (PKA) signalling that gets activated through this pathway. Further support for this mechanism comes from observations of weight loss attenuation in animal models that have undergone hepatic vagotomy, hence suggesting involvement of the liver-brain-adipose axis in mediating part of the weight loss effect.[41]

Body composition studies confirm that the major component of weight loss achieved through SGLT2-induced is due to fat mass, with minimal or negligible effect on skeletal muscle mass and no significant decrease in muscle strength. The selective reduction of adiposity is clinically meaningful, as it can improve insulin sensitivity, hepatic steatosis and the cardiometabolic risk profile.[40]

2.1.5 | Autonomic effects

SGLT2is are increasingly recognized not only for their metabolic and renal effects, but also for their modulation of autonomic nervous system activity. Evidence from both preclinical and clinical studies indicates that SGLT2is reduce blood pressure and do not elicit reflex tachycardia, which is typically observed when sympathoinhibition occurs.[42] The normal circadian patterning of both blood pressure and sympathetic nerve activity (SNA) by these agents in animal models of metabolic syndrome and hypertension further supports their role in autonomic regulation.[43]

The mechanisms underlying these effects are multifactorial. At the level of hemodynamics, SGLT2is promoted natriuresis and osmotic diuresis by contracting plasma volume, thereby reducing cardiac preload. This would be described as volume reduction, increasing the probability of lowering pressure; however, it is not accompanied by compensatory increases in heart rate. This suggests that SGLT2is blunt sympathetic outflow, potentially through central or renal mechanisms.[44]

At the renal level, experimental data have revealed several pathways by which SGLT2is may reduce the sympathetic nerve activity. Norepinephrine has been found to upregulate SGLT2 expression, such that its inhibition reverses this upregulation and normalizes diuretic responses, particularly in models of heart failure.[45] Also, improving the intrarenal milieu by reducing hypoxia, inflammation, oxidative stress and congestion, SGLT2is may suppress afferent renal nerve signalling. This, in turn, reduces central sympathetic outflow to the kidneys and other organs.[46]

Molecular markers also support these findings. Reductions in the expression of tyrosine hydroxylase—the key enzyme involved in the synthesis of catecholamines—have been noted both in the heart and kidney, elicited by SGLT2 inhibition, independent of any changes in glycaemia or blood pressure.[35,47]

Taken together, current evidence supports a consistent sympathoinhibitory effect of SGLT2is across various levels of regulation. By reducing systemic and renal sympathetic tone, these agents can enhance the cardiovascular and renal protective benefits they have already established.[48]

2.2 | Mechanisms of blood pressure reduction with GLP-1 receptor agonists

GLP-1 RAs lower BP through mechanisms that are distinctively neurohormonal and metabolic, with pronounced central and endothelial effects. Although dual GLP-1/GIP RAs, such as tirzepatide, may share overlapping mechanisms, their specific impact on blood pressure regulation remains insufficiently elucidated in the current literature and is therefore not discussed further in this section.

2.2.1 | Appetite suppression and substantial weight loss

GLP-1 RAs are among the most effective pharmacotherapeutic agents capable of inducing significant and sustained weight loss in individuals with overweight or obesity. They primarily act by suppressing appetite centrally through complicated neuroendocrine signalling mechanisms. Centrally, GLP-1 RAs activate important hypothalamic nuclei and change nerve pathways in areas like the lateral septum—a part now known to play a significant role in controlling feeding actions. Studies in animals have shown that activating GLP-1R-carrying nerve cells in this area is necessary for drugs like liraglutide to induce less eating, and disrupting this pathway weakens both the reduction in food intake and weight loss.[49–51]

Clinically, GLP-1 RAs, including liraglutide and semaglutide generate dramatic dose-dependent reductions in bodyweight, often independent of glycaemic status. Recent studies consistently report mean weight losses ranging from approximately 5% with liraglutide over treatment durations of 26 to 72 weeks.[52,53] Semaglutide is singled out as the best single agent GLP-1 RA for weight reduction among non-diabetics. Reductions in waist circumference and improvements in several markers for cardiometabolic risk usually accompany weight loss.[54]

A distinguishing feature of GLP-1 RAs is their multifaceted mechanism of action. In addition to central appetite regulation, they delay gastric emptying and modulate gastrointestinal hormone secretion, further enhancing satiety and reducing caloric intake.[55] Peripherally, they enhance insulin secretion, suppress glucagon release, improve lipid metabolism and mitigate adipose tissue inflammation, collectively supporting broader metabolic benefits. Reduction in visceral adiposity associated with GLP-1 RA therapy may attenuate sympathetic overactivity and improve insulin sensitivity; however, GLP-1– sympathetic nervous system (SNS) interactions extend beyond adiposity changes and are further detailed in section 2.2.4. These downstream effects may help ameliorate vascular tone and lower blood pressure, further reinforcing the cardiometabolic profile of these agents.[54]

GLP-1 RAs are generally well tolerated, with gastrointestinal adverse events the most common and presenting as nausea, vomiting, diarrhoea and constipation. These events are typically transient and dose-related. Serious adverse outcomes and treatment discontinuations remain relatively rare. Discontinuation of therapy results in weight regain, thereby emphasizing the need for either long-term pharmacologic treatment or the integration of lifestyle interventions to maintain clinical benefit.[52,53]

Beyond gastrointestinal effects, hemodynamic adverse events such as orthostatic hypotension and transient syncope may occasionally occur, particularly in individuals with long-standing diabetes, autonomic dysfunction, or those receiving concomitant antihypertensive therapy. While these phenomena are generally mild and self-limiting, they warrant clinical attention given the frequent polypharmacy and potential for cumulative volume depletion in this population.[56] Both SGLT2 inhibitors and GLP-1 receptor agonists can modestly lower intravascular volume or alter vascular tone, which may unmask postural symptoms in susceptible patients. Accordingly, careful dose titration and individualized adjustment of concomitant antihypertensive agents are advised to minimize the risk of symptomatic hypotension without compromising cardiometabolic benefit.[57]

2.2.2 | Renal sodium handling and natriuresis

The clinically relevant effects of GLP-1 RAs on renal sodium handling include natriuresis primarily through a direct tubular mechanism and by modulating the RAAS. The natriuresis observed with GLP-1 is unrelated to glycosuria, unlike the case with SGLT2is, as it is glucose-independent and sustained across various glycaemic states. Studies in healthy humans and animal models acutely infused with GLP-1 have shown increased urinary sodium excretion in the absence of changes in glomerular filtration rate (GFR) or renal plasma flow (RPF), which supports a tubular site of action rather than a hemodynamic effect. That this effect is mediated explicitly by GLP-1 receptor activation is evidenced by attenuation of natriuresis when the selective GLP-1RA, exendin 9–39, is administered.[58]

At the mechanistic level, GLP-1R expressed in the proximal tubule inhibits the activity of NHE3, likely via a phosphorylation cascade mediated by a PKA-dependent pathway. As such, inhibition will result in reduced proximal sodium reabsorption, leading to an increase in the fractional excretion of both sodium and lithium. Molecular studies further support increased phosphorylation of NHE3 and decreased transporter activity elicited by exposure to GLP-1, thereby confirming this as a tubular mechanism.[59,60]

Apart from their tubular effects, GLP-1 RAs also involve hormonal mediators of fluid balance. They suppress the circulating levels of

angiotensin II, thereby lowering activation of the RAAS and permitting natriuresis independent of any changes in either GFR or RPF. The natriuretic effect of GLP-1 demonstrates volume-dependence: that is, it is enhanced in states of volume expansion. This supports a putative functional GLP-1–renal axis, most probably coming into play in pathological states characterized by extracellular fluid overload.[61]

In models of diabetic nephropathy, GLP-1 and agents that increase endogenous GLP-1 levels, such as dipeptidyl peptidase-4 (DPP-4) inhibitors, further reduce sodium reabsorption by lowering the expression and activity of the epithelial sodium channel (ENaC). This mechanism may be involved in sensitivity to salt and water retention.[62] The other way around, there is less natriuresis or diuresis induced by GLP-1 RA in states of hypertension. This is most probably explained by reduced expression of renal receptors for GLP-1 and increased degradation of the peptide.[63]

2.2.3 | Endothelial function and NO bioavailability

GLP-1 RAs exert notable vascular benefits, particularly through enhancement of endothelial nitric oxide synthase (eNOS) activity and attenuation of oxidative stress. These effects improve endothelial-dependent vasodilation, reduce arterial stiffness and promote microvascular recruitment in peripheral tissues—mechanisms that collectively contribute to cardiovascular protection. Preclinical and clinical evidence consistently demonstrate that GLP-1 RAs, including exenatide and liraglutide, improve endothelial function in individuals with and without T2DM. Importantly, many of these vascular effects appear to be at least partially independent of glycaemic control. Mechanistically, GLP-1 RAs stimulate eNOS phosphorylation, leading to increased NO production and enhanced vasodilatory capacity of the endothelium. These findings are supported by in vitro and in vivo studies, which have demonstrated increased NO generation and eNOS activity in human endothelial cells and isolated arterioles following exposure to GLP-1 Ras.[64,65]

The vasoprotective actions of these agents are mediated via the GLP-1 receptor, as evidenced by the reversal of these effects upon administration of receptor antagonists. Downstream signalling involves activation of the AMPK/PI3K-Akt/eNOS axis, which promotes NO bioavailability and counters oxidative stress, thereby safeguarding endothelial integrity under metabolic stressors such as hyperglycaemia and dyslipidaemia. Additionally, GLP-1 RAs reduce the expression of endothelial activation markers, including soluble intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1), further underscoring their anti-inflammatory and anti-atherogenic potential.[66]

Clinical studies corroborate these findings, reporting improvements in coronary flow velocity reserve and peripheral microvascular perfusion in patients treated with GLP-1 RAs. Although the magnitude of improvement in flow-mediated dilation (FMD) varies across populations and comparator treatments, the prevailing consensus is that GLP-1 RAs contribute to vascular health through NO-dependent mechanisms and suppression of oxidative pathways.[67]

2.2.4 | Sympathetic nervous system modulation

These mechanisms operate independently of weight change, underscoring that GLP-1–SNS interactions are not solely explained by reductions in visceral adiposity. A distinctive characteristic of GLP-1 RAs is their capacity to penetrate the blood–brain barrier and modulate activity of the autonomic nervous system. They act on important brain stem structures, including the nucleus tractus solitarius (NTS) and area postrema, to reduce central sympathetic outflow, increasing parasympathetic tone. This pathway mainly explains their effects on lowering both systolic and diastolic blood pressure.

GLP-1 RAs act through both the central and peripheral pathways. Experimental findings suggest that the application of GLP-1 in both central and peripheral locations may induce a dose-dependent increase in sympathetic activity. This is due to the activation of GLP-1 receptors located within medullary autonomic regulatory centres, which are associated with catecholaminergic neurons projecting to sympathetic preganglionic neurons. Activation of these pathways is associated with upregulation of markers involved in neuronal excitation and catecholamine biosynthesis.[68,69]

In human studies, GLP-1 infusion has been shown to increase muscle sympathetic nerve activity (MSNA), but not accompanied by significant changes in cardiac autonomic balance, as measured by heart rate variability (HRV) spectral analysis. Clinically, this translates to modest increases in resting heart rate observed with GLP-1 RA therapy. This phenomenon is considered a class effect and may result from direct stimulation of the sinoatrial node or mild sympathoexcitation.[70]

Despite these autonomic effects, large-scale cardiovascular outcome trials have not shown an elevated risk of heart failure hospitalization with GLP-1 RA use. Conversely, these agents are safe to use and confer benefit among patients with T2DM who have established cardiovascular disease. They cannot be characterized as drugs for the management of heart failure since their effect on cardiac outcomes is relatively neutral.[71]

Evidence interestingly suggests a bidirectional interaction between the sympathetic nervous system and endogenous GLP-1 secretion. Sympathetic activation through adrenergic signalling inhibits the release of GLP-1 from intestinal L cells, which may be involved in regulating postprandial glucose levels as well as central glucose sensing.[72] This feedback loop underscores the complexity of GLP-1 signalling in metabolic and autonomic control.

2.2.5 | Anti-inflammatory and antioxidant effects

GLP-1 RAs exhibit potent anti-inflammatory and antioxidant properties that significantly contribute to vascular protection and improved endothelial function. Recent studies have indicated that GLP-1 RAs reduce circulating levels of inflammatory biomarkers, such as tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6) and C-reactive protein, as well as malondialdehyde, a marker of oxidative stress. At the same time, they increase the expression of adiponectin, an anti-

inflammatory adipokine, thereby promoting a more favourable vascular environment.[73,74]

Notably, these effects occur independently of glycaemic control and are associated with reductions in systolic blood pressure, accompanied by improvements in endothelial-dependent vasodilation. The underlying mechanisms relate to increased bioavailability of NO and reduced oxidative damage to the endothelium.[75,76]

At the molecular level, GLP-1 RAs reduce vascular inflammation by downregulating leukocyte adhesion to the endothelium and inhibiting the infiltration of inflammatory cells into the vascular wall. They also act to prevent eNOS uncoupling, which is associated with oxidative stress and related vasodilatory pathology. Preserved eNOS coupling would most likely preserve NO-mediated vascular tone, accompanying a reduction in peripheral vascular resistance.[57,77]

Preclinical and clinical studies support the ability of GLP-1 RAs to restore or preserve endothelial function across the spectrum of cardiometabolic conditions, including diabetes, obesity and hypertension. Vasoprotective effects are attributable, at least in part, to direct actions on endothelial cells. This further supports the therapeutic relevance of GLP-1 RAs in cardiovascular risk reduction.[78]

However, the relationship between these anti-inflammatory and antioxidant effects and blood pressure regulation is more nuanced. Meta-analyses consistently show modest reductions in systolic blood pressure, with the magnitude of lowering more closely linked to weight loss and glycaemic improvement than to direct anti-inflammatory pathways.[79] One analysis nevertheless demonstrated a strong correlation between CRP reduction and systolic pressure decline, suggesting that inflammation may contribute to hemodynamic benefit.[73] Conversely, ambulatory blood pressure studies in patients with type 2 diabetes did not confirm a significant effect, indicating that these vascular effects may occur independently of blood pressure modulation.[80]

2.3 | Overlapping and distinct mechanisms between the two classes

Despite targeting different molecular sites, these two classes of antihyperglycaemic agents have several downstream effects that lead to lowering blood pressure, improving metabolism and protecting organs.

