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Review

Overview of salt restriction in the Dietary Approaches to Stop Hypertension (DASH) and the Mediterranean diet for blood pressure reduction

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Abstract

Despite considerable advances in pharmacological treatments, hypertension remains a major cause of premature morbidity and mortality worldwide since elevated blood pressure (BP) adversely influences cardiovascular and renal outcomes. Accordingly, the current hypertension guidelines recommend the adoption of dietary modifications in all subjects with suboptimal BP levels. These modifications include salt intake reduction and a healthy diet, such as the Dietary Approaches to Stop Hypertension (DASH) diet or the Mediterranean diet (MedDiet), independently of the underlying antihypertensive drug treatment. However, dietary modifications for BP reduction in adults with prehypertension or hypertension are usually examined as stand-alone interventions and, to a lesser extent, in combination with other dietary changes. The purpose of the present review was to summarize the evidence regarding the BP effect of salt restriction in the context of the DASH diet and the MedDiet. We also summarize the literature regarding the effects of these dietary modifications when they are applied as the only intervention for BP reduction in adults with and without hypertension and the potent physiological mechanisms underlying their beneficial effects on BP levels. Available data of randomized controlled trials (RCTs) provided evidence about the significant BP-lowering effect of each one of these dietary strategies, especially among subjects with hypertension since they modulate various physiological mechanisms controlling BP. Salt reduction by 2.3 g per day in the DASH diet produces less than half of the effect on systolic blood pressure (SBP)/diastolic blood pressure (DBP) (–3.0/–1.6 mmHg) as it does without the DASH diet (–6.7/–3.5 mmHg). Although their combined effect is not fully additive, low sodium intake and the DASH diet produce higher SBP/DBP reduction (–8.9/–4.5 mmHg) than each of these dietary regimens alone. It is yet unsettled whether this finding is also true for salt reduction in the MedDiet.

Keywords: Salt; Sodium; Dietary approaches to stop hypertension; DASH; Mediterranean diet; Blood pressure; Hypertension; Review

1. Stating the problem

Elevated blood pressure (BP) is the leading modifiable risk factor contributing to the global burden of cardiovascular disease (CVD) [1]. To date, the number of adults with hypertension has doubled worldwide since 1990, reaching 2019 1.28 billion adults, meaning that the global age-standardized prevalence rate of hypertension is on average 32% for women and 34% for men [2]. Cardiovascular causes principally drive the number of deaths due to high BP, but chronic kidney disease (CKD) also remains an important contributor. An estimated 7.7–10.4 million annual deaths from ischemic heart disease, stroke, and CKD are attributable to systolic blood pressure (SBP) levels higher than 115 mmHg [3]. When BP is reduced within goal among patients with hypertension, it is accompanied by a significant reduction in fatal and non-fatal outcomes [4].

The pathophysiological mechanisms of hypertension are rather complex. The "mosaic theory" hypothesized that abnormal BP stems from altered regulatory systems involving cardiovascular, renal, neuroendocrine, and inflammatory pathways. The overall cardiovascular homeostasis is also influenced by multiple genetic and environmental factors [5]. Visceral obesity and ectopic fat storage in organs and tissues controlling cardiovascular function (heart, blood vessels and, kidneys) appear to be a pivotal component in the pathogenesis of hypertension since both systolic and diastolic functions are being impaired [6]. Among dietary factors, excessive sodium consumption is a major contributor to the development of hypertension, and sodium restriction has been regarded as a popular recommendation for BP reduction, which is being included in lifestyle modification, irrespectively of BP levels [7].

In the last decades, a substantial number of interventional and observational studies investigated the relationship between dietary sodium intake and BP levels. As a result, mounting evidence supports a direct association between sodium intake and BP increase [8]. However, sodium restriction as a measure to promote BP reduction has usu-

ally been examined in randomized controlled trials (RCTs) separately from other interventions and less likely in combination with other lifestyle changes, such as weight loss, physical exercise, or adoption of a specific dietary pattern [9,10]. Examples of dietary patterns that have been recognized as effective dietary interventions to reduce BP are the Dietary Approaches to Stop Hypertension (DASH) diet and the Mediterranean diet (MedDiet) [11,12]. However, the contribution of salt restriction under and above these dietary patterns on BP reduction remains by and large unclear.

In the present review, we summarized the available evidence from RCTs for the BP effects of salt restriction in the context of the DASH diet and the MedDiet. First, we focused on studies examining the BP effects of salt restriction when it is applied as the only intervention for BP reduction in adults with and without hypertension. Second, we reported the literature summary regarding the BP effect of the DASH and the MedDiet in subjects with or without hypertension, without a concomitant salt restriction. Finally, we considered the BP-lowering effect of salt restriction in the context of the DASH and the MedDiet. In each section, we presented evidence from RCTs to avoid methodological bias of observational studies. To select eligible meta-analyses of RCTs, we performed a literature search in PubMed, combining appropriate keywords for each examined dietary strategy. The filter "Meta-Analysis" was activated. In addition, references of the retrieved meta-analyses were searched to identify any missing meta-analyses.

2. The interplay between sodium intake and blood pressure

Salt is necessary for human health, consisting mainly of sodium chloride (NaCl) [13]. One sodium chloride molecule represents a 1:1 sodium (Na^+) and chloride (Cl^-) ions ratio. However, chloride contributes more than sodium to the molecule's weight, and one gram of sodium chloride provides 0.4 g of sodium and 0.6 g of chloride [14]. Thus, one of these two elements' main functions lies in the homeostatic control of the extracellular fluid volume, strictly regulated by mechanisms triggered by sodium and chloride concentrations changes. Thereby, salt intake, through the concomitant provision of sodium and chloride, is involved in regulating total body water, blood volume, and by extension, the level of BP values [15,16].

The gastrointestinal tract absorbs almost entirely dietary salt, and the kidneys retain more than 90% of the filtered sodium [17]. Therefore, sodium handling became one of the kidneys' main physiologic functions, because, for several million years, people in Prehistoric times consumed a diet naturally low in sodium, with less than 1 gram of salt per day [18]. However, nowadays, this sodium conservation mechanism may not be beneficial since people consume through their diets almost 10 times higher sodium than what is deemed physiologically necessary [19]. The proposed physiologically necessary sodium amount is less than 500 mg per day (i.e., less than 1.25 g of salt per day) [20]. The food industry's abundance of salty processed foods is mainly responsible for the high dietary salt intake, estimated at 9–12 g per day in most countries. However, there are marked differences between countries and regions within countries [21]. Furthermore, this increase in salt intake took place in a short period in the evolutionary timescale. As a result, kidneys programmed for a low salt diet may at some time fail to excrete chronic excessive salt intake and contribute to the elevation of BP levels [22].