Volume adjustment is a major overlapping pathway. SGLT2is precipitate rapid plasma volume reduction through glucosuria-induced osmotic diuresis and natriuresis, primarily by inhibiting proximal sodium transport and NHE3 activity.[81,82] On the other hand, GLP-1RAs induce natriuresis without glucosuria, primarily by inhibiting NHE3 in the proximal tubule through cAMP-PKA signalling, while also altering RAAS activity. These effects are glucose-independent and explain the distinct temporal profiles of blood pressure lowering—early onset with SGLT2is and gradual with GLP-1Ras.[83,84]

Another benefit, common in both, is weight reduction. SGLT2is induces modest weight loss by calorie loss through urinary glucose excretion, which may be partially offset by compensatory hyperphagia. GLP-1RAs, in contrast, precipitate potent central appetite suppression, delay gastric emptying and more pronounced and sustained weight loss. These downstream metabolic effects reduce sympathetic activity and vascular resistance.[85]

Both classes improve endothelial function, reduce oxidative stress and lower systemic inflammation, which in turn reduces arterial stiffness. SGLT2is increase NO bioavailability-related mechanisms and reductions in NADPH oxidase activity, whereas GLP-1RAs increase eNOS phosphorylation together and activate anti-inflammatory pathways.[86,87]

Autonomic modulation is substantially different between the two classes. SGLT2is primarily decreases sympathetic tone through peripheral mechanisms, including renal afferent nerve modulation and improved renal milieu. GLP-1RAs penetrate the blood–brain barrier, thereby acting directly at central autonomic nuclei (NTS, area postrema), resulting in robust sympathetic outflow inhibition concomitantly with vagal tone facilitation.[88,89]

Regarding glycaemic control, both classes lower glucose levels by mechanisms independent of insulin, with a low risk of hypoglycaemia. SGLT2is by producing glucosuria, and GLP1-RAs increase the secretion of insulin, suppress glucagon secretion and delay gastric emptying. More specifically, SGLT2is may increase the secretion of glucagon that GLP-1RAs would suppress through their inhibitory effect mediated via somatostatin, supporting the notional mechanistic rationale for combination therapy.[90]

These converging and diverging actions not only explain their efficacy but also suggest complementary therapeutic value when used in combination. A comparative summary provides an overview of these mechanisms and their relative contributions (Table 1).

Though different in mechanistic profiles, they share overlapping pleiotropic effects on weight, endothelial function, inflammation and blood pressure. Therefore, these agents are intended to be complementary in the management of T2DM with coexisting hypertension and cardiovascular risk.[91] Their combination leverages renal and neurohormonal pathways, justifying integrated use in appropriately selected patients.

3 | GLP-1 RAS AND GLP-1/GIP RAS – EVIDENCE FROM PIVOTAL RCTS

Pivotal randomized trials of GLP-1 RAs and dual GLP-1/GIP RAs have consistently demonstrated modest but clinically relevant reductions in blood pressure, in addition to their established glucose-lowering and cardiometabolic benefits. In cardiovascular outcome trials (CVOTs) among patients with T2DM, these agents appear to exert a greater influence on systolic blood pressure (SBP) than diastolic blood pressure (DBP), likely reflecting their effects on arterial compliance, natriuresis and weight loss-mediated hemodynamic changes.

In the LEADER trial, which evaluated liraglutide *vs.* placebo in patients living with T2DM at high cardiovascular risk, statistically significant BP effects were observed over 36 months. Compared to placebo, liraglutide reduced systolic BP by 1.2 mmHg (95% CI, −1.9 to −0.5), while diastolic BP was paradoxically 0.6 mmHg higher (95% CI, 0.2 to 1.0). These findings highlight a modest net antihypertensive effect, with the greater SBP reduction suggestive of improved vascular tone or reduced central arterial stiffness.[92]

TABLE 1 SGLT2 inhibitors *vs.* GLP-1 receptor agonists - comparative mechanisms of blood pressure reduction.

Mechanism	SGLT2 inhibitors	GLP-1 RAs/GLP-1-GIP RAs
Osmotic diuresis	+++ (glucosuria-induced volume loss)	____
Natriuresis	++ (transient; proximal tubule/NHE3 inhibition)	+ (GLP-1R-mediated NHE3 inhibition)
Appetite suppression	____[1]	+++ (central hypothalamic GLP-1R activation)
Weight loss	+ (caloric loss via glucosuria)	+++ (substantial; appetite and gastric emptying)
Endothelial function improvement	++ (↓ oxidative stress and AGE)	++ (↑ NO, ↓ inflammation)
Sympathetic modulation	+ (indirect; kidney-mediated)[2]	+++ (direct CNS-mediated)[3]
Arterial stiffness reduction	++ (endothelial and smooth muscle effects)	+ (partly through weight loss and NO enhancement)
Central autonomic modulation	____[3]	+++ (via NTS, area postrema)
Onset of BP effect	Rapid (within days)	Gradual, dose-dependent

+ mild effects;++ moderate effects; +++ strong effect; −-- no direct effects.

[1]Although SGLT2 expression has been observed in the hypothalamus and may modulate AMPK signalling in preclinical models, SGLT2 inhibitors do not exert clinically relevant appetite-suppressing effects. Increased appetite has been reported as a compensatory response to caloric loss through glucosuria.

[2]SGLT2 inhibitors may indirectly reduce sympathetic activity through renal mechanisms, including decreased afferent signalling, volume contraction and improved tubuloglomerular feedback. These effects are peripherally mediated.

[3]*GLP-1 RAs act directly on central autonomic control centres, such as the nucleus tractus solitarius and area postrema, reducing sympathetic tone and enhancing vagal output. SGLT2 inhibitors do not appreciably cross the blood–brain barrier and therefore lack direct CNS-mediated autonomic effects.*

In SUSTAIN-6, which investigated subcutaneous semaglutide in two doses (0.5 mg and 1.0 mg weekly) among patients with T2DM and high cardiovascular risk, a dose-dependent reduction in SBP was observed. The 0.5 mg dose resulted in a mean SBP decrease of 1.3 mmHg *vs.* placebo ($P = 0.10$, not statistically significant), while the 1.0 mg dose yielded a 2.6 mmHg reduction ($P < 0.001$), underscoring a potentially pharmacodynamic gradient in BP-lowering efficacy.[93]

Beyond diabetes-focused CVOTs, trials in people without diabetes, primarily targeting obesity, demonstrate a more pronounced antihypertensive effect, likely mediated by greater weight reduction. Meta-analytic evidence supports a direct, dose–response relationship between weight loss and BP reduction. A BMI decrease of 2.27 kg/m^2 is associated with SBP and DBP reductions of 5.79 mmHg and 3.36 mmHg, respectively, while a BMI decrease of 4.12 kg/m^2 confers even greater reductions (−6.65 mmHg SBP, −3.63 mmHg DBP). Notably, individuals achieving ≥3 kg/m^2 reduction experience amplified benefits, reinforcing the synergistic role of weight loss in BP control.[94]

In the SCALE trial, liraglutide 3.0 mg daily resulted in 8.0% mean weight loss from baseline, alongside a significant SBP reduction of −2.8 mmHg (difference vs placebo; 95% CI, −3.56 to −2.09; $P < 0.001$) and DBP reduction of −0.9 mmHg (95% CI, −1.41 to −0.37; $P < 0.001$). While absolute BP reductions were modest, the directionally consistent results support an adjunct role in hypertension management, particularly in obese patients.[95]

The STEP 1 trial, evaluating semaglutide 2.4 mg weekly in adults with obesity, reported a placebo-adjusted SBP reduction of 5.10 mmHg (−6.16 mmHg with semaglutide vs − 1.06 mmHg with placebo), accompanying a substantial 14.9% mean bodyweight reduction. The impact on DBP was not specified, but the magnitude of systolic reduction highlights semaglutide's relevance beyond glycaemic control.[96]

In the SELECT trial, which assessed semaglutide 2.4 mg in a non-diabetic obese population with established cardiovascular disease, BP-lowering effects were again evident. Semaglutide reduced SBP by 3.82 mmHg *vs.* 0.51 mmHg with placebo, resulting in a placebo-corrected reduction of −3.31 mmHg (95% CI, −3.75 to −2.88). DBP decreased by 1.02 mmHg with semaglutide *vs.* 0.47 mmHg with placebo (difference −0.55 mmHg; 95% CI, −0.83 to −0.27), affirming a preferential effect on SBP.[97]

Dual agonist tirzepatide has shown even greater efficacy. In SURMOUNT-1, participants receiving tirzepatide achieved mean SBP reductions of 6.2 mmHg compared to 1.0 mmHg with placebo, alongside unprecedented mean weight loss of up to 20.9%.[98] These findings suggest superior cardiorenal and hemodynamic benefits, although long-term CVOT data are still pending.

The upcoming SURPASS-CVOT and SURMOUNT-MMO trials are expected to clarify the full cardiometabolic and BP-lowering effects of tirzepatide in both diabetic and non-diabetic populations.[99,100] Given its dual incretin mechanism and brilliant weight reduction efficacy, tirzepatide may emerge as the most powerful pharmacological adjunct for hypertension in the context of metabolic disease.[101]

4 | GLP-1 RAS AND GLP-1/GIP RAS – REAL-WORLD DATA AND META-ANALYSES

4.1 | GLP-1 receptor agonists – evidence from meta-analyses

Two early meta-analyses of first-generation GLP-1RAs provided early evidence for exenatide twice daily, exenatide every week and liraglutide once daily in reducing blood pressure.[102,103] In a Bayesian

TABLE 2 Effects of GLP-1 RA and blood pressure outcomes in meta-analyses.

Authors	Study type included (no. of studies quantitatively synthesized)*	Population	Intervention	Comparator	Outcomes	Certainty of evidence
[104]	RCTs (n = 35)	Not specified	GLP-1 RA	Placebo and NMA to indirectly compare specific GLP-1RA medications	**Versus Placebo** SBP: −3.1 mmHg (95% CI − 3.6 to −2.7)	Generally low to moderate certainty using GRADE
[105]	RCTs (n = 75)	Adults ≥ 18 years	GLP-1 RA	NMA with indirect comparisons to placebo and 14 distinct GLP-1 RA medication regimens	**Semaglutide (subcutaneous) Versus Placebo** SBP: −4.5 mmHg (95% CI − 5.6 to −3.3) DBP: −1.9 mmHg (95% CI − 2.6 to −1.2)	Low certainty using CINeMA
[106]	RCTs (n = 164)	Not specified	GLP-1 RA or SGLT2i	Placebo or active control	SBP: −2.9 mmHg (95% CI − 3.0 to −2.6) DBP: −0.9 mmHg (95% CI − 1.0 to −0.8)	Not assessed
[102]	RCTs (n = 33)	Adults, most with T2DM	GLP-1 RA	Placebo or active control	SBP: −2.2 mmHg (95% CI − 3.0 to −1.5) DBP: −0.5 mmHg (95% CI − 1.2 to 0.3)	Not assessed
[79]	RCTs (n = 63)	Adults (trials must mention diabetes status)	Semaglutide, liraglutide, dulaglutide and exenatide	Placebo	**SBP** Semaglutide: −3.4 mmHg (95% CI − 4.2 to −2.6) Liraglutide: −2.6 mmHg (95% CI − 3.5 to −1.7) Dulaglutide: −1.5 mmHg (95% CI − 2.2 to −0.7) Exenatide: −3.3 mmHg (95% CI − 3.7 to −2.9) **DBP** Semaglutide: −0.7 mmHg (95% CI − 1.5 to −0.1) Liraglutide: −0.2 mmHg (95% CI − 0.6 to 0.1) Dulaglutide: 0.3 mmHg (95% CI − 0.1 to 0.6) Exenatide: −1.0 mmHg (95% CI − 1.8 to −0.1)	Not assessed
[103]	RCTs (n = 53)	T2DM	GLP-1 RA	Pairwise and NMA with indirect comparisons to placebo, active comparators and 9 distinct GLP-1 RA medication regimens	**SBP** Exenatide 10 mcg twice daily: −2.3 mmHg (95% CI − 3.3 to −1.3) Exenatide 2 mg weekly: −1.9 mmHg (95% CI − 3.5 to −0.5) Exenatide 5 mcg twice daily: −1.2 mmHg (95% CI − 2.9 to 0.5) **DBP** Exenatide 10 mcg twice daily: −1.1 mmHg (95% CI − 1.8 to −0.3) Exenatide 5 mcg twice daily: −0.7 mmHg (95% CI − 1.8 to 0.4) Liraglutide 1.2 mg daily: −0.5 mmHg (95% CI − 1.8 to 0.8) **Estimates for the three most effective GLP-1 RA regimens in NMA *vs.* placebo**	Not assessed

(Continues)

TABLE 2 (Continued)

Authors	Study type included (no. of studies quantitatively synthesized)*	Population	Intervention	Comparator	Outcomes	Certainty of evidence
107	RCTs (n = 204)	T2DM	GLP-1 RA	NMA with indirect comparisons to placebo and nine other antidiabetic drug classes	**vs. Placebo** SBP: −2.9 mmHg (95% CI − 3.4 to −2.4) DBP: −0.3 mmHg (95% CI − 0.5 to 0.0) **vs. SGLT2i** SBP: 0.6 mmHg (95% CI − 0.1 to 1.2) DBP: 1.2 mmHg (95% CI 0.9 to 1.5)	Generally high to moderate certainty using CINeMA
108	RCTs (n = 30)	Overweight or obese adults with or without diabetes	GLP-1 RA	Placebo	SBP: −3.4 mmHg (95% CI − 4.0 to −2.8) DBP: −1.1 mmHg (95% CI − 1.5 to −0.7)	Moderate certainty (SBP) and low certainty (DBP) using GRADE

*Number of individual studies included in the largest meta-analysis of a blood pressure outcome.

Abbreviations: *CINeMA: Confidence In Network Meta-Analysis framework; DPB: diastolic blood pressure; GLP-1RA: glucagon-like peptide-1 receptor agonists; GRADE: Grading of Recommendations Assessment, Development and Evaluation; NMA: network-meta analysis; RCT: randomized controlled trial; SBP: systolic blood pressure; SGLT2i: sodium-glucose co-transporter 2 inhibitor; T2DM: type 2 diabetes mellitus.*

network meta-analysis, Sun et al. estimated the probability rankings of the best treatments for SBP and DBP, indicating potential differences in the effects of distinct GLP-1 RAs medications and dose regimens. The top three regimens and corresponding estimated reductions in SBP and DBP are summarized in Table 2.

Recent meta-analyses have synthesized studies of semaglutide. For example, Ali et al. evaluated the effects of specific GLP-1 RA medications on SBP in 35 placebo-controlled RCTs using network meta-analysis.[104] As compared to placebo, the largest reductions in SBP occurred with liraglutide and exenatide 10 mcg twice daily among individuals with diabetes, while efpeglenatide < 6 mg daily and semaglutide once weekly resulted in the largest reductions among individuals without diabetes. By contrast, An et al. reported that oral and subcutaneous semaglutide were most effective for SBP and subcutaneous semaglutide for DBP, in a network meta-analysis comparing GLP-1 RAs medications.[105] In a pairwise meta-analysis of 30 studies enrolling adults with overweight or obesity, Wong et al. reported that patients receiving oral *vs.* subcutaneous formulations of GLP-1 RA and trials with larger reductions in bodyweight were associated with greater reductions in SBP and DBP. They also found that changes in SBP, but not DBP, were greater among studies enrolling patients without diabetes *vs.* those with diabetes.[108]

When indirectly compared to SGLT2is in a network meta-analysis, GLP-1 RAs as a class had limited evidence of a difference in reductions in SBP, but were associated with a significant increase in DBP.[107] Among individual GLP-1-RAs, semaglutide (oral and subcutaneous) and exenatide (twice daily) were associated with the largest reductions in SBP, yet only exenatide (twice daily) was associated with reductions in DBP as compared to placebo. Rivera et al. also found that semaglutide and exenatide produced the largest reductions in SBP and DBP.[79]

Collectively, the evidence from meta-analyses demonstrates that GLP-1 receptor agonists reduce both systolic and diastolic blood pressure, with the magnitude of diastolic reduction approximately half that observed for systolic pressure—a proportional pattern consistent with most established antihypertensive classes. Importantly, these trial-derived estimates likely underestimate the true clinical effect, as many participants were normotensive at baseline and some antihypertensive agents were discontinued during study periods.[109] Moreover, data from ambulatory blood pressure monitoring (ABPM) indicate a more pronounced and sustained reduction, particularly in hypertensive individuals, further supporting the antihypertensive relevance of GLP-1-based therapies.[110]

4.2 | GLP1 receptor agonists Real-world evidence

Owing to their limited uptake in many countries, real-world evidence investigating the effects of GLP-1 RAs on blood pressure are currently limited to small-scale studies, with early evidence from these studies demonstrating the effects of GLP-1 RAs on blood pressure in clinical practice (Table 3). A large cohort study conducted at a single diabetes clinic and South Korea examined a wide range of clinical

TABLE 3 Effects of GLP-1 RA on blood pressure outcomes in select real-world studies.

Authors	Design	Population	Intervention	Comparator	Outcomes	Effect	Limitations
[111]	Cohort study, electronic health records	Mayo Clinic Health System (USA) Individuals with BMI ≥ 27 kg/m^2 who were prescribed at least 3 months of subcutaneous semaglutide for the purpose of weight loss with any dose (0.25, 0.5, 1, 1.7, 2 and 2.4 mg) n = 304 Mean age 49 years	Semaglutide subcutaneous injections	None	1) Change in SBP and DBP from baseline to last follow-up visit 2) Change in no. of antihypertensive medications from baseline to last follow-up visit	**SBP:** −6.8 mmHg (95% CI − 8.5 to −5.1) DBP: −2.6 mmHg (95% CI − 3.9 to −1.2) **No. of antihypertensive medications:** 3.6 (0.8) to 2.9 (1.2)	1) Treated group only pre- post-comparison (not adjusted for comparator group) 2) Estimates not adjusted for confounding factors 3) Descriptive analysis only 4) No information on other GLP-1/GIP medications or follow-up data beyond 12 months
[112]	Cross-sectional study, survey data	Patients who visit clinicians of members of the Kanagawa Physicians Association (Japan) T2DM (and CKD for SGLT2i group), prevalent use of SGLT2i or GLP-1 RA for at least one year and blood pressure > 130/80 mmHg n = 544 Mean age 58 to 64 years	SGLT2i (n = 384)	GLP-1 RA (n = 160)	Change in office SBP and DBP from baseline	**SBP:** −4.5 to −7.1 mmHg **DBP:** −3.2 to −4.2 mmHg Most point estimates from different analyses were not statistically significant	1) Restricted to prevalent users and adherent patients could result in selection bias of a healthier cohort 2) Different eligibility criteria for exposure groups (CKD for SGLT2i survey) 3) Appears to be a one-time survey from a group of physicians, may not be broadly generalizable
[113]	Cohort study, clinical records	Diabetes clinic at Seoul National University Bundang Hospital (South Korea) Adults with T2DM n = 2112 Mean age 56 years	Initiate GLP-1 RA (n = 528)	Initiate SGLT2i (n = 1584)	Seated SBP and DBP mean change from baseline	Effect size not reported, but numerically lower in SGLT2i group	1) Blood pressure not primary outcome of the study 2) Magnitude of effect not reported 3) Single-centre study from South Korea, and findings may not be broadly generalizable

Abbreviations: CKD: chronic kidney disease; DPB: diastolic blood pressure; GLP-1RA: glucagon-like peptide-1 receptor agonists; SBP: systolic blood pressure; SGLT2i: sodium-glucose co-transporter 2 inhibitor; T2DM: type 2 diabetes mellitus.

outcomes, including blood pressure, between patients using GLP-1 RAs and SGL2Tis.[113] Over four years of follow-up, SBP and DBP were on average lower among individuals prescribed SGL2Ti during the first two years, but were not statistically different between treatments at four years. Using physician survey data, Kobayashi et al. found that patients with T2DM had increased odds of achieving better blood pressure control with SGLT2is as compared to GLP-1 RAs treatment, although differences in SBP and DBP changes were not statistically different.[112] Ghusn et al. described decreases in systolic and diastolic blood pressure up to 12 months among patients with recorded blood pressure information who were prescribed weekly subcutaneous semaglutide injections for weight loss.[111] Further real-world studies in more diverse populations are therefore needed to understand the comparative long-term effects of different GLP-1/GIP RAs drugs in clinical practice.

5 | SGLT2 INHIBITORS – EVIDENCE FROM PIVOTAL RCTS

Although a limited number of randomized controlled trials (RCTs) have been specifically designed to investigate the effects of SGLT2is on

TABLE 4 Randomized controlled trials evaluating the impact of SGLT2 inhibitors on blood pressure.

Authors	Study population	HTN, n (%)	Intervention	Follow-up	Outcome
[116]	Patients with T2DM n = 7020 Age: 63.2 years	6667 (95)	Empagliflozin *vs.* placebo	3.1 years	Higher reduction in office SBP (−4.0 mmHg) and DBP (−1.5 mmHg) with empagliflozin
[117]	Patients with T2DM and HTN n = 825 Age: 60.2 years	825 (100)	Empagliflozin *vs.* placebo	12 weeks	Greater decrease in office SBP (−3.9 mmHg) and DBP (−1.9 mmHg) and in ABPM SBP (−3.4 mmHg) and DBP (−1.4 mmHg) with empagliflozin 10 mg Higher decrease in office SBP (−4.8 mmHg) and DBP (−1.9 mmHg) and in ABPM SBP (−4.2 mmHg) and DBP (−1.7 mmHg) with empagliflozin 25 mg
[118]	Patients with T2DM and uncontrolled nocturnal HTN n = 132 Age: 70 years	132 (100)	Empagliflozin *vs.* placebo	12 weeks	Reduction in office SBP (−8.6 mmHg) and DBP (−2.0 mmHg) with empagliflozin 10 mg Decrease in ABPM SBP (−7.7 mmHg) and DBP (−2.9 mmHg) with empagliflozin 10 mg
[119]	HFrEF patients (NYHA class II-IV) n = 3730 Age: 66.8 years	2698 (72.3)	Empagliflozin *vs.* placebo	52 weeks	Reduction in office SBP (−2.4 mmHg) with empagliflozin 10 mg compared to placebo
[120]	HF patients with LVEF> 40% (NYHA class II-IV) n = 5988 Age: 71.9 years	5424 (90.5)	Empagliflozin *vs.* placebo	52 weeks	Reduction in office SBP (−1.8 mmHg) with empagliflozin 10 mg
[121]	Patients with CKD (eGFR) of at least 20 but less than 45 mL per minute per 1.73 m^2 n = 6609 Age:63.8 years	NA	Empagliflozin *vs.* placebo	2 years	SBP (−2.6 ± 0.3 mmHg) and DBP (−0.5 ± 0.2 mmHg) were lower in the empagliflozin arm compared to placebo arm at the end of follow-up
[122]	Diabetic patients at high CV risk n = 17 160 Age: 64 years	NA	Dapagliflozin *vs.* placebo	4.2 years	Reduction in office SBP (−2.7 mmHg) and DBP (−0.7 mmHg) with dapagliflozin 10 mg
[123]	HFrEF patients (NYHA class II-IV) n = 4744 Age: 66.4 years	3510 (74)	Dapagliflozin *vs.* placebo	18.2 months	Reduction in office SBP (−1.3 mmHg) with dapagliflozin 10 mg
[124]	HF patients with LVEF> 40% (NYHA class II-IV) n = 6263 Age: 71.6 years	5553 (88.6)	Dapagliflozin *vs.* placebo	2.3 years	Beneficial effect of dapagliflozin on clinical outcomes was more pronounced in patients with a baseline SBP > 128 mmHg.
[125]	Patients with CKD eGFR of 25 to 75 mL per minute per 1.73 m2 n = 4304 Age: 61.9 years	NA	Dapagliflozin *vs.* placebo	2.4 years	Changes in BP were not assessed. Increase in BP was defined as safety endpoint and no such events were reported in the dapagliflozin treatment arm.
[126]	Diabetic patients with HTN n = 613 Age:56.3 years	613 (100)	Dapagliflozin *vs.* placebo	12 weeks	Dapagliflozin on top of renin angiotensin system blockade resulted in a reduction in office SBP (−3.1 mmHg) and ABPM SBP (−2.9 mmHg) compared to placebo
[127]	Diabetic patients with HTN n = 449 Age:57 years	449 (100)	Dapagliflozin *vs.* placebo	12 weeks	Dapagliflozin on top of combined antihypertensive therapy led to a reduction in office SBP (−4.3 mmHg) compared to placebo
[128]	Diabetic patients at high CV risk n = 10 142 Age:63.3 years	9125 (90)	Canagliflozin *vs.* placebo	188.2 weeks	Greater reduction compared to placebo in office SBP (−3.9 mmHg) and DBP (−1.4 mmHg) with canagliflozin

TABLE 4 (Continued)

Authors	Study population	HTN, n (%)	Intervention	Follow-up	Outcome
[129]	Diabetic patients with HTN n = 113 Age:58.6 years	113 (100)	Canagliflozin *vs.* placebo	6 weeks	Greater reduction compared to placebo in ABPM SBP (−3.3 mmHg) and DBP (−1.9 mmHg) with canagliflozin 100 mg, and reduction in ABPM SBP (−4.9 mmHg) and DBP (−2.9 mmHg) with canagliflozin 300 mg were observed.
[130]	Patients with diabetes n = 139 Age:57.5 years	NA	Ipragliflozin *vs.* placebo	24 weeks	Decline in office SBP (−1.2 mmHg) and DBP (−1.3 mmHg) with ipragloflozin 50 mg
[131]	Patients with diabetes n = 158 Age:59.3 years	NA	Luseogliflozin *vs.* placebo	24 weeks	Reduction in office SBP (−5.6 mmHg) and DBP (−2.5 mmHg) with luseogliflozin 2.5 mg
[132]	Patients with diabetes n = 229 Age:57.3 years	NA	Tofogliflozin *vs.* placebo	24 weeks	Reduction in office SBP (−3.6 mmHg) and DBP (−4.2 mmHg) with tofogliflozin 10 mg

Abbreviations: ABPM: Ambulatory blood pressure monitoring, CKD: Chronic kidney disease, CV: Cardiovascular, DBP: Diastolic blood pressure, eGFR: Estimated glomerular filtration rate, HFrEF: Heart failure with reduced ejection fraction, LVEF: Left ventricular ejection fraction, NA: Not available, NYHA: New York Heart Association, SBP: Systolic blood pressure; T2DM: Type 2 Diabetes Mellitus.

blood pressure, their impact on blood pressure has been assessed as secondary or safety endpoints across a range of patient populations, including individuals with T2DM, atherosclerotic cardiovascular disease, heart failure and chronic kidney disease.[114,115] An overview of representative RCTs is provided in Table 4.