Excessive sodium consumption (i.e., more than 5000 mg sodium or 12.5 grams of salt per day) is an important risk factor for hypertension [23]. Indeed, it increases BP by (1) a volume-dependent mechanism due to plasma expansion [24] and (2) a volume-independent mechanism due to the activation of the renin-angiotensin-aldosterone system (RAAS) [25] and the sympathetic nervous system (SNS) [26]. Also, increased sodium intake is associated with endothelial dysfunction [27] and peripheral vascular resistance increments [28]. These pathophysiological mechanisms linking excessive salt consumption with hypertension have been extensively reviewed. Regarding volume-dependent mechanisms, the osmolarity of extracellular fluid increases since ingested sodium is confined mainly to the extracellular space [29]. In an attempt to excrete excess sodium and restore osmolarity, the body enhances the action of anti-diuretic hormone. It also inhibits the action of aldosterone at the kidney level, resulting in a decrease in the amount of urine excreted and an increase in their sodium concentration [30]. These mechanisms restore osmolarity at the expense of water retention, extracellular fluid volume expansion, and increased cardiac output [31]. Subsequently, different mechanisms are activated, such as pressure natriuresis and diuresis [32,33]. High salt and water excretion are accomplished through the increased intraglomerular pressure until the blood volume is sufficiently reduced and BP levels are lowered [34,35].

However, BP levels are not changing predictably for all individuals [36]. In some people, the so-called salt-sensitive, BP exhibits changes parallel to the changes in salt intake [37]. The pathophysiological mechanisms of underlying salt-sensitivity remain elusive. However, they may be influenced by genetic to environmental factors and seem associated with older age, black race, CKD, obesity, and metabolic syndrome [38,39]. Salt-sensitive individuals cannot excrete increased dietary salt amounts, and BP elevation is a regulatory mechanism to address sodium overload effectively [40]. Suppose a salt-sensitive individual consumes for prolonged time intervals excessive salt. In that case, the kidneys are constantly "forced" to excrete large amounts of sodium until their excretory ability is deteriorated [41], and hypertension develops to produce sufficient excretion of sodium and water [42,43]. The latter is mediated by resetting the pressure-sodium excretion curve,

preventing BP from returning to normal levels [44].

3. To what extent should sodium intake be lowered?

According to the 2012 World Health Organization's (WHO) recommendations, in adults over 16 years, sodium intake should be reduced to less than 2000 mg per day (equivalent to <5 g salt per day) [45]. Furthermore, the 2018 European Society of Cardiology (ESC)/European Society of Hypertension (ESH) guidelines for the management of arterial hypertension also recommend sodium intake to be limited to approximately to 2000 mg per day in the general population and to try to achieve this goal in all hypertensive patients [46]. In addition, the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for the prevention and management of high BP in adults propose to reduce sodium intake to <1500 mg per day (equivalent to <3.75 g salt per day) [47]. These guidelines about sodium intake concern both patients with hypertension and normotensive individuals.

The effect of dietary salt on BP levels was first noted in 1904 in France by Ambard and Beaujard, who studied 6 patients with high BP for 3 weeks and observed that when the dietary salt was decreased, BP fell, while the increase in salt intake had the opposite effect and BP rose [48]. In the early 1920s, Allen and Sherrill in the United States confirmed this finding [49]. Kempner offered confirmatory findings in 1948, who used a rice diet with less than 0.5 g salt per day in 500 patients with severe hypertension and showed that this rice diet with strict salt restriction could produce remarkably lower BP levels [50]. Subsequently, beginning in the 1970s, the effect of moderate salt restriction in patients with less severe hypertension or normotensive adults was studied in experimental trials. The first double-blind controlled study providing evidence about the BP-lowering effect of moderate salt restriction in patients with mild to moderate hypertension was conducted in 1982 by MacGregor *et al*. [51], followed by subsequent research in the field.

Dietary interventions mostly compare low sodium intake to usual or high sodium intake in the context of the habitual diet either by dietary modification (e.g., counseling to reduce salt during cooking and at the table and to avoid highly salty processed foods) or by supplementation with sodium or placebo tablets. However, the definitions of "low", "usual", and "high" sodium intake are unclear, and consequently, these terms indicate different ranges of sodium intake. Generally, and according to health institutions' recommendations, low sodium intake is below 2000 mg per day, usual sodium intake is between 2000 and 5000 mg per day, and high sodium intake is above 5000 mg per day. Through the years, several meta-analyses of RCTs have also been conducted to estimate the effect of a salt-restricted diet compared to the control diet on BP reduction. The most recent update of meta-analytical approaches is presented in Table 1 (Ref. [52–60]).

Almost all meta-analyses provided evidence about the significant lowering effect of sodium reduction on BP, ranging from –2.5 (95% CI: –3.8 to –1.2) to –4.8 (95% CI: –3.9 to –5.7) mmHg, regarding SBP and from –1.2 (95% CI: –1.8 to –0.7) to –2.1 (95% CI: –2.7 to –1.5) mmHg, regarding diastolic blood pressure (DBP) [52–57,59,60], for a median sodium reduction ranging from –1.13 (range: –1.50 to –0.74) to –2.30 (range: –7.54 to –0.46) g per day [52–55,57,60]. All meta-analyses agreed that for the same reduction in salt intake BP reduction was greater in patients with hypertension compared to individuals without hypertension. In hypertensive patients SBP/DBP reduction ranged from –4.1 (95% CI: –5.1 to –2.9) to –8.0 (95% CI: –15.7 to –0.3)/–2.3 (95% CI: –3.0 to –1.5) to –4.3 (95% CI: –7.1 to –1.6) mmHg, while in normotensive individuals SBP/DBP reduction ranged from –1.1 (95% CI: –1.7 to –0.6) to –2.4 (95% CI: –3.6 to –1.3)/0.0 (95% CI: –0.4 to 0.4) to –1.2 (95% CI: –1.8 to –0.6) mmHg [52–58].

The main differential component that distinguishes the presented meta-analyses is the duration of the included trials, i.e., some meta-analyses included salt restriction trials of less than one week, while others excluded short-duration trials. The modification effect of trial duration for the impact of salt reduction on BP is challenging and yet unclear. Indeed, the inclusion of salt restriction trials of less than one week produced significant BP-lowering in hypertension and a trivial effect in normotensive individuals [52,58]. It has also been suggested that the effect of a sustained salt restriction on BP levels is not different after the first week from baseline [58,61,62]. Thus, the indifferent BP-lowering effect following salt restriction in normotensive individuals is potentially related to differential activation of neuro-hormonal factors compared to patients with hypertension [58]. However, in additional meta-analyses, the exclusion of short-duration trials was associated with a significant BP-lowering effect independently of hypertension status [53–57,60].

In a step further, Graudal *et al*. [58], in their meta-analysis, studied the effect of reducing dietary sodium from about 4700 to about 1500 mg per day, i.e., from a level corresponding to the present usual intake of the world's populations to a low level following the recommendations of the health institutions. The authors concluded that white normotensives do not benefit from sodium reduction but may experience potential harm due to the adverse effects on hormones and lipids. In contrast, white hypertensives may benefit from BP-lowering but may also be exposed to potential harms. Therefore, since sodium reduction does not have net beneficial effects in a population of white people with normal BP, a small BP-lowering does not justify the recommendation for sodium reduction in the general population [58].

Overall, the conflicting findings of the above meta-analyses question the current recommendations to reduce salt intake from 9–12 to 5–6 g per day. Thus, the question

regarding the optimum level of sodium intake is still controversial. Indeed, the meta-analysis by Graudal *et al*. [58] about the absence of public health benefits when sodium is reduced in non-hypertensive individuals is driven by the results from the very short-term trials in which time-limited and large reductions in salt intake were pursued. By contrast, modest and long-term reduction in salt intake can have important public health benefits, since even a relatively small BP-lowering effect of decreased sodium intake across the entire population, including the subjects without high BP, may contribute to CVD reduction [53–57,60].

Regarding the adverse effects of sodium reduction on hormones and blood lipids, Aburto *et al*. [56] showed that reducing sodium intake for at least one month had no impact on catecholamine levels or blood lipids. Authors raised the hypothesis that metabolic changes occurring after large and rapid reductions in salt intake do not occur with moderate and sustained salt reduction. Also, He, *et al*. [57] stated that the compensatory mechanisms involving the activation of the RAAS and the SNS are more extensive with sudden and large decreases in salt intake. Huang *et al*. [59] included in their meta-analysis trials regardless of the length of the intervention duration to examine its effect on the studied outcomes. They found that the duration of the sodium reduction intervention was not associated with the magnitude of either SBP or DBP reduction. However, they identified in studies of longer than two weeks' duration an approximately twice as large effect of sodium reduction on BP compared with short-term studies of less than 15 days' duration. The authors suggested that (1) the short-term responses of the RAAS and the SNS, and (2) the unfavorable metabolic effects associated with extreme falls in dietary sodium are not sustained in longer-term interventions and do not outweigh the long-term benefits anticipated from BP-lowering.

The dose-response relationship between the reduction in salt intake and the magnitude of BP-lowering has also been demonstrated, i.e., the greater the reduction in salt intake, the greater the fall in BP levels [52,53,57,59,60]. In the largest meta-analysis of RCTs [60], an almost linear relationship was identified between attained sodium intake and BP levels with no flattening of the curve or a threshold for the effect of sodium reduction on BP across the entire range of dietary sodium exposure (0 to 6900 mg per day of sodium excretion). However, the curve for SBP was steeper than for DBP. In linear regression analysis, every 2300 mg per day reduction in urinary sodium excretion was associated with a lower mean SBP of –5.6 mmHg (95% CI: –4.5 to –6.6) and a lower mean DBP of –2.3 mmHg (95% CI: –1.7 to –3.0). The roughly linear association between the achieved sodium intake and BP change was observed in hypertensive patients and individuals without hypertension. However, after sodium reduction, participants with hypertension than normotension showed a steeper decrease in BP. The only exception were participants without hypertension whose sodium intake was <2 g per day, for whom there was little evidence regarding the BP effect of sodium reduction. Moreover, a higher baseline sodium intake (<2.5 g versus ≥ 2.5 g per day) resulted in greater BP-lowering at a given change in sodium intake. Thus, reducing sodium consumption has a greater capacity to lower BP in high sodium consumers [60].

4. DASH diet and blood pressure reduction

The DASH diet is a dietary pattern that emphasizes the consumption of fruits, vegetables, and low-fat dairy products, including whole grains, legumes, nuts, fish, and poultry while containing decreased amounts of fat, red meat, and sweets/sugar-containing beverages. Also, the DASH diet is naturally low in sodium [63]. The high content in potassium, calcium, magnesium, and fiber, along with the reduced-sodium, trans/saturated/total fat, and dietary cholesterol content, are considered the beneficial components of the DASH diet [64]. The various effects of the dietary patterns are linked to the synergistic effects produced by the combination of foods and nutrients being habitually consumed in their context [65]. Although the DASH diet is widely recognized as an effective dietary intervention to reduce BP, the mechanisms exerting its antihypertensive effect are not fully known. However, several potential physiological effects of the DASH diet have been proposed and correlated to BP reduction [66].

Particularly, the DASH diet seems to interact with the RAAS, enhancing some of the physiologic effects of angiotensin-converting enzyme (ACE) inhibition and resulting in a natriuretic and diuretic effect [67]. Regarding the DASH diet effect on the pressure-natriuresis curve (arterial BP-urinary sodium output relationship), the slope of the pressure-natriuresis curve is increased without shifting the curve along the BP axis. Accordingly, the DASH diet acts as a diuretic, enhancing the salt output at each BP level. For this reason, the DASH diet has a greater BP-lowering effect in salt-sensitive individuals whose slopes are depressed [68]. The natriuretic action of the DASH diet has been mainly attributed to its high content in potassium and calcium, coming from its high content in fruits, vegetables, and low-fat dairy products. Potassium is known for its role in regulating BP, and its natriuretic action [69], while calcium has also been shown to blunt the pressure effects of dietary sodium [70]. Other important nutrients of the DASH diet are numerous vitamins, phytochemicals, and antioxidants, such as polyphenols and especially flavonoids, which attenuate oxidative stress. Moreover, it has been found that they inhibit or decrease inflammation through the lowering of high-sensitivity C-reactive protein (hs-CRP) and reduce subclinical cardiac injury through the lowering of high-sensitivity cardiac troponin I (hs-cTnI) [71]. Also, the consumption of fruits and vegetables rich in inorganic nitrate improves endothelial function, reduces arterial stiffness, and decreases platelet aggregation through nitric oxide-related mechanisms because nitrate can be

Table 1. Effect of salt reduction on BP: results from published meta-analyses of RCTs examining the effect of salt reduction on SBP and DBP in adults.