The EMPA-REG OUTCOME trial is a landmark randomized controlled trial that evaluated the effects of empagliflozin on cardiovascular outcomes in patients with T2DM. In addition to its established cardiovascular benefits, empagliflozin was associated with higher reductions in SBP and DBP (−4 mmHg and −1.5 mmHg) compared to placebo.[116] A subsequent trial, the EMPA-REG BP study, specifically examined the antihypertensive effects of empagliflozin and demonstrated significant reductions in both office-based and 24-hour ambulatory systolic and diastolic blood pressure. The extent of the reduction in blood pressure was found to be dependent on the dosage administered, with a greater decrease observed in patients receiving 25 mg once daily in comparison to those receiving 10 mg once daily.[117] Further post hoc analyses by Mancia et al. explored the influence of the number and class of concomitant antihypertensive medications on blood pressure responses to empagliflozin. Their findings confirmed that the blood pressure-lowering effect of empagliflozin was sustained and consistent across subgroups receiving none, one or two antihypertensive agents. Moreover, this effect was independent of the specific class of antihypertensive therapy.[133] The blood pressure–lowering effect of empagliflozin was further confirmed in a multicentre RCT conducted in Japan, which demonstrated significant reductions in both systolic and diastolic blood pressure among patients with T2DM and uncontrolled hypertension.[118]

Empagliflozin studies in patients with heart failure revealed extremely positive results, establishing it as the standard treatment for all types of heart failure.[134] In the EMPEROR-Reduced trial, which included patients with heart failure with reduced ejection fraction (HFrEF), treatment with empagliflozin led to a reduction in SBP of 2.4 mmHg after 52 weeks of follow-up.[119] Similarly, in patients with heart failure with preserved ejection fraction (HFpEF), empagliflozin was associated with a 1.8 mmHg decrease in SBP at the end of 52 weeks.[120] The EMPA-KIDNEY trial evaluated the impact of empagliflozin on the progression of chronic kidney disease (CKD). After 2 years of follow-up, the SBP and DBP were lower in the empagliflozin group than in the placebo group: −2.6 ± 0.3 mmHg and −0.5 ± 0.2 mmHg, respectively.[121]

The DECLARE-TIMI 58 trial constitutes the pivotal RCT assessing the effects of dapagliflozin in individuals with type 2 diabetes on cardiovascular outcomes. Over a median follow-up of 4.2 years, administration of dapagliflozin 10 mg once daily was associated with a higher decline in office-measured SBP (−2.7 mmHg) and DBP (−0.7 mmHg) compared to placebo arm.[122] Weber et al. demonstrated that dapagliflozin exerts additional blood pressure–lowering effects when administered alongside either RAAS blockade monotherapy or combination antihypertensive regimens, as shown in placebo-controlled randomized trials involving hypertensive patients with T2DM.[126,127] The blood pressure-lowering effect of dapagliflozin was also evident in the DAPA-HF trial, which enrolled patients with HFrEF. Beyond its demonstrated efficacy in reducing the composite outcome of worsening heart failure or cardiovascular death, dapagliflozin compared to placebo was related to a greater reduction of 1.3 mmHg in office-measured systolic blood pressure.[123] The DELIVER trial included patients with heart failure and a left ventricular ejection fraction (LVEF) of more than 40%, randomizing them into dapagliflozin and placebo groups. Dapagliflozin was found to be associated with better cardiovascular outcomes, with greater benefits observed in patients with a SBP of over 128 mmHg.[124] The DAPA-CKD trial established the benefits of dapagliflozin for renal outcomes in patients with CKD, but changes in blood pressure were not evaluated. However, an increase in blood pressure was not observed in any cases in the dapagliflozin group.[125]

Canagliflozin, another SGLT2i was evaluated in patients with T2DM and increased cardiovascular risk. In the CANVAS Programme,

canagliflozin significantly reduced the incidence of the primary composite endpoint—comprising cardiovascular death, nonfatal myocardial infarction or nonfatal stroke—although it was concomitantly associated with an increased risk of lower-limb amputations. Blood pressure was assessed as a secondary endpoint, with canagliflozin producing higher reductions compared to placebo in office SBP and DBP of −3.9 mmHg and −1.4 mmHg.[128] Another RCT involving patients with diabetes and hypertension also demonstrated the blood pressure-lowering effect of canagliflozin after six weeks of follow-up. The blood pressure reduction was greater with higher doses of canagliflozin.[129]

Tofogliflozin, luseogliflozin and ipragliflozin are SGLT2is primarily utilized in Asian populations. Their antihypertensive effects in individuals with T2DM have been demonstrated in RCTs with relatively small sample sizes. Among these agents, tofogliflozin exhibited a dose-dependent reduction in blood pressure when compared to placebo, suggesting a potential pharmacodynamic relationship between dosage and antihypertensive efficacy.[130–132]

In summary, SGLT2is appear to exert a blood pressure–lowering effect that is consistent across various patient populations. This antihypertensive effect is generally dose-dependent, with higher doses associated with greater reductions in blood pressure. Given these properties, SGLT2is may hold potential as an adjunctive therapy in the management of resistant hypertension. Although studies conducted in Japan and Korea have reported findings consistent with those from trials conducted in European and North American populations, it remains important to acknowledge that geographic and ethnic differences may modulate the extent of blood pressure response to SGLT2is therapy.

6 | SGLT2 INHIBITORS – REAL-WORLD DATA AND META-ANALYSES

6.1 | SGLT2 and combined SGLT1/2 inhibitors – evidence from meta-analyses

Several meta-analyses have investigated the effects of SGLT2is on blood pressure outcomes from randomized controlled trials. Among these meta-analyses, the range of average reductions in office SBP/DBP was 2.4–5.0/1.4–2.3 mmHg and 24 h ambulatory SBP/DBP was 3.3–3.8/1.7–1.8 mmHg (Table 5). In a network meta-analysis, Tsapas et al. reported that among nine antidiabetic drug classes, SGLT2is produced the largest reductions in SBP.[107] When compared to placebo, specific SGLT2i medications associated with the largest reductions in SBP were canagliflozin, ertugliflozin and dapagliflozin, while those with the largest associated reductions in DPB were empagliflozin, dapagliflozin and canagliflozin. The availability of combined SGLT1/2 inhibitors has also raised the question about whether they impact blood pressure beyond the effects observed with SGLT2i. To answer this question, Teo et al. performed a network meta-analysis to compare the effects of SGLT2i (dapagliflozin, empagliflozin, canagliflozin, ipragliflozin, ertugliflozin and luseogliflozin) and SGLT1/2 inhibitors (licogliflozin and sotagliflozin) on blood pressure in patients with diabetes.[141] There was little evidence of a difference between SGLT2 and SGLT1/2 inhibitors, with low to moderate certainty. The evidence available from meta-analyses to date supports similar effects of SGLT2i and SGLT1/2i on blood pressure, which have recently been reproduced in several real-world (observational) studies.

Although the absolute reductions in blood pressure appear modest—typically in the range of 2 to 5 mmHg—their clinical significance is far greater than the numbers suggest. Large-scale meta-analyses and major clinical guidelines consistently demonstrate that even small declines in systolic blood pressure (SBP) yield measurable reductions in cardiovascular risk. A 2 mmHg lower SBP is associated with significant decreases in stroke mortality and ischemic heart disease deaths at the population level, while a 5 mmHg reduction corresponds to an approximate 10% relative reduction in major cardiovascular events, including stroke and myocardial infarction, irrespective of baseline blood pressure or cardiovascular status.[143] The relationship between SBP and cardiovascular risk is log-linear, with no clear lower threshold and benefits extend even to individuals in the high-normal range.[144]

For stroke prevention specifically, a 5 mmHg reduction in SBP confers around a 10% lower relative risk of recurrent stroke and other major cardiovascular events in both primary and secondary prevention contexts.[145] More intensive BP lowering—such as targeting SBP < 130 mmHg—yields further reductions in stroke and ischemic outcomes, as confirmed by network meta-analyses and recent guideline recommendations.[146] The absolute benefit is most pronounced in high-risk groups, yet the proportional risk reduction per mmHg of SBP lowering remains remarkably consistent across different risk strata.[147]

From a clinical standpoint, these data underscore that the blood pressure reductions achieved with SGLT2 inhibitors and GLP-1 receptor agonists are not merely ancillary effects but carry tangible prognostic value. Their consistent 2–5 mmHg average decrease translates into meaningful population-level cardiovascular protection—comparable to the benefit expected from first-line antihypertensive therapies.

6.2 | SGLT2 inhibitors – Real-world evidence

Emerging real-world evidence indicates that SGLT2i treatment is associated with reductions in blood pressure, reductions in the use of antihypertensive medications and a lower risk of incident hypertension (Table 6). Two well-performed cohort studies using primary care data from the UK reproduced results from RCTs, reporting similar average reductions in office SBP of 1.8–3.1 mmHg as compared with DPP4i or sulfonylureas, but they did not assess DBP.[149–152] A smaller cohort study from Spain also found similar reductions in SBP and DBP for SGLT2i *vs.* DPP4i and sulfonylureas.[151] An et al. used electronic health records from California to evaluate changes pre-post SGLT2i initiation, but did not have a comparator group.[148] SGLTi use was associated with reductions in both SBP and DBP, as well as reductions in the number of antihypertensive drugs used. After SGLT2i initiation,

TABLE 5 Effects of SGLT2 and SGLT1/2 inhibitors on blood pressure outcomes in select meta-analyses.

Citation	Study type included (no. of studies quantitatively synthesized)*	Population	Intervention	Comparator	Outcomes	Certainty of evidence
135	RCTs (n = 27)	Not specified	SGLT2i	Placebo or active control	SBP: −4.0 mmHg (95% CI − 4.4 to −3.5) DBP: −1.6 mmHg (95% CI − 1.9 to −1.3) Orthostatic Hypotension: RR 0.72 (95% CI 0.47 to 1.09)	Not assessed
136	RCTs (n = 6)	Not specified	SGLT2i	Placebo	**ABPM 24 h** SBP: −3.8 mmHg (95% CI − 4.2 to −2.3) DBP: −1.8 mmHg (95% CI − 2.4 to −1.3) **ABPM Daytime** SBP: −4.3 mmHg (95% CI − 5.1 to −3.6) DBP: − 2.1 mmHg (95% CI − 2.6 to −1.5) **ABPM Night-time** SBP: − 2.6 mmHg (95% CI − 3.1 to −2.1) DBP: −1.5 mmHg (95% CI − 2.2 to −0.8)	Not assessed
137	RCTs (n = 7)	T2DM	Sotagliflozin	Placebo or active control	SBP: −2.4 mmHg (95% CI − 2.79 to −1.97)	Not assessed
138	RCTs (n = 7)	T2DM	SGLT2i	Placebo or active control or hydrochlorothiazide	**APBM 24 h** SBP: −3.6 mmHg (95% CI − 4.2 to −2.9) DBP: −1.7 mmHg (95% CI − 2.1 to −1.3) **ABPM Daytime** SBP: −4.3 mmHg (95% CI − 5.0 to −3.6) DBP: − 2.0 mmHg (95% CI − 2.5 to −1.5) **ABPM Night-time** SBP: − 2.6 mmHg (95% CI − 3.5 to −1.8) DBP: −1.4 mmHg (95% CI − 2.0 to −0.8)	Not assessed
106	RCTs (n = 208)	Not specified	SGLT2i	Placebo or active control	SBP: −4.3 mmHg (95% CI − 4.5 to −4.2) DBP: −2.3 mmHg (95% CI − 2.4 to −2.2)	Not assessed
114	RCTs (n = 9)	T2DM	Empagliflozin	Placebo or active control	**Empagliflozin 25 mg *vs.* Placebo** SBP: −4.2 mmHg (95% CI − 5.2 to −3.2) DBP: −1.9 mmHg (95% CI − 2.7 to −1.0)	Not assessed
139	RCTs (not reported)	Not specified	SGLT2i	Placebo or active control	SBP: −2.5 mmHg (95% CI − 2.8 to −2.0) DBP: −1.5 mmHg (95% CI − 1.8 to −1.1)	Not assessed
140	RCTs (n = 9)	Participants with hypertension and pre-hypertension (excluded patients with secondary hypertension, chronic kidney disease or heart failure)	SGLT2i	Placebo	**Office BP** SBP: − 5.0 mmHg (95% CI − 6.3 to −3.8; high certainty) DBP: −1.7 mmHg; 95% CI − 2.5 to −0.9; high certainty)	Yes, using GRADE

(Continues)

TABLE 5 (Continued)

Citation	Study type included (no. of studies quantitatively synthesized)*	Population	Intervention	Comparator	Outcomes	Certainty of evidence
					ABPM Daytime SBP: −4.6 mmHg (95% CI − 5.4 to −3.7; high certainty) **ABPM Night-time** SBP: − 2.8 mmHg (95% CI − 3.8 to −1.8; high certainty)	
141	RCTs (n = 109)	With and without diabetes mellitus	SGLT2i or combined SGLT1/2i	Placebo or active control	**Office BP** SBP: − 3.3 mmHg (95% CI − 3.9 to −2.7) DBP: −1.5 mmHg; 95% CI − 1.8 to −1.3) **ABPM 24 h** SBP: −3.3 mmHg (95% CI − 4.2 to −2.3) DBP: −1.8 mmHg (95% CI − 2.4 to −1.3) **ABPM Daytime** SBP: −4.4 mmHg (95% CI − 5.4 to −3.4) DBP: − 2.0 mmHg (95% CI − 3.2 to −0.9) **ABPM Night-time** SBP: − 2.4 mmHg (95% CI − 3.3 to −1.5) DBP: −1.2 mmHg (95% CI − 2.8 to 0.4)	Low (office BP and ABPM 24 h SBP) and moderate to high certainty (other outcomes) using GRADE
107	RCTs (n = 204)	T2DM	SGLT2i	NMA with indirect comparisons to placebo and nine other antidiabetic drug classes	***vs.* Placebo** SBP: −2.9 mmHg (95% CI − 3.4 to −2.4) DBP: −1.4 mmHg (95% CI − 1.7 to −1.2)	Generally high to moderate certainty using CINeMA
142	RCTs (n = 21)	T2DM	SLGT2i	Placebo or active control	***vs.* Placebo** SBP: −3.8 mmHg (95% CI − 4.6 to −2.9) DBP: −1.8 mmHg (95% CI − 2.3 to −1.2) ***vs.* Active Control** SBP: −4.5 mmHg (95% CI − 5.7 to −3.2) DBP: −2.0 mmHg (95% CI − 2.6 to −1.4)	Moderate certainty (SBP) using GRADE

*Number of individual studies included in the largest meta-analysis of a blood pressure outcome.

Abbreviations: ABPM, ambulatory blood pressure monitoring; CINeMA: Confidence In Network Meta-Analysis framework; DBP: diastolic blood pressure; GLP-1RA: glucagon-like peptide-1 receptor agonists; GRADE: Grading of Recommendations Assessment, Development and Evaluation; NMA: network-meta analysis; RCT: randomized controlled trial; RR: risk ratio; SBP: systolic blood pressure; SGLT2i: sodium-glucose co-transporter 2 inhibitor; T2DM: type 2 diabetes mellitus.

TABLE 6 Effects of SGLT2i on blood pressure outcomes in select real-world studies.

Citation	Design	Population	Intervention	Comparator	Outcomes	Effect	Limitations
[148]	Cohort study, electronic health records	Kaiser Permanent Southern California (USA) ≥ 1BP measurement at baseline and during follow-up; n = 12 960 patients receiving treatment for hypertension; mean age 64.5 years	Initiate SGLT2i	None	1) Outpatient systolic and diastolic blood pressure mean change from baseline 2) Mean (SD) number of antihypertensive medications change from baseline 3) Proportion with any antihypertensive medication discontinuation during follow-up	**SBP:** −5.3 mmHg (p-value <0.001) **DBP:** −2.5 mmHg (p-value <0.001) **No. of antihypertensive medications:** 3.6 (0.8) to 2.9 (1.2) **Any antihypertensive medication discontinuation:** 33.4%	1) Treated group only pre- post-comparison (not adjusted for comparator group) 2) Estimates not adjusted for confounding factors 3) Descriptive analysis
[149]	Cohort study, electronic health records	Linked CPRD-Hospital Episodes Statistics (United Kingdom) T2DM treated with metformin n = 75 739 Mean age 56–62 years	Initiate SGLT2i	1) Initiate DPP4i 2) Initiate sulfonylurea	Change in SBP at one and two years after treatment initiation	**SGLT2i *vs.* DPP4i** One year: −1.8 mmHg (95% CI − 3.0 to −0.5) Two years: −2.5 mmHg (95% CI − 4.0 to −1.0) **SGLT2i *vs.* sulfonylurea** One year: −2.1 mmHg (95% CI − 3.1 to −1.0) Two years: −3.0 mmHg (95% CI − 4.3 to −1.6)	1) Used the observational analogue of the intention-to-treat approach so effect size may be underestimated if patients discontinue treatment (biased towards the null) 2) Long-term reduction in SBP beyond two years was not assessed 3) No information on comparing to GLP-1RA
[150]	Cohort study, administrative claims	JMDC (Japan) ≥ 20 years with diagnosis of diabetes but no history of hypertension or antihypertensive medication use N = 11 416, mean age 50 years	Initiate SGLT2i	Initiate DPP4i	Diagnosis of hypertension (ICD-10 codes I10-I15)	HR 0.91 (95% CI 0.84 to 0.97)	1) Does not directly evaluate blood pressure change 2) Comparator is DPP4i, no information on comparing to GLP-1RA 3) Imprecise estimates because of propensity score matching
[151]	Cohort study, electronic health records	SIDIAP (Spain) T2DM and HbA1c ≥ 7% Mean age 60–61 years n = 6310	SGLT2i	1) Initiate DPP4i 2) Initiate sulfonylurea	Mean difference in SBP and DBP at 2 years	**SGLT2i *vs.* DPP4i** SBP: −1.8 mmHg (95% CI − 3.3 to −0.3) DBP: −1.0 mmHg (95% CI − 2.0 to −0.0) **SGLT2i *vs.* sulfonylurea** SBP: −1.9 mmHg (95% CI − 3.4 to −0.4) DBP: −1.1 mmHg (95% CI − 2.1 to −0.1) (All statistically significant in adjusted complete case analysis)	1) Long-term reduction in blood pressure beyond two years was not assessed 2) No information on comparing to GLP-1RA 3) Imprecise estimates because of propensity score matching

(Continues)

TABLE 6 (Continued)

Citation	Design	Population	Intervention	Comparator	Outcomes	Effect	Limitations
[152]	Cohort study, electronic health records	Linked CPRD-Hospital Episodes Statistics (United Kingdom) Adults treated with metformin who intensify to second-line treatment Mean age 60 years n = 7958 (SBP cohort)	SGLT2i	1) Initiate DPP4i 2) Initiate sulfonylurea	Mean difference in SBP at 2 years	**SGLT2i *vs.* DPP4i** −1.8 mmHg (95% CI − 3.2 to −0.5) **SGLT2i *vs.* sulfonylurea** −3.1 mmHg (95% CI − 4.4 to −1.7)	1) Required to have baseline and follow-up BP, could result in selection bias for more adherent patients 2) Long-term reduction in SBP beyond two years was not assessed 3) No information on comparing to GLP-1RA

Abbreviations: DPP4i: dipeptidyl peptidase-4 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; HR: hazard ratio; SGLT2i: sodium-glucose co-transporter 2 inhibitor; T2DM: type 2 diabetes mellitus.

one-third of participants were able to discontinue at least one antihypertensive medication. In a cohort study in Japan, among individuals without hypertension at baseline, Suzuki et al. found that SGLT2i use was associated with a 9% relative decrease in an incident diagnosis of hypertension.[150] Taken together, these real-world studies complement findings from meta-analyses of RCTs and demonstrate that reductions in the use of antihypertensive medications occur frequently in clinical practice.

7 | FUTURE DIRECTIONS AND RESEARCH AGENDA

Although there are solid data demonstrating that both SGLT2is and GLP-1 RAs produce modest but clinically relevant reductions in BP, there are important gaps that should be addressed by further research. BP-specific trials need to be at the top of the research agenda and in the development of clinical practice.

Most of the evidence comes from diabetes and cardiovascular outcome studies in which BP is quantified as a secondary endpoint. Well-controlled, prospective clinical trials with primary endpoints for hypertension are needed to confirm the antihypertensive efficacy and safety profile of these drugs, especially in people with hypertension but not obesity or diabetes.

Recent high-quality syntheses highlight what the next generation of trials should include: hypertension-dedicated RCTs with prespecified BP endpoints; standardized and reproducible BP assessment anchored in ABPM; and direct head-to-head comparisons both across classes (SGLT2 inhibitors vs GLP-1 receptor agonists) and within classes (different molecules). These features would improve comparability and sharpen causal inference for BP-mediated benefit.[153]

There is a need for mechanistic studies to clarify the relative role of weight loss, natriuresis, increased arterial compliance and other hemodynamic changes in lowering BP.

In addition, head-to-head comparison studies between different SGLT2is, GLP-1 RAs and dual GLP-1/GIP agonists are needed to differentiate class- and drug-specific BP effects and comparative efficacy *vs.* standard antihypertensives.

More research should be conducted to investigate long-term BP variability, durability of response and outcomes such as hypertension-mediated organ damage or major cardiovascular events.

Studies should be designed to assess blood pressure response by ethnicity, gender, age and baseline blood pressure to detect potential heterogeneity of antihypertensive response in patient subgroups and identify those most likely to benefit.

More attention needs to be paid to standardization of blood pressure measurement, such as the use of ambulatory blood pressure monitoring (ABPM), unattended automated office BP measurement and inclusion of populations with different hypertension phenotypes with or without cardiometabolic disease.

In addition, studies with longer follow-up are needed to investigate the sustained antihypertensive effect and long-term safety in real-world populations.

Shown evidence suggests a potential additive role for these agents in the treatment of hypertension, particularly in patients with obesity, metabolic syndrome or type 2 diabetes. Future hypertension guidelines should consider the inclusion of SGLT2is and GLP-1 RAs as adjunctive antihypertensive therapies, depending on the results of relevant trials. Altogether, ongoing studies should strive to close these important knowledge gaps and maximize the inclusion of these therapeutics in personalized hypertension management. Incorporating the blood pressure–lowering effects of SGLT2 inhibitors and GLP-1 receptor agonists into current ESC/ESH and AHA/ACC guidelines could enhance cardiovascular risk reduction, particularly in patients with diabetes or obesity.

Dedicated trials of SGLT2 inhibitors combined with GLP-1 receptor agonists, with primary outcomes specifically designed for blood pressure reduction, are crucial to unlock their complementary potential and maximize cardiovascular benefit. Such studies would not only delineate additive hemodynamic effects but also clarify mechanistic interactions across renal, metabolic and vascular domains—ultimately shaping future guideline integration.

Given their high cost and uneven global availability, addressing implementation challenges and health-equity considerations is essential to ensure that the benefits of SGLT2 inhibitors and GLP-1 receptor agonists reach patients in low- and middle-income settings.

8 | CONCLUSION

SGLT2 inhibitors and GLP-1 receptor agonists lower blood pressure consistently across populations with type 2 diabetes, obesity, cardiovascular disease and chronic kidney disease. Although the magnitude of reduction is modest, the effect is reproducible, clinically meaningful and largely independent of glycaemic control.

The available evidence supports a conceptual shift: from viewing these drugs solely as antidiabetic agents to recognizing their role within an integrated, multi-system treatment strategy, in which blood pressure reduction contributes to broader cardiovascular and renal protection. Their distinct yet complementary mechanisms also provide a rationale for combination therapy in selected high-risk individuals.

Nonetheless, key limitations persist. Few trials have prioritized blood pressure as a primary endpoint, leading to heterogeneity in measurement approaches and limited precision in effect estimates. Long-term outcomes related to blood pressure, particularly with newer agents such as dual agonists, remain insufficiently characterized.

Future research should prioritize trials specifically designed to evaluate blood pressure effects, including direct comparisons between drug classes and assessment across clinically relevant subgroups. In the interim, optimal implementation will require multidisciplinary collaboration to align therapeutic strategies with the overlapping pathophysiology of metabolic, cardiovascular, renal and hypertensive disease.

8.1 | Nomenclature of targets and ligands

Key protein targets and ligands in this article are hyperlinked to corresponding entries in http://www.guidetopharmacology.org, and are permanently archived in the Concise Guide to PHARMACOLOGY 2023/24.[154,155]

AUTHOR CONTRIBUTIONS

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

No new data were generated.