Author, year	Studies, n	Participants, n	Duration of trials			BP difference (mmHg)						Sodium intake (mg per day)					
			Median (range)			SBP			DBP			Baseline			Change during intervention		
						Mean (95% CI)			Mean (95% CI)			Median (range)			Median (range)		
			All subjects	Patients with hypertension	Normotensive individuals	All subjects	Patients with hypertension	Normotensive individuals	All subjects	Patients with hypertension	Normotensive individuals	All subjects	Patients with hypertension	Normotensive individuals	All subjects	Patients with hypertension	Normotensive individuals
Midgley, *et al*., 1996 [52]	56	3505	14 (4–1095) days	29 (4–730) days	14 (4–1095) days	–3.4 (–4.3; –2.5)	–5.9 (–7.8; –4.1)	–1.6 (–2.4; –0.9)	–2.0 (–2.7; –1.4)	–3.8 (–4.8; –2.9)	–0.5 (–1.2; 0.1)	3680 (1564; 6693)	3634 (1564; 5244)	3772 (1656; 6693)	–2300 (–7544; –46)	–1817 (–7544; –46)	–3059 (–7199; –368)
Cutler, *et al*., 1997 [53]	32	2635	NR	2 (1–24) months	1 (0.5–36) months	–2.8 (–3.4; –2.2)	–4.8 (–5.9; –3.8)	–1.9 (–2.6; –1.2)	–1.5 (–1.9; –1.1)	–2.5 (–3.1; –1.9)	–1.1 (–1.5; –0.7)	NR	NR	NR	NR	–1633 (–612; –3933)	–1633 (–368; –2691)
Hooper, *et al*., 2002 [54]	7	2549	NR	12 (12–12) months	6 (6–12) months	–2.5 (–3.8; –1.2)	–8.0 (–15.7; –0.3)	–2.3 (–3.1; –1.6)	–1.2 (–1.8; –0.7)	–4.3 (–7.1; –1.6)	–1.2 (–1.8; –0.6)	NR	NR	NR	–1127 (–1495; –736)	–1104 (–759; –1449)	–989 (–368; –1610)
Geleijnse, *et al*., 2003 [55]	40	NR	4 (2–156) weeks	NR	NR	–2.5 (–3.2; –1.9)	–5.2 (–6.6; –3.9)	–1.3 (–2.1; –0.4)	–1.9 (–2.4; –1.5)	–3.7 (–4.7; –2.7)	–1.1 (–1.8; –0.5)	3519 ± 759 *	NR	NR	–2093 ± 1196 *	NR	NR
Aburto, *et al*., 2013 [56]	36	6736	>4 weeks	NR	NR	–3.4 (–4.3; –2.5)	–4.1 (–5.1; –2.9)	–1.4 (–2.7; –0.1)	–1.5 (–2.1; –0.9)	–2.3 (–3.0; –1.5)	–0.6 (–1.3; 0.1)	NR	NR	NR	NR	NR	NR
He, *et al*., 2013 [57]	34	3230	4 (4–156) weeks	5 (4–52) weeks	4 (4–156) weeks	–4.2 (–5.2; –3.2)	–5.4 (–6.6; –4.2)	–2.4 (–3.6; –1.3)	–2.1 (–2.7; –1.5)	–2.8 (–3.5; –2.1)	–1.0 (–1.9; –0.2)	3680 (2875; 4600)	3726 (2875; 4393)	3519 (2944; 4600)	–1725 (–920; –2714)	–1725 (–1219; –2691)	–1725 (–920; –2714)
Graudal, *et al*., 2020 [58]	195	12,296	>3 days	NR	NR	NR	–5.7 (–6.7; –4.7)	–1.1 (–1.7; –0.6)	NR	–2.9 (–3.4; –2.3)	0.0 (–0.4; 0.4)	4692 (NR) **	NR	NR	–3220 (NR) **	NR	NR
Huan, *et al*., 2020 [59]	133	12,197	≤7 days–>6 months	NR	NR	–4.3 (–4.9; –3.6)	NR	NR	–2.1 (–2.5; –1.7)	NR	NR	NR	NR	NR	–2990 (–3335; –2645) ***	NR	NR
Filippini, *et al*., 2021 [60]	85	>10,000	4 weeks–36 months	NR	NR	–4.8 (–3.9; –5.7)	NR	NR	–2.0 (–1.4; –2.6)	NR	NR	NR	NR	NR	–1840 (–115; –7107)		

BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; NR, not reported; RCT, randomized controlled trial; SBP, systolic blood pressure.
*Mean ± SD, **Mean (SD), ***Mean (95% CI).

Table 2. Effect of the DASH diet on BP: Results from published meta-analyses of RCTs examining the effect of the DASH diet on SBP and DBP in adults.

Author, year	Studies, n	Participants, n	Duration of trials	BP difference (mmHg)					
				SBP			DBP		
				Mean (95% CI)			Mean (95% CI)		
			Range	All subjects	Patients with hypertension	Normotensive individuals	All subjects	Patients with hypertension	Normotensive individuals
Saneei, *et al*., 2014 [78]	17	2561	2–26 weeks	–6.7 (–8.3; –5.3)	–6.8 (–8.6; –5.1)	–2.5 (–3.9; –1.0)	–3.5 (–4.3; –2.8)	–3.6 (–4.4; –2.8)	–1.7 (–2.7; –0.7)
Siervo, *et al*., 2015 [79]	16	1581	2–24 weeks	–5.2 (–7.0; –3.4)	NR	NR	–2.6 (–3.5; –1.7)	NR	NR
Ndanuko, *et al*., 2016 [80]	10	2798	8 weeks–12 months	–4.9 (–6.2; –3.6)	NR	NR	–2.6 (–3.3; –1.9)	NR	NR
Gay, *et al*., 2016 [81]	4	668	6–12 months	–7.6 (–9.9; –5.3)	NR	NR	–4.2 (–5.9; –2.6)	NR	NR
Filippou, *et al*., 2020 [11]	30	5545	2–52 weeks	–3.2 (–4.2; –2.3)	–3.9 (–5.5; –2.4)	–3.9 (–6.0; –1.8)	–2.5 (–3.5; –1.5)	–2.5 (–3.9; –1.1)	–2.1 (–4.0; –0.2)
Lari, *et al*., 2021 [82]	34	6011	2–52 weeks	–3.9 (–5.2; –2.6)	NR	NR	–2.4 (–3.4; –1.5)	NR	NR

BP, blood pressure; CI, confidence interval; DASH, dietary approaches to stop hypertension; DBP, diastolic blood pressure; RCT, randomized controlled trial; SBP, systolic blood pressure.

metabolized to nitric oxide [72]. Collectively, these data suggest that the DASH diet induces hormonal and vascular responses related to its hypotensive effect and additional responses in end-diastolic volume and stroke volume related to its beneficial effect on left ventricular function [73].

The 2017 ACC/AHA guidelines for preventing and managing high BP in adults recommend a heart-healthy diet, such as the DASH diet, for adults with elevated BP or hypertension [47]. The 2020 International Society of Hypertension (ISH) global hypertension practice guidelines also recommend preventing or delaying high BP by eating a diet like the DASH. In addition, these guidelines highlighted the increased intake of vegetables high in nitrates known to reduce BP, such as leafy vegetables and beetroot [74].

The BP-lowering effect of the DASH diet was first noted almost 25 years ago, when the initial DASH clinical trial, which was a controlled feeding trial, tested the effects of 3 different diets on BP levels in adults with stage 1 hypertension and without hypertension. The "combination" diet, which was rich in fruits, vegetables, and low-fat dairy products, currently named the "DASH" diet, reduced SBP/DBP compared to the control diet by –5.5 (95% CI: –7.4 to –3.7)/–3.0 (95% CI: –4.3 to –1.6) mmHg and compared to the fruits-and-vegetables diets by –2.7 (95% CI: –4.6 to –0.9)/–1.9 (95% CI: –3.3 to –0.6) mmHg. The salient BP reduction between diets suggests that (1) some components of the fruits-and-vegetables diet, and (2) additional components of the "combination" (DASH) diet may synergistically contribute to BP-lowering. The results were even more pronounced among subjects with stage 1 hypertension, in whom compared to the control diet, SBP/DBP was reduced by –11.4 (95% CI: –15.9 to –6.9)/–5.5 (95% CI: –8.2 to –2.7) mmHg [75].

This study demonstrated that the effects of the original DASH diet on BP occurred without energy or sodium restriction since bodyweight was kept constant and the sodium content of each diet was similar (approximately 3000 mg per day). Given the body of evidence regarding the BP-lowering effect of salt restriction, the DASH trial research group subsequently conducted a second controlled feeding trial to determine the BP effects of sodium restriction alone and in combination with the DASH diet. Specifically, the DASH-Sodium trial investigated among adults with stage 1 hypertension and without hypertension the extent to which reducing sodium intake at 3 different sodium levels lowers BP within the context of the DASH and the control diet. The participants were randomly assigned to the control or the DASH diet. They were fed for 30 consecutive days on their assigned diet in a crossover design with 3 different sodium levels: low, intermediate, and high (1150, 2300, and 3450 mg, respectively, at 2100 kcal). The high level reflected the average sodium intake in the United States. The medium level corresponded to prevailing sodium recommendations, whereas the lower level represented a level that might further lower BP [76].

Confirming the results by Appel *et al.* [75], the DASH-Sodium trial showed that the DASH diet significantly reduced BP than the control diet. Extending the previous results, it was found that this was true for SBP at every sodium level, i.e., at the high [–5.9 (95% CI: –8.0 to –3.7) mmHg], the intermediate [–5.0 (95% CI: –7.6 to –2.5) mmHg] and the low level [–2.2 (95% CI: –4.4 to –0.1) mmHg] and for DBP only at the high [–2.9 (95% CI: –4.3 to –1.5) mmHg] and the intermediate level [–2.5 (95% CI: –4.1 to –0.8) mmHg]. Compared to the control diet, the effect of the DASH diet on both SBP and DBP was larger at the high than at the intermediate and the low sodium levels. This study also showed that in the context of the control diet, the reduction of sodium intake lowered SBP/DBP significantly in a stepwise manner from the high to the intermediate [–2.1 (95% CI: –3.4 to –0.8)/–1.1 (95% CI: –1.9 to –0.2) mmHg] and from the intermediate to the low level of sodium [–4.6 (95% CI: –5.9 to –3.2)/–2.4 (95% CI: –3.3 to –1.5) mmHg]. Notably, going from the intermediate to the low sodium intake level, the effects on SBP and DBP were greater. In the context of the DASH diet, sodium reduction reduced SBP from the high to the intermediate [–1.3 (95% CI: –2.6 to 0.0) mmHg] and from the intermediate to the low level of sodium intake [–1.7 (95% CI: –3.0 to –0.4) mmHg], but DBP was reduced only from the intermediate to the low level of sodium intake [–1.0 (95% CI: –1.9 to –0.1) mmHg]. An almost similar pattern as in the control diet was observed. However, the progressive reduction in sodium intake from the high to the low level had an almost double effect on SBP/DBP in the context of the control [–6.7 (95% CI: –5.4 to –8.0)/–3.5 (95% CI: –2.6 to –4.3) mmHg], as it did in the context of the DASH diet [–3.0 (95% CI: –1.7 to –4.3)/–1.6 (95% CI: –0.8 to –2.5) mmHg] [76].

Finally, the greatest benefit on BP was observed when the low sodium intake was coupled with the DASH diet, especially among subjects with hypertension. In a secondary analysis of the DASH-Sodium trial, according to baseline levels of SBP, compared to the control diet with high sodium, the DASH diet with low sodium lowered SBP by –9.7 (95% CI: –13.3 to –6.6) mmHg among those with a baseline SBP of 140 to 149 mmHg and by –20.8 (95% CI: –30.9 to –10.7) mmHg among those with a baseline SBP $\geq$ 150 mmHg. Thus, although the combined effects on BP of low sodium intake and the DASH diet were greater than the effects of either intervention alone, they were not as great as they would have been if the effects of each dietary intervention were strictly additive [76,77].

The less pronounced effects of sodium reduction in the context of the DASH compared to the control diet may occur because of the already low BP resulting from each of these dietary regimens. Sacks *et al.* [76] assumed that low amounts of dietary sodium attenuated the hypotensive effects of potassium in the DASH diet or, inversely, the

high potassium or calcium content of the DASH diet attenuated the effects of low amounts of sodium. The lack of an additive effect resulting from low sodium intake and the DASH diet could be explained by considering the data of the pressure-natriuresis relationship mentioned earlier. Since the DASH diet increases the slope of the pressure-natriuresis curve, as if it was a diuretic, it is assumed that it lowers BP effectively in subjects with high sodium sensitivity by making BP less sodium-sensitive. For this reason, the BP-lowering effect of sodium restriction may be attenuated in the context of the DASH compared to the control diet. By extension, their combined effect is smaller rather than fully additive. Also, it is of note that the pressure-natriuresis curves suggest that the effect of the DASH diet on BP would be diminished at very low sodium intakes, e.g., 500 or 700 mg per day [68].

The DASH and the DASH-Sodium trials provided strong evidence that both the DASH diet and sodium restriction, alone or together, significantly reduce BP. These two clinical trials have been extensively discussed and reviewed and, in the meanwhile, numerous subsequent RCTs confirmed these findings. However, the DASH diet was often examined alone and to a lesser extent in combination with sodium restriction. Through the past years, several meta-analyses of RCTs have also been conducted to estimate the effect of the DASH diet compared to the control diet on BP reduction, with or without concomitant sodium reduction, which are presented in Table 2 (Ref. [11,78–82]). In the meta-analysis conducted recently by our group [11], we moved on a step further. We examined the modification effect of salt intake on BP reduction in the context of the DASH diet. We performed a subgroup analysis according to daily sodium intake and compared the results to the DASH-Sodium clinical trial.