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REFERENCES

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. *Nat Rev Nephrol*. 2020;16(4):223-237. doi:10.1038/s41581-019-0244-2
2. Jia G, Sowers JR. Hypertension in diabetes: an update of basic mechanisms and clinical disease. *Hypertension (Dallas, Tex.: 1979)*. 2021;78(5):1197-1205. doi:10.1161/HYPERTENSIONAHA.121.17981
3. Petrie JR, Guzik TJ, Touyz RM. Diabetes, hypertension, and cardiovascular disease: clinical insights and vascular mechanisms. *Can J Cardiol*. 2018;34(5):575-584. doi:10.1016/j.cjca.2017.12.005
4. GBD 2017 Risk Factor Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the global burden of disease study 2017. *Lancet (London, England)*. 2018;392(10159):1923-1994. doi:10.1016/S0140-6736(18)32225-6
5. Cheung BM, Li C. Diabetes and hypertension: is there a common metabolic pathway? *Curr Atheroscler Rep*. 2012;14(2):160-166. doi:10.1007/s11883-012-0227-2
6. Wei GS, Coady SA, Goff DC Jr, et al. Blood pressure and the risk of developing diabetes in African Americans and whites: ARIC, CARDIA, and the Framingham heart study. *Diabetes Care*. 2011;34(4):873-879. doi:10.2337/dc10-1786

7. Hall JE, do Carmo JM, da Silva AA, Wang Z, Hall ME. Obesity, kidney dysfunction and hypertension: mechanistic links. *Nat Rev Nephrol*. 2019;15(6):367-385. doi:10.1038/s41581-019-0145-4
8. Xiao LX, Wang ZY, Li JT, et al. Association of cardiometabolic multimorbidity with all-cause and cardiovascular disease mortality among Chinese hypertensive patients. *Journal of Geriatric Cardiology: JGC*. 2024;21(2):211-218. doi:10.26599/1671-5411.2024.02.003
9. Sowers JR, Epstein M, Frohlich ED. Diabetes, hypertension, and cardiovascular disease: an update. *Hypertension (Dallas, Tex.: 1979)*. 2001;37(4):1053-1059. doi:10.1161/01.hyp.37.4.1053
10. Yuan Y, Isasi CR, Al-Rousan T, et al. Associations of concurrent hypertension and type 2 diabetes with mortality outcomes: a prospective study of U.S. adults. *Diabetes Care*. 2025;48(7):1241-1250. doi:10.2337/dca24-0118
11. Ndumele CE, Neeland IJ, Tuttle KR, et al. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation*. 2023;148(20):1636-1664. doi:10.1161/CIR.0000000000001186
12. Piskorz D. Hypertension and metabolic disorders, a glance from different phenotypes. *Am J Prev Cardiol*. 2020;2:100032. doi:10.1016/j.ajpc.2020.100032
13. *Hexose transporter family: sodium/glucose cotransporter 2*Last modified on 12/06/2025. Accessed on 14/10/2025. IUPHAR/BPS Guide to PHARMACOLOGY. https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=916
14. Liakos A, Karagiannis T, Athanasiadou E, et al. Efficacy and safety of empagliflozin for type 2 diabetes: a systematic review and meta-analysis. *Diabetes Obes Metab*. 2014;16(10):984-993. doi:10.1111/dom.12307
15. Rastogi A, Januzzi JL Jr. Pleiotropic effects of sodium-glucose cotransporter-2 inhibitors in cardiovascular disease and chronic kidney disease. *J Clin Med*. 2023;12(8):2824. doi:10.3390/jcm12082824
16. Wu Q, Zhang J, Zhang F, Li D. SGLT2 inhibitors as metabolic modulators: beyond glycemic control in type 2 diabetes. *Front Endocrinol*. 2025;16:1601633. doi:10.3389/fendo.2025.1601633
17. Bataille D, Chan SL, Delagrange P, et al. Glucagon receptor family in GtoPdb v.2023.1. *IUPHAR/BPS Guide to Pharmacology CITE*. 2023;2023(1) Available from. doi:10.2218/gtopdb/F29/2023.1
18. Al Qassab M, Mneimneh M, Jradi A, et al. The expanding role of GLP-1 receptor agonists: advancing clinical outcomes in metabolic and mental health. *Curr Issues Mol Biol*. 2025;47(4):285. doi:10.3390/cimb47040285
19. Zheng Z, Zong Y, Ma Y, et al. Glucagon-like peptide-1 receptor: mechanisms and advances in therapy. *Signal Transduct Target Ther*. 2024;9(1):234. doi:10.1038/s41392-024-01931-z
20. Diallo A, Carlos-Bolumbu M, Galtier F. Blood pressure-lowering effects of SGLT2 inhibitors and GLP-1 receptor agonists for preventing of cardiovascular events and death in type 2 diabetes: a systematic review and meta-analysis. *Acta Diabetol*. 2023;60(12):1651-1662. doi:10.1007/s00592-023-02154-4
21. Sarzani R, Giulietti F, Di Pentima C, Spannella F. Sodium-glucose co-transporter-2 inhibitors: peculiar "hybrid" diuretics that protect from target organ damage and cardiovascular events. *Nutrition, Metabolism, and Cardiovascular Diseases: NMCD*. 2020;30(10):1622-1632. doi:10.1016/j.numecd.2020.05.030
22. Tang J, Ye L, Yan Q, Zhang X, Wang L. Effects of sodium-glucose cotransporter 2 inhibitors on water and sodium metabolism. *Front Pharmacol*. 2022;13:800490. doi:10.3389/fphar.2022.800490
23. Ferrannini E. Sodium-glucose co-transporters and their inhibition: clinical physiology. *Cell Metab*. 2017;26(1):27-38. doi:10.1016/j.cmet.2017.04.011
24. Kimura G. Diuretic action of sodium-glucose cotransporter 2 inhibitors and its importance in the management of heart failure. *Circ J*. 2016;80(11):2277-2281. doi:10.1253/circj.CJ-16-0780
25. Fonseca-Correa JI, Correa-Rotter R. Sodium-glucose cotransporter 2 inhibitors mechanisms of action: a review. *Front Med*. 2021;8:777861. doi:10.3389/fmed.2021.777861
26. Scheen AJ. Sodium-glucose cotransporter type 2 inhibitors for the treatment of type 2 diabetes mellitus. *Nat Rev Endocrinol*. 2020;16(10):556-577. doi:10.1038/s41574-020-0392-2
27. Rajasekeran H, Lytvyn Y, Cherney DZ. Sodium-glucose cotransporter 2 inhibition and cardiovascular risk reduction in patients with type 2 diabetes: the emerging role of natriuresis. *Kidney Int*. 2016;89(3):524-526. doi:10.1016/j.kint.2015.12.038
28. Verma S. Potential mechanisms of sodium-glucose co-transporter 2 inhibitor-related cardiovascular benefits. *Am J Cardiol*. 2019;124-(Suppl 1):S36-S44. doi:10.1016/j.amjcard.2019.10.028
29. Kitada K, Kidoguchi S, Nakano D, Nishiyama A. Sodium/glucose cotransporter 2 and renoprotection: from the perspective of energy regulation and water conservation. *J Pharmacol Sci*. 2021;147(3):245-250. doi:10.1016/j.jphs.2021.07.006
30. Chiriacò M, Tricò D, Solini A. Mechanisms of cardio-renal protection of sodium-glucose cotransporter-2 inhibitors. *Curr Opin Pharmacol*. 2022;66:102272. doi:10.1016/j.coph.2022.102272
31. Li X, Preckel B, Hermanides J, Hollmann MW, Zuurbier CJ, Weber NC. Amelioration of endothelial dysfunction by sodium glucose co-transporter 2 inhibitors: pieces of the puzzle explaining their cardiovascular protection. *Br J Pharmacol*. 2022;179(16):4047-4062. doi:10.1111/bph.15850
32. Pandey AK, Bhatt DL, Pandey A, et al. Mechanisms of benefits of sodium-glucose cotransporter 2 inhibitors in heart failure with preserved ejection fraction. *Eur Heart J*. 2023;44(37):3640-3651. doi:10.1093/eurheartj/ehad389
33. Rangaswami J, Bhalla V, de Boer IH, et al. Cardiorenal protection with the newer antidiabetic agents in patients with diabetes and chronic kidney disease: a scientific statement from the American Heart Association. *Circulation*. 2020;142(17):e265-e286. doi:10.1161/CIR.0000000000000920
34. Patoulias D, Papadopoulos C, Kassimis G, et al. Effect of sodium-glucose co-transporter-2 inhibitors on arterial stiffness: a systematic review and meta-analysis of randomized controlled trials. *Vascular Medicine (London, England)*. 2022;27(5):433-439. doi:10.1177/1358863X221101653
35. Castoldi G, Carletti R, Ippolito S, et al. Cardioprotective effects of sodium glucose cotransporter 2 inhibition in angiotensin II-dependent hypertension are mediated by the local reduction of sympathetic activity and inflammation. *Int J Mol Sci*. 2023;24(13):10710. doi:10.3390/ijms241310710
36. Durante W, Behnammanesh G, Peyton KJ. Effects of sodium-glucose co-transporter 2 inhibitors on vascular cell function and arterial remodeling. *Int J Mol Sci*. 2021;22(16):8786. doi:10.3390/ijms22168786
37. Reed JW. Impact of sodium-glucose cotransporter 2 inhibitors on blood pressure. *Vasc Health Risk Manag*. 2016;12:393-405. doi:10.2147/VHRM.S111991
38. Pereira MJ, Eriksson JW. Emerging role of SGLT-2 inhibitors for the treatment of obesity. *Drugs*. 2019;79(3):219-230. doi:10.1007/s40265-019-1057-0
39. Ferrannini G, Hach T, Crowe S, Sanghvi A, Hall KD, Ferrannini E. Energy balance after sodium-glucose cotransporter 2 inhibition. *Diabetes Care*. 2015;38(9):1730-1735. doi:10.2337/dc15-0355
40. Volpe S, Vozza A, Lisco G, et al. Sodium-glucose cotransporter 2 inhibitors improve body composition by increasing the skeletal muscle mass/fat mass ratio in patients with type 2 diabetes: a

52-week prospective real-life study. *Nutrients*. 2024;16(22):3841. doi:10.3390/nu16223841

41. Sawada Y, Izumida Y, Takeuchi Y, et al. Effect of sodium-glucose cotransporter 2 (SGLT2) inhibition on weight loss is partly mediated by liver-brain-adipose neurocircuitry. *Biochem Biophys Res Commun*. 2017;493(1):40-45. doi:10.1016/j.bbrc.2017.09.081
42. Dimova R, Tankova T. Does SGLT2 inhibition affect sympathetic nerve activity in type 2 diabetes? *Hormone and Metabolic Research = Hormon- Und Stoffwechselforschung = Hormones et Metabolisme*. 2021;53(2):75-84. doi:10.1055/a-1298-4205
43. Wan N, Rahman A, Hitomi H, Nishiyama A. The effects of sodium-glucose cotransporter 2 inhibitors on sympathetic nervous activity. *Front Endocrinol*. 2018;9:421. doi:10.3389/fendo.2018.00421
44. Heerspink HJ, Perkins BA, Fitchett DH, Husain M, Cherney DZ. Sodium glucose cotransporter 2 inhibitors in the treatment of diabetes mellitus: cardiovascular and kidney effects, potential mechanisms, and clinical applications. *Circulation*. 2016;134(10):752-772. doi:10.1161/CIRCULATIONAHA.116.021887
45. Katsurada K. Interaction between SGLT2 and the sympathetic nervous system in normal and various cardiovascular metabolic disease states. *Hypertens Res*. 2025;48(7):2072-2078. doi:10.1038/s41440-025-02216-w
46. Gronda E, Vanoli E, Iacoviello M, Caldarola P, Gabrielli D, Tavazzi L. The benefit of sodium-glucose co-transporter inhibition in heart failure: the role of the kidney. *Int J Mol Sci*. 2022;23(19):11987. doi:10.3390/ijms231911987
47. Ansary TM, Nakano D, Nishiyama A. Diuretic effects of sodium glucose cotransporter 2 inhibitors and their influence on the renin-angiotensin system. *Int J Mol Sci*. 2019;20(3):629. doi:10.3390/ijms20030629
48. Azzam O, Matthews VB, Schlaich MP. Interaction between sodium-glucose co-transporter 2 and the sympathetic nervous system. *Curr Opin Nephrol Hypertens*. 2022;31(2):135-141. doi:10.1097/MNH.0000000000000767
49. Chen Z, Deng X, Shi C, et al. GLP-1R-positive neurons in the lateral septum mediate the anorectic and weight-lowering effects of liraglutide in mice. *J Clin Invest*. 2024;134(17):e178239. doi:10.1172/JCI178239
50. Kumar N, D'Alessio DA. Slow and steady wins the race: 25 years developing the GLP-1 receptor as an effective target for weight loss. *J Clin Endocrinol Metab*. 2022;107(8):2148-2153. doi:10.1210/clinem/dgac276
51. Moiz A, Filion KB, Tsoukas MA, Yu OH, Peters TM, Eisenberg MJ. Mechanisms of GLP-1 receptor agonist-induced weight loss: a review of central and peripheral pathways in appetite and energy regulation. *Am J Med*. 2025;138(6):934-940. doi:10.1016/j.amjmed.2025.01.021
52. Liu Y, Ruan B, Jiang H, et al. The weight-loss effect of GLP-1RAs glucagon-like peptide-1 receptor agonists in non-diabetic individuals with overweight or obesity: a systematic review with meta-analysis and trial sequential analysis of randomized controlled trials. *Am J Clin Nutr*. 2023;118(3):614-626. doi:10.1016/j.ajcnut.2023.04.017
53. Mozaffarian D, Agarwal M, Aggarwal M, et al. Nutritional priorities to support GLP-1 therapy for obesity: a joint advisory from the American College of Lifestyle Medicine, the American Society for Nutrition, the obesity medicine association, and the Obesity Society. *Obesity*. 2025;33(8):1475-1503. doi:10.1002/oby.24336
54. Drucker DJ. GLP-1-based therapies for diabetes, obesity and beyond. *Nat Rev Drug Discov*. 2025;24(8):631-650. doi:10.1038/s41573-025-01183-8
55. Gudzune KA, Kushner RF. Medications for obesity: a review. *Jama*. 2024;332(7):571-584. doi:10.1001/jama.2024.10816
56. Xie Y, Choi T, Al-Aly Z. Mapping the effectiveness and risks of GLP-1 receptor agonists. *Nat Med*. 2025;31(3):951-962. doi:10.1038/s41591-024-03412-w
57. Das SR, Everett BM, Birtcher KK, et al. 2020 expert consensus decision pathway on novel therapies for cardiovascular risk reduction in patients with type 2 diabetes: a report of the American College of Cardiology solution set oversight committee. *J am Coll Cardiol*. 2020;76(9):1117-1145. doi:10.1016/j.jacc.2020.05.037
58. Asmar A, Cramon PK, Asmar M, et al. The renal extraction and the natriuretic action of GLP-1 in humans depend on interaction with the GLP-1 receptor. *J Clin Endocrinol Metab*. 2021;106(1):e11-e19. doi:10.1210/clinem/dgaa643
59. Crajoinas RO, Oricchio FT, Pessoa TD, et al. Mechanisms mediating the diuretic and natriuretic actions of the incretin hormone glucagon-like peptide-1. *Am J Physiol Renal Physiol*. 2011;301(2):F355-F363. doi:10.1152/ajprenal.00729.2010
60. Skov J, Dejgaard A, Frøkiær J, et al. Glucagon-like peptide-1 (GLP-1): effect on kidney hemodynamics and renin-angiotensin-aldosterone system in healthy men. *J Clin Endocrinol Metab*. 2013;98(4):E664-E671. doi:10.1210/jc.2012-3855
61. Asmar A, Cramon PK, Simonsen L, et al. Extracellular fluid volume expansion uncovers a natriuretic action of GLP-1: a functional GLP-1-renal axis in man. *J Clin Endocrinol Metab*. 2019;104(7):2509-2519. doi:10.1210/jc.2019-00004
62. Kodama G, Taguchi K, Ito S, et al. Glucagon like peptide-1 modulates urinary sodium excretion in diabetic kidney disease via ENaC activation. *Sci Rep*. 2025;15(1):11486. doi:10.1038/s41598-025-95673-9
63. Savignano FA, Crajoinas RO, Pacheco BPM, et al. Attenuated diuresis and natriuresis in response to glucagon-like peptide-1 in hypertensive rats are associated with lower expression of the glucagon-like peptide-1 receptor in the renal vasculature. *Eur J Pharmacol*. 2017;811:38-47. doi:10.1016/j.ejphar.2017.05.054
64. Aung MM, Slade K, Freeman LAR, et al. Locally delivered GLP-1 analogues liraglutide and exenatide enhance microvascular perfusion in individuals with and without type 2 diabetes. *Diabetologia*. 2019;62(9):1701-1711. doi:10.1007/s00125-019-4918-x
65. Koska J, Sands M, Burciu C, et al. Exenatide protects against glucose- and lipid-induced endothelial dysfunction: evidence for direct vasodilation effect of GLP-1 receptor agonists in humans. *Diabetes*. 2015;64(7):2624-2635. doi:10.2337/db14-0976
66. Almutairi M, Al Batran R, Ussher JR. Glucagon-like peptide-1 receptor action in the vasculature. *Peptides*. 2019;111:26-32. doi:10.1016/j.peptides.2018.09.002
67. Nomoto H, Miyoshi H, Furumoto T, et al. A comparison of the effects of the GLP-1 analogue liraglutide and insulin glargine on endothelial function and metabolic parameters: a randomized, controlled trial Sapporo Athero-incretin study 2 (SAIS2). *PLoS ONE*. 2015;10(8):e0135854. doi:10.1371/journal.pone.0135854
68. Jessen L, Smith EP, Ulrich-Lai Y, et al. Central nervous system GLP-1 receptors regulate islet hormone secretion and glucose homeostasis in male rats. *Endocrinology*. 2017;158(7):2124-2133. doi:10.1210/en.2016-1826
69. Yamamoto H, Lee CE, Marcus JN, et al. Glucagon-like peptide-1 receptor stimulation increases blood pressure and heart rate and activates autonomic regulatory neurons. *J Clin Invest*. 2002;110(1):43-52. doi:10.1172/JCI15595
70. Bharucha AE, Charkoudian N, Andrews CN, et al. Effects of glucagon-like peptide-1, yohimbine, and nitrergic modulation on sympathetic and parasympathetic activity in humans. *Am J Physiol Regul Integr Comp Physiol*. 2008;295(3):R874-R880. doi:10.1152/ajpregu.00153.2008
71. Pop-Busui R, Januzzi JL, Bruemmer D, et al. Heart failure: an underappreciated complication of diabetes. A consensus report of the American Diabetes Association. *Diabetes Care*. 2022;45(7):1670-1690. doi:10.2337/dci22-0014
72. Ren W, Chen J, Wang W, et al. Sympathetic nerve-enteroendocrine L cell communication modulates GLP-1 release, brain glucose

utilization, and cognitive function. *Neuron*. 2024;112(6):972-990.e8. doi:10.1016/j.neuron.2023.12.012
73. Bray JJH, Foster-Davies H, Salem A, et al. Glucagon-like peptide-1 receptor agonists improve biomarkers of inflammation and oxidative stress: a systematic review and meta-analysis of randomised controlled trials. *Diabetes Obes Metab*. 2021;23(8):1806-1822. doi:10.1111/dom.14399
74. Park B, Bakbak E, Teoh H, et al. GLP-1 receptor agonists and atherosclerosis protection: the vascular endothelium takes center stage. *Am J Physiol Heart Circ Physiol*. 2024;326(5):H1159-H1176. doi:10.1152/ajpheart.00574.2023
75. Ceriello A, Novials A, Ortega E, et al. Glucagon-like peptide 1 reduces endothelial dysfunction, inflammation, and oxidative stress induced by both hyperglycemia and hypoglycemia in type 1 diabetes. *Diabetes Care*. 2013;36(8):2346-2350. doi:10.2337/dc12-2469
76. Helmstädter J, Frenis K, Filippou K, et al. Endothelial GLP-1 (glucagon-like peptide-1) receptor mediates cardiovascular protection by liraglutide in mice with experimental arterial hypertension. *Arterioscler Thromb Vasc Biol*. 2020;40(1):145-158. doi:10.1161/atv.0000615456.97862.30
77. Hullon D, Subeh GK, Volkova Y, Janiec K, Trach A, Mnevets R. The role of glucagon-like peptide-1 receptor (GLP-1R) agonists in enhancing endothelial function: a potential avenue for improving heart failure with preserved ejection fraction (HFpEF). *Cardiovasc Diabetol*. 2025;24(1):70. doi:10.1186/s12933-025-02607-w
78. Engin A. Endothelial Dysfunction in Obesity and Therapeutic Targets. In: *Adv exp med biol*. Vol.1460; 2024:489-538. doi:10.1007/978-3-031-63657-8_17
79. Rivera FB, Lumbang GNO, Gaid DRM, et al. Glucagon-like peptide-1 receptor agonists modestly reduced blood pressure among patients with and without diabetes mellitus: a meta-analysis and meta-regression. *Diabetes Obes Metab*. 2024;26(6):2209-2228. doi:10.1111/dom.15529
80. Patoulias D, Papadopoulos C, Siskos F, Stavropoulos K, Doumas M. The effect of glucagon-like peptide-1 receptor agonists on 24-hour ambulatory blood pressure: a confirmatory meta-analysis. *Blood Press Monit*. 2021;26(4):284-287. doi:10.1097/MBP.0000000000000537
81. Ahwin P, Martinez D. The relationship between SGLT2 and systemic blood pressure regulation. *Hypertension Research: Official Journal of the Japanese Society of Hypertension*. 2024;47(8):2094-2103. doi:10.1038/s41440-024-01723-6
82. Wilcox CS. Antihypertensive and renal mechanisms of SGLT2 (sodium-glucose linked transporter 2) inhibitors. *Hypertension (Dallas, Tex: 1979)*. 2020;75(4):894-901. doi:10.1161/HYPERTENSIONAHA.119.11684
83. De Oliveira-Gomes D, Pingili A, Inglis S, Mandras SA, Loro-Ferrer JF, daSilva-deAbreu A. Impact of glucagon-like peptide-1 receptor agonists on hypertension management: a narrative review. *Curr Opin Cardiol*. 2025;40(4):185-192. doi:10.1097/HCO.0000000000001225
84. Puglisi S, Rossini A, Poli R, et al. Effects of SGLT2 inhibitors and GLP-1 receptor agonists on renin-angiotensin-aldosterone system. *Front Endocrinol*. 2021;12:738848. doi:10.3389/fendo.2021.738848
85. Palmer SC, Tendal B, Mustafa RA, et al. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. *BMJ (Clinical Research Ed)*. 2021;372:m4573. doi:10.1136/bmj.m4573
86. Sternlicht H, Bakris GL. Blood pressure lowering and sodium-glucose co-transporter 2 inhibitors (SGLT2is): more than osmotic diuresis. *Curr Hypertens Rep*. 2019;21(2):12. doi:10.1007/s11906-019-0920-4
87. Thomas MC, Cherney DZI. The actions of SGLT2 inhibitors on metabolism, renal function and blood pressure. *Diabetologia*. 2018;61(10):2098-2107. doi:10.1007/s00125-018-4669-0
88. Ribeiro-Silva JC, Tavares CAM, Girardi ACC. The blood pressure lowering effects of glucagon-like peptide-1 receptor agonists: a mini-review of the potential mechanisms. *Curr Opin Pharmacol*. 2023;69:102355. doi:10.1016/j.coph.2023.102355
89. Ussher JR, Drucker DJ. Glucagon-like peptide 1 receptor agonists: cardiovascular benefits and mechanisms of action. *Nat Rev Cardiol*. 2023;20(7):463-474. doi:10.1038/s41569-023-00849-3
90. Saponaro C, Gmyr V, Thévenet J, et al. The GLP1R agonist liraglutide reduces hyperglucagonemia induced by the SGLT2 inhibitor dapagliflozin via somatostatin release. *Cell Rep*. 2019;28(6):1447-1454.e4. doi:10.1016/j.celrep.2019.07.009
91. Shepard BD, Ecelbarger CM. Sodium glucose transporter, type 2 (SGLT2) inhibitors (SGLT2i) and glucagon-like peptide 1-receptor agonists: newer therapies in whole-body glucose stabilization. *Semin Nephrol*. 2021;41(4):331-348. doi:10.1016/j.semnephrol.2021.06.005
92. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2016b;375(4):311-322. doi:10.1056/NEJMoa1603827
93. Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med*. 2016a;375(19):1834-1844. doi:10.1056/NEJMoa1607141
94. Yang S, Zhou Z, Miao H, Zhang Y. Effect of weight loss on blood pressure changes in overweight patients: a systematic review and meta-analysis. *J Clin Hypertens (Greenwich)*. 2023;25(5):404-415. doi:10.1111/jch.14661
95. Pi-Sunyer X, Astrup A, Fujioka K, et al. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. *N Engl J Med*. 2015;373(1):11-22. doi:10.1056/NEJMoa1411892
96. Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989-1002. doi:10.1056/NEJMoa2032183
97. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al. Semaglutide and cardiovascular outcomes in obesity without diabetes. *N Engl J Med*. 2023;389(24):2221-2232. doi:10.1056/NEJMoa2307563
98. Jastreboff AM, Aronne LJ, Ahmad NN, et al. Tirzepatide once weekly for the treatment of obesity. *N Engl J Med*. 2022;387(3):205-216. doi:10.1056/NEJMoa2206038
99. Nicholls SJ, Bhatt DL, Buse JB, et al. Comparison of tirzepatide and dulaglutide on major adverse cardiovascular events in participants with type 2 diabetes and atherosclerotic cardiovascular disease: SURPASS-CVOT design and baseline characteristics. *Am Heart J*. 2024;267:1-11. doi:10.1016/j.ahj.2023.09.007
100. https://clinicaltrials.gov/study/NCT05556512
101. Aronne LJ, Horn DB, le Roux CW, et al. Tirzepatide as compared with semaglutide for the treatment of obesity. *N Engl J Med*. 2025;393(1):26-36. doi:10.1056/NEJMoa2416394
102. Katout M, Zhu H, Rutsky J, et al. Effect of GLP-1 mimetics on blood pressure and relationship to weight loss and glycemia lowering: results of a systematic meta-analysis and meta-regression. *Am J Hypertens*. 2014;27(1):130-139. doi:10.1093/ajh/hpt196
103. Sun F, Wu S, Guo S, et al. Impact of GLP-1 receptor agonists on blood pressure, heart rate and hypertension among patients with type 2 diabetes: a systematic review and network meta-analysis. *Diabetes Res Clin Pract*. 2015;110(1):26-37. doi:10.1016/j.diabres.2015.07.015
104. Ali A, Siddiqui AA, Usman MS, Shahid I, Khan MS, Perswani P. Effect of glucagon-like peptide 1 receptor agonists on systolic blood pressure in patients with obesity, with or without diabetes: a systematic review and network meta-analysis. *Clin Obes*. 2025;15(4):e70012. doi:10.1111/cob.70012
105. An X, Sun W, Wen Z, et al. Comparison of the efficacy and safety of GLP-1 receptor agonists on cardiovascular events and risk factors: a review and network meta-analysis. *Diabetes Obes Metab*. 2025;27(4):1735-1751. doi:10.1111/dom.16228