All these meta-analyses of RCTs investigating the effect of the DASH diet on BP demonstrated that the DASH diet significantly reduced both SBP and DBP and confirmed its effectiveness as a nutritional strategy for the prevention and management of hypertension [11,78–82]. However, except for the meta-analysis conducted recently by our group [11], BP estimates presented the absolute mean BP difference as a change from baseline BP [78–82]. Consequently, the reported BP reduction, ranging from –3.9 (95% CI: –5.2 to –2.6) to –7.6 (95% CI: –9.9 to –5.3) mmHg, regarding SBP and from –2.4 (95% CI: –3.4 to –1.5) to –4.2 (95% CI: –5.9 to –2.6) mmHg, regarding DBP, introduced outcome-related bias. At variance with the previous evidence, we considered the attained mean SBP/DBP difference between the two randomized arms during follow-up. We found that it was –3.2 (95% CI: –4.2 to –2.3) and –2.5 (95% CI: –3.5 to –1.5) mmHg for SBP and DBP, respectively [11]. Considering hypertension status, three of these meta-analyses found that the BP-lowering effect of the DASH diet was greater among individuals with hypertension compared to those without hypertension [78,79,81]. We observed no differential SBP/DBP-lowering between the two randomized arms according to hypertension status. The underlying “regression to the mean” phenomenon or different operating pathophysiological pathways in hypertension, such as endothelial dysfunction and increased sympathetic tone, may limit but not neutralize the BP-lowering effect of the DASH diet [11].

Regarding the influence of sodium intake on BP in the context of the DASH diet, two of the meta-analyses mentioned above also reported meta-regression analyses for the relationship between the difference in dietary sodium intake and the attained BP levels [78,79]. Saneei *et al*. [78] found that the difference in sodium intake between the intervention and the control groups was significantly associated with the fall in SBP but not in DBP. On the other hand, Siervo *et al*. [79] reported that both SBP and DBP changes were independent of the differences in dietary sodium intake. Therefore, the authors stated that the lack of a significant association between dietary sodium intake and BP was not anticipated. This phenomenon might be due to the differences between the trials concerning dietary sodium intake in both the DASH and the control groups, the assessment of sodium intake (dietary intake or 24-h urinary excretion assessment), and the type of the dietary intervention (controlled feeding study or provision of dietary advice).

In the meta-analysis conducted by our group, the univariate meta-regression analysis of change in 24-h urinary sodium exertion during follow-up revealed that it had no significant modifying effect on SBP or DBP reduction. However, the subgroup analysis conducted according to daily sodium intake showed that the treatment effect of the DASH diet was more pronounced regarding SBP reduction in trials with sodium intake $>$2400 mg per day compared to trials with sodium intake $\leq$2400 mg per day. The graphical displays of the estimated SBP results from the included studies according to sodium intake are presented in the forest plots of Fig. 1. These findings agree with the results of the DASH-Sodium trial, proving that higher levels of daily sodium intake enhance the BP-lowering effect of the DASH diet [11].

5. Mediterranean diet and blood pressure reduction

The MedDiet is a dietary pattern that emphasizes whole grains, fruits, vegetables, legumes, and nuts. It is characterized by increased total fat consumption, with olive oil being the principal source of added fat. It also includes fish and seafood, low-fat dairy products, poultry, and eggs and contains decreased amounts of red meat and sweets/sugar-containing beverages. Finally, moderate consumption of alcohol, mainly red wine during meals, is present in the MedDiet [83]. The high content in antioxidants and anti-inflammatory nutrients, fibers, ω-3 poly- and mono-unsaturated fat, the moderate content in ethanol, and the low content in trans/saturated fat and dietary cholesterol

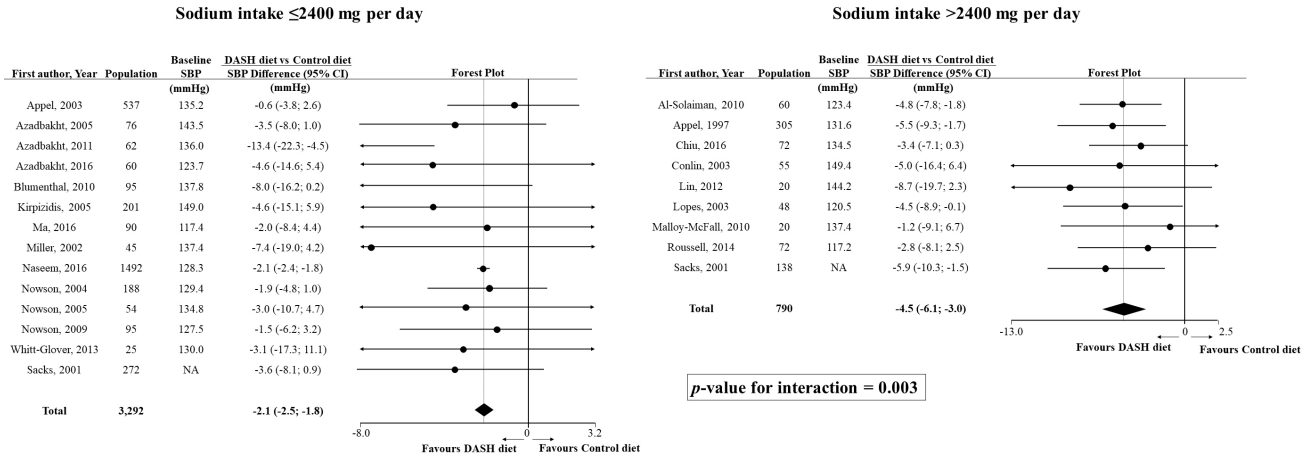

Fig. 1. Blood pressure-lowering effect of the DASH diet in adults with and without hypertension: Subgroup analysis of trials for SBP outcome, according to daily sodium intake. CI, confidence interval; DASH, dietary approaches to stop hypertension; NA, not applicable; SBP, systolic blood pressure. Difference in means of the attained SBP difference in trials with sodium intake ≤2400 mg per day (left forest plot) and in trials with sodium intake >2400 mg per day (right forest plot) for the effect of the DASH diet compared to control diet. In each subgroup of trials, from left to right, the columns indicate first author, year, the number of subjects in the two randomized arms, the difference in mean and 95% CIs for SBP outcome (the minus sign indicates a lower BP value in the first group), and the forest plot of the difference in means and 95% CIs. Blood pressure in mmHg.

are considered the beneficial components of the MedDiet diet [84]. The synergetic action of these components attenuates the intermediate CVD pathways of atherosclerosis and thrombosis since they exert a protective effect on endothelial function by mitigating the processes of oxidative stress and inflammation [85]. Moreover, the components of the MedDiet improve multiple CVD risk factors, including elevated BP levels, although the way the MedDiet induces BP changes is not fully understood [86].

It seems that olive oil might be the component of the MedDiet with a favorable effect on BP. First, the high content in mono-unsaturated fatty acids, vitamin E, and polyphenols, especially flavonoids, may increase nitric oxide availability, promote vasodilation, and improve endothelial function [87]. Second, fruits and vegetables, which are rich in (1) vitamins (e.g., vitamin C), (2) minerals (e.g., potassium), (3) fibers, (4) numerous bioactive compounds (e.g., like phytosterols, inorganic nitrate), and (5) phytochemicals (i.e., polyphenols-flavonoids) may contribute to endothelium-dependent vasodilation and inhibition of platelet aggregation [88]. Third, regarding whole grains, the potential beneficial effects on BP may be associated with the high dietary fiber content and minerals highly linked to fiber intake [89]. Last, red wine is a complex blend of ingredients, such as polyphenols (including resveratrol), having a positive biological effect on the cardiovascular system since they exert antioxidant and anti-inflammatory effects [90].

The 2018 ESC/ESH guidelines for hypertension management recommend that hypertensive patients should be advised to eat a healthy, balanced diet, such as the MedDiet [46]. Also, the 2021 ESC Guidelines for CVD prevention recommend adopting a MedDiet or a similar diet to lower CVD risk. Specifically, it is recommended to choose a more plant- and less animal-based food pattern [91].

The very first evidence about the cardioprotective effect of the MedDiet came in 1970 from the Seven Countries Study. It was first described and studied by Ancel Keys, as he observed that certain populations dwelling around the Mediterranean Sea had some special dietary habits. It had been hypothesized that these dietary habits may have a favorable effect on CVD mortality observed at variance with Northern Europe and the United States [92]. Over the past decades, the MedDiet has been the most studied dietary pattern, and the definition originally introduced by Keys has been evolved [93]. For a long now, there has been a substantial body of evidence, which has established the health benefits associated with the adherence to the MedDiet, mainly about metabolic syndrome, type 2 diabetes (T2D), CVD, and some neurodegenerative diseases and cancers [94,95]. Regarding the BP effect of the MedDiet, several studies have found that consuming foods typical of the MedDiet might reduce the risk of hypertension. In contrast, foods not typical of this dietary pattern, such as red and processed meat, have an opposite effect on BP levels [96].

The PREvención con DIeta MEDiterránea (PREDIMED) study, was designed to assess the influence of the MedDiet on primary CVD prevention. A landmark study conducted on nearly 7500 participants at high cardiovascular risk. It investigated the effects of two MedDiets, the one supplemented with extra-virgin olive oil and the other supplemented with mixed nuts, compared to the control diet, a low-fat diet. Participants were not subjected to any caloric

Table 3. Effect of the MedDiet on BP: Results from published meta-analyses of RCTs examining the effect of the MedDiet on SBP and DBP in adults.

Author, year	Studies, n	Participants, n	Duration of trials	BP difference (mmHg)	
			Range	SBP	DBP
				Mean (95% CI)	Mean (95% CI)
Nordmann, *et al*., 2011 [98]	6	2650	2–4 years	Versus low-fat diet –1.7 (–3.3; –0.1)	Versus low-fat diet –1.5 (–2.1; –0.8)
Nissensohn, *et al*., 2016 [99]	6	7987	2–4 years	Versus low-fat diet –1.5 (–2.9; 0.0)	Versus low-fat diet –0.7 (–1.3; –0.1)
Ndanuko, *et al*., 2016 [80]	3	535	1–2 years	Versus usual/low-fat/prudent diet –3.0 (–3.5; –2.6)	Versus usual/low-fat/prudent diet –1.9 (–2.3; –1.7)
Gay, *et al*., 2016 [81]	4	7703	2–4 years	Versus usual/low-fat/prudent diet –1.2 (–2.8; 0.5)	Versus usual/low-fat/prudent diet –1.5 (–2.1; –0.8)
Rees, *et al*., 2019 [100]	Versus no/minimal intervention 2	Versus no/minimal intervention 269	Versus no/minimal intervention 3–24 months	Versus no/minimal intervention –2.9 (–3.5; –2.5)	Versus no/minimal intervention –2.0 (–2.3; –1.7)
	Versus another dietary intervention 4	Versus another dietary intervention 448	Versus another dietary intervention 3–12 months	Versus another dietary intervention –1.5 (–3.9; 0.9)	Versus another dietary intervention –0.2 (–2.4; 1.9)
Cowell, *et al*., 2021 [101]	19	4137	1.5 week–5 years	Versus habitual/low–fat/other diet –1.4 (–2.4; –0.4)	Versus habitual/low–fat/other diet –1.5 (–2.7; –0.3)
Filippou, *et al*., 2021 [12]	35	13,943	6 weeks–3.7 years	Versus usual diet/other dietary intervention –1.5 (–2.8; –0.1) Versus usual diet –3.1 (–4.8; –1.3) Versus all other dietary interventions –0.2 (–1.9; 1.5) Versus low-fat diet –0.1 (–1.1; 0.9)	Versus usual diet/other dietary intervention –0.9 (–1.5; –0.3) Versus usual diet –1.6 (–2.6; –0.6) Versus all other dietary interventions –0.6 (–1.3; 0.1) Versus low-fat diet –0.7 (–1.5; 0.1)

BP, blood pressure; CI, confidence interval; DBP, diastolic blood pressure; RCT, randomized controlled trial; SBP, systolic blood pressure.

or sodium restriction. All groups received dietary counseling (including group sessions specific for each intervention group) to increase adherence to the assigned diet. At the same time, participants in the two intervention groups were also given supplementary foods, either extra-virgin olive oil or mixed nuts, to ensure high consumption of these key elements. The results over a median follow-up period of 3.8 years showed that compared to the low-fat diet, greater reductions in DBP were seen for both MedDiets [–1.5 (95% CI: –2.0 to –1.0) and –0.7 (95% CI: –1.2 to –0.2) mmHg for MedDiet with extra-virgin olive oil and mixed nuts, respectively]. Regarding differences in SBP up to 4 years of follow-up, they were apparent only in crude analyses and became non-significant after multivariate adjustment [97].

Although the MedDiet was mainly examined against cardiovascular risk factors, the results regarding the effect on BP levels were, until recently, by and large undetermined. Indeed, the available studies showed converging results due to methodological and clinical differences. At the same time, some studies were designed with a different purpose than that to explore the MedDiet BP-lowering effect. However, several meta-analyses of these RCTs have been conducted through the past years aiming to determine the effect of the MedDiet on BP, which are presented in Table 3 (Ref. [12,80,81,98–101]).