106. Hu M, Cai X, Yang W, Zhang S, Nie L, Ji L. Effect of hemoglobin A1c reduction or weight reduction on blood pressure in glucagon-like peptide-1 receptor agonist and sodium-glucose cotransporter-2 inhibitor treatment in type 2 diabetes mellitus: a meta-analysis. *J Am Heart Assoc*. 2020;9(7):e015323. doi:10.1161/JAHA.119.015323
107. Tsapas A, Karagiannis T, Kakotrichi P, et al. Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: a systematic review and network meta-analysis. *Diabetes Obes Metab*. 2021;23(9):2116-2124. doi:10.1111/dom.14451
108. Wong HJ, Toh KZX, Teo YH, et al. Effects of glucagon-like peptide-1 receptor agonists on blood pressure in overweight or obese patients: a meta-analysis of randomized controlled trials. *J Hypertens*. 2025;43(2):290-300. doi:10.1097/HJH.0000000000003903
109. Basile C, Merolla A, Mancusi C, et al. Effect of incretin-based therapies on blood pressure: a systematic review and meta-analysis. *Eur J Prev Cardiol*. 2025;zwaf560. Advance online publication. doi:10.1093/eurjpc/zwaf560
110. Ferdinand KC, White WB, Calhoun DA, et al. Effects of the once-weekly glucagon-like peptide-1 receptor agonist dulaglutide on ambulatory blood pressure and heart rate in patients with type 2 diabetes mellitus. *Hypertension (Dallas, Tex.: 1979)*. 2014;64(4):731-737. doi:10.1161/HYPERTENSIONAHA.114.03062
111. Ghusn W, Fansa S, Anazco D, et al. Weight loss and cardiovascular disease risk outcomes of semaglutide: a one-year multicentered study. *Int J Obes (Lond)*. 2024;48(5):662-667. doi:10.1038/s41366-023-01456-5
112. Kobayashi K, Toyoda M, Hatori N, et al. Comparison of the blood pressure management between sodium-glucose cotransporter 2 inhibitors and glucagon-like peptide 1 receptor agonists. *Sci Rep*. 2022;12(1):16106. doi:10.1038/s41598-022-20313-5
113. Sohn M, Nam S, Nauck MA, Lim S. Long-term comparison of renal and metabolic outcomes after sodium-glucose co-transporter 2 inhibitor or glucagon-like peptide-1 receptor agonist therapy in type 2 diabetes. *BMC Med*. 2024;22(1):273. doi:10.1186/s12916-024-03483-z
114. Liakos CI, Papadopoulos DP, Sanidas EA, et al. Blood pressure-lowering effect of newer antihyperglycemic agents (SGLT-2 inhibitors, GLP-1 receptor agonists, and DPP-4 inhibitors). *Am J Cardiovasc Drugs*. 2021;21(2):123-137. doi:10.1007/s40256-020-00423-z
115. Vallon V. State-of-the-art-review: mechanisms of action of SGLT2 inhibitors and clinical implications. *Am J Hypertens*. 2024;37(11):841-852. doi:10.1093/ajh/hpae092
116. Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med*. 2015;373(22):2117-2128. doi:10.1056/NEJMoa1504720
117. Tikkanen I, Narko K, Zeller C, et al. Empagliflozin reduces blood pressure in patients with type 2 diabetes and hypertension. *Diabetes Care*. 2015;38(3):420-428. doi:10.2337/dc14-1096
118. Kario K, Okada K, Kato M, et al. Twenty-four-hour blood pressure-lowering effect of a sodium-glucose cotransporter 2 inhibitor in patients with diabetes and uncontrolled nocturnal hypertension: results from the randomized, placebo-controlled SACRA study. *Circulation*. 2019;139(18):2089-2097. doi:10.1161/CIRCULATIONAHA.118.037076
119. Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med*. 2020;383(15):1413-1424. doi:10.1056/NEJMoa2022190
120. Anker SD, Butler J, Filippatos G, et al. Empagliflozin in heart failure with a preserved ejection fraction. *N Engl J Med*. 2021;385(16):1451-1461. doi:10.1056/NEJMoa2107038
121. The EMPA-KIDNEY Collaborative Group, Herrington WG, Staplin N, et al. Empagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2023;388(2):117-127. doi:10.1056/NEJMoa2204233
122. Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med*. 2019;380(4):347-357. doi:10.1056/NEJMoa1812389
123. McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;381(21):1995-2008. doi:10.1056/NEJMoa1911303
124. Solomon SD, McMurray JJV, Claggett B, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. *N Engl J Med*. 2022;387(12):1089-1098. doi:10.1056/NEJMoa2206286
125. Heerspink HJL, Stefánsson BV, Correa-Rotter R, et al. Dapagliflozin in patients with chronic kidney disease. *N Engl J Med*. 2020;383(15):1436-1446. doi:10.1056/NEJMoa2024816
126. Weber MA, Mansfield TA, Alessi F, Iqbal N, Parikh S, Ptaszynska A. Effects of dapagliflozin on blood pressure in hypertensive diabetic patients on renin-angiotensin system blockade. *Blood Press*. 2016a;25(2):93-103. doi:10.3109/08037051.2015.1116258
127. Weber MA, Mansfield TA, Cain VA, Iqbal N, Parikh S, Ptaszynska A. Blood pressure and glycaemic effects of dapagliflozin versus placebo in patients with type 2 diabetes on combination antihypertensive therapy: a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Diabetes Endocrinol*. 2016b;4(3):211-220. doi:10.1016/S2213-8587(15)00417-9
128. Neal B, Perkovic V, Matthews DR. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med*. 2017;377(21):2097-2099. doi:10.1056/NEJMc1712572
129. Townsend RR, Machin I, Ren J, et al. Reductions in mean 24-hour ambulatory blood pressure after 6-week treatment with canagliflozin in patients with type 2 diabetes mellitus and hypertension. *J Clin Hypertens (Greenwich)*. 2016;18(1):43-52. doi:10.1111/jch.12747
130. Han KA, Chon S, Chung CH, et al. Efficacy and safety of ipragliflozin as an add-on therapy to sitagliptin and metformin in Korean patients with inadequately controlled type 2 diabetes mellitus: a randomized controlled trial. *Diabetes Obes Metab*. 2018;20(10):2408-2415. doi:10.1111/dom.13394
131. Seino Y, Sasaki T, Fukatsu A, Ubukata M, Sakai S, Samukawa Y. Efficacy and safety of luseogliflozin as monotherapy in Japanese patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled, phase 3 study. *Curr Med Res Opin*. 2014;30(7):1245-1255. doi:10.1185/03007995.2014.912983
132. Kaku K, Watada H, Iwamoto Y, et al. Efficacy and safety of monotherapy with the novel sodium/glucose cotransporter-2 inhibitor tofogliflozin in Japanese patients with type 2 diabetes mellitus: a combined phase 2 and 3 randomized, placebo-controlled, double-blind, parallel-group comparative study. *Cardiovasc Diabetol*. 2014;13:65. doi:10.1186/1475-2840-13-65
133. Mancia G, Cannon CP, Tikkanen I, et al. Impact of empagliflozin on blood pressure in patients with type 2 diabetes mellitus and hypertension by background antihypertensive medication. *Hypertension (Dallas, Tex.: 1979)*. 2016;68(6):1355-1364. doi:10.1161/HYPERTENSIONAHA.116.07703
134. McDonagh TA, Metra M, Adamo M, et al. 2023 focused update of the 2021 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J*. 2023;44(37):3627-3639. doi:10.1093/eurheartj/ehad195
135. Baker WL, Smyth LR, Riche DM, Bourret EM, Chamberlin KW, White WB. Effects of sodium-glucose co-transporter 2 inhibitors on blood pressure: a systematic review and meta-analysis. *Journal of the American Society of Hypertension: JASH*. 2014;8(4):262-75.e9. doi:10.1016/j.jash.2014.01.007
136. Baker WL, Buckley LF, Kelly MS, et al. Effects of sodium-glucose cotransporter 2 inhibitors on 24-hour ambulatory blood pressure: a systematic review and meta-analysis. *J am Heart Assoc*. 2017;6(5):e005686. doi:10.1161/JAHA.117.005686
137. Bantounou MA, Sardellis P, Plascevic J, et al. Meta-analysis of sotagliflozin, a dual sodium-glucose-cotransporter 1/2 inhibitor, for

heart failure in type 2 diabetes. *ESC Heart Failure*. 2025;12(2):968-979. doi:10.1002/ehf2.15036
138. Georgianos PI, Agarwal R. Ambulatory blood pressure reduction with SGLT-2 inhibitors: dose-response meta-analysis and comparative evaluation with low-dose hydrochlorothiazide. *Diabetes Care*. 2019;42(4):693-700. doi:10.2337/dc18-2207
139. Mazidi M, Rezaie P, Gao HK, Kengne AP. Effect of sodium-glucose Cotransport-2 inhibitors on blood pressure in people with type 2 diabetes mellitus: a systematic review and meta-analysis of 43 randomized control trials with 22 528 patients. *J am Heart Assoc*. 2017;6(6):e004007. doi:10.1161/JAHA.116.004007
140. Ren B, Chen M. Effect of sodium-glucose cotransporter-2 inhibitors on patients with essential hypertension and pre-hypertension: a meta-analysis. *Ther Adv Endocrinol Metab*. 2022;13:20420188221142450. doi:10.1177/20420188221142450
141. Teo YN, Ting AZH, Teo YH, et al. Effects of sodium/glucose cotransporter 2 (SGLT2) inhibitors and combined SGLT1/2 inhibitors on cardiovascular, metabolic, renal, and safety outcomes in patients with diabetes: a network meta-analysis of 111 randomized controlled trials. *Am J Cardiovasc Drugs*. 2022;22(3):299-323. doi:10.1007/s40256-022-00528-7
142. Vasilakou D, Karagiannis T, Athanasiadou E, et al. Sodium-glucose cotransporter 2 inhibitors for type 2 diabetes: a systematic review and meta-analysis. *Ann Intern Med*. 2013;159(4):262-274. doi:10.7326/0003-4819-159-4-201308200-00007
143. Blood Pressure Lowering Treatment Trialists' Collaboration. Pharmacological blood pressure lowering for primary and secondary prevention of cardiovascular disease across different levels of blood pressure: an individual participant-level data meta-analysis. *Lancet (London, England)*. 2021;397(10285):1625-1636. doi:10.1016/S0140-6736(21)00590-0
144. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet (London, England)*. 2016;387(10022):957-967. doi:10.1016/S0140-6736(15)01225-8
145. Hsu CY, Saver JL, Ovbiagele B, Wu YL, Cheng CY, Lee M. Association between magnitude of differential blood pressure reduction and secondary stroke prevention: a meta-analysis and meta-regression. *JAMA Neurol*. 2023;80(5):506-515. doi:10.1001/jamaneurol.2023.0218
146. Bushnell C, Kernan WN, Sharrief AZ, et al. 2024 guideline for the primary prevention of stroke: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2024;55(12):e344-e424. doi:10.1161/STR.0000000000000475
147. Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J am Coll Cardiol*. 2019;74(10):e177-e232. doi:10.1016/j.jacc.2019.03.010
148. An J, Sim JJ, Zhou MM, et al. Blood pressure reduction and changes in antihypertensive medication use among patients with hypertension who initiated sodium-glucose cotransporter-2 inhibitors. *J Clin Hypertens (Greenwich)*. 2024;26(11):1318-1321. doi:10.1111/jch.14915
149. Bidulka P, Lugo-Palacios DG, Carroll O, et al. Comparative effectiveness of second line oral antidiabetic treatments among people with type 2 diabetes mellitus: emulation of a target trial using routinely collected health data. *BMJ (Clinical Research Ed)*. 2024;385:e077097. doi:10.1136/bmj-2023-077097
150. Suzuki Y, Kaneko H, Okada A, et al. Comparison of incident hypertension between SGLT2 inhibitors vs. DPP4 inhibitors. *Hypertens Res*. 2024;47(7):1789-1796. doi:10.1038/s41440-024-01649-z
151. Vlacho B, Mundet-Tudurí X, Mata-Cases M, et al. Analysis of the effectiveness of second oral glucose-lowering therapy in routine clinical practice from the Mediterranean area: a retrospective cohort study. *Diabetes Res Clin Pract*. 2021;171:108616. doi:10.1016/j.diabres.2020.108616
152. Wilkinson S, Williamson E, Pokrajac A, et al. Comparative effects of sulphonylureas, dipeptidyl peptidase-4 inhibitors and sodium-glucose co-transporter-2 inhibitors added to metformin monotherapy: a propensity-score matched cohort study in UK primary care. *Diabetes Obes Metab*. 2020;22(5):847-856. doi:10.1111/dom.13970
153. Aristizábal-Colorado D, Corredor-Rengifo D, Sierra-Castillo S, et al. A decade of progress in type 2 diabetes and cardiovascular disease: advances in SGLT2 inhibitors and GLP-1 receptor agonists - a comprehensive review. *Front Endocrinol*. 2025;16:1605746. doi:10.3389/fendo.2025.1605746
154. Alexander SPH, Christopoulos A, Davenport AP, et al. The concise guide to PHARMACOLOGY 2023/24: G protein-coupled receptors. *Br J Pharmacol*. 2023;180:S23-S144. doi:10.1111/bph.16177
155. Alexander SPH, Fabbro D, Kelly E, et al. The concise guide to PHARMACOLOGY 2023/24: transporters. *Br J Pharmacol*. 2023;180:S374-S469. doi:10.1111/bph.16182

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