The main differential component that distinguishes the above meta-analyses of RCTs is the comparator diet against which the BP effect of the MedDiet is reported. In two meta-analyses, the MedDiet was compared to the low-fat diet [98,99]. Nordmann *et al*. [98] found that the MedDiet produced more favorable changes in both SBP and DBP [–1.7 (95% CI: –3.3 to –0.1) and –1.5 (95% CI: –2.1 to –0.8) mmHg, respectively] [98], while Nissensohn *et al*. [99] found that compared to the low-fat diet the MedDiet reduced DBP [–0.7 (95% CI: –1.3 to –0.1) mmHg], but not SBP [–1.5 (95% CI: –2.9 to 0.0) mmHg] [99]. In two other meta-analyses, the MedDiet was compared to the usual or another diet (low-fat or prudent) using the results of a limited number of studies, and no separate analyses according to the type of the comparator were conducted [80,81]. Ndanuko *et al*. [80] found that the MedDiet reduced both SBP and DBP [–3.0 (95% CI: –3.5 to –2.6) and –1.9 (95% CI: –2.3 to –1.7) mmHg, respectively] [80], while Gay *et al*. [81] found that compared to the usual or another diet the MedDiet reduced DBP [–1.5 (95% CI: –2.1 to –0.8) mmHg], but not SBP [–1.2 (95% CI: –2.8 to 0.5) mmHg] [81].

Rees *et al*. [100] conducted two separate comparisons about the effect of the MedDiet intervention against no/minimal intervention or another dietary intervention on CVD risk factors and CVD mortality in people with or without CVD. In studies concerning the primary prevention of CVD, the MedDiet reduced both SBP and DBP when compared to no/minimal intervention [–2.9 (95% CI: –3.5 to –2.5) and –2.0 (95% CI: –2.3 to –1.7) mmHg, respectively], but when compared to another dietary intervention, the MedDiet resulted in no significant SBP or DBP reduction [–1.5 (95% CI: –3.9 to 0.9) and –0.2 (95% CI: –2.4 to 1.9) mmHg, respectively] [100]. A more recent meta-analysis conducted by Cowell *et al*. [101] included a larger number of RCTs. It showed that compared to the habitual or the low-fat or another diet, the MedDiet reduced SBP by –1.4 (95% CI: –2.4 to –0.4) mmHg and DBP by –1.5 (95% CI: –2.7 to –0.3) mmHg. At the same time, subgroup anal-

ysis revealed no influence of the type of the comparator diet on the BP effect of the MedDiet.

These meta-analyses provided mixed results regarding the effect of the MedDiet on BP reduction. Moreover, BP estimates were evaluated as the difference from baseline levels in each arm, introducing outcome-related bias. At variance with previous evidence, in the meta-analysis conducted recently by our group, we aimed to address the issues mentioned above and estimate the effect of the MedDiet compared to the usual diet or another dietary intervention on the attained BP reduction during follow-up [12]. The results showed that compared to all other diets (usual diet/other dietary intervention), the MedDiet reduced SBP by –1.5 (95% CI: –2.8 to –0.1) mmHg and DBP by –0.9 (95% CI: –1.5 to –0.3) mmHg. Compared only to the usual diet, the MedDiet reduced SBP and DBP [–3.1 (95% CI: –4.8 to –1.3) and –1.6 (95% CI: –2.6 to –0.6) mmHg, respectively], while compared to all other active intervention diets or only to the low-fat diet the MedDiet did not reduce SBP and DBP, meaning that it proved equally effective to reduce BP as the low-fat and all other dietary interventions taken together (e.g., prudent, hypolipidemic, low- or high-carbohydrate diet). We were unable to compare the BP effect of the MedDiet between hypertensive and non-hypertensive patients since the majority of studies were conducted in mixed populations. However, in a limited number of studies conducted in normotensive individuals, the BP effect of the MedDiet was not significant [12].

The influence of sodium intake on BP in the context of the MedDiet remains undetermined. The MedDiet was not "invented" for BP-lowering purposes, like the DASH diet, and the effects of its adoption on BP were examined along with the effects on the other CVD risk factors, such as overweight/obesity, raised blood glucose and, abnormal blood lipids, because of the evidence indicating its association with lower CVD mortality. Accordingly, the RCTs examining the BP effects of the MedDiet usually were performed without a parallel salt reduction strategy. Although MedDiet does not impose a certain level of sodium intake, it promotes the consumption of foods that are naturally low in sodium, like fruits and vegetables. Thus, individuals with higher adherence to the MedDiet have a lower salt intake. A reduction in sodium intake usually follows the adoption of the MedDiet in dietary interventions [102]. However, based on the results of the existing RCTs, it is not possible to determine whether salt reduction contributes towards the BP-lowering effects of the MedDiet. Unlike some trials that examined the DASH diet in combination with sodium restriction, there is a lack of a similar effort in MedDiet trials since they do not give sufficient data regarding the change in sodium intake. Nevertheless, it may be hypothesized that the MedDiet exerts beneficial effects towards hypertension risk because of its overall better micro-, macro-nutrient, and mineral content, which seems to decrease the level of oxidation and inflammation and reduce the exposure to harmful components of the diet, including salt [103].

6. Conclusions

Hypertension increases the risk for adverse cardiovascular and renal outcomes. However, it should be pointed out that premature morbidity and mortality begin to increase among persons whose SBP/DBP is above 115/75 mmHg. Therefore, although BP-lowering by drugs should be reserved for patients with hypertension or high cardiovascular risk and high normal BP, non-pharmacological measures, including appropriate dietary and lifestyle changes, should be implemented to all individuals irrespectively of BP levels. In overweight and obese hypertensive patients, a core recommendation is weight reduction through reduced energy intake and increased physical activity to reduce fat storage and ectopic lipid deposition in key target organs of BP control. Such measures, in general, may increase the net clinical benefit, contribute to BP control with fewer antihypertensive drugs, and exert properties independent of BP reduction, decreasing CVD risk more than expected.

Regarding the dietary strategies, they reduce sodium intake and promote a healthful dietary pattern, such as the DASH diet or the MedDiet, which influence various physiological mechanisms controlling BP and have beneficial effects on BP levels and overall cardiovascular health. Salt intake levels should be reduced progressively to accomplish a modest, long-term salt reduction, rather than an extreme and sudden fall in dietary consumption of salt. In the context of the DASH diet, salt restriction produces a less pronounced reduction in BP, which could be because of the overlapping mechanisms of action, resulting in a reduced capacity to lower BP with salt reduction further, when accounting for the effects of the DASH diet. Evidence about the contribution of salt reduction in the context of the MedDiet is yet insufficient.

Abbreviations

BP, blood pressure; CVD, cardiovascular disease; CDK, chronic kidney disease; DASH, dietary approaches to stop hypertension; DBP, diastolic blood pressure; MedDiet, Mediterranean diet; RCT, randomized controlled trial; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure; SNS, sympathetic nervous system.

Author contributions

CF, FT, and DP designed the paper; CF, FT and CT performed the literature search; CF, FT and CT wrote the paper; DP, EM, PN, DT, and KT assisted in the revision of the manuscript; CF, FT, DP, EM, CT, PN, DT, and KT had primary responsibility for final content.

Ethics approval and consent to participate

Not applicable.

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Conflict of interest

The authors declare no conflict of interest.

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