REVIEW ARTICLE

Dietary interventions in blood pressure lowering: current evidence in 2020

Larysa Strilchuk[1], Raffaele I. Cincione[2], Federica Fogacci[3], Arrigo F. G. Cicero[3]

1 1st Department of Therapy, Medical Diagnostics and Hematology and Transfusiology, Lviv National Medical University, Lviv, Ukraine
2 Department of Clinical and Experimental Medicine, University of Foggia, Foggia, Italy
3 Hypertension and Cardiovascular Risk Research Group, Department of Medical and Surgical Sciences, University of Bologna, Bologna, Italy

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ABSTRACT
Dietary modification is one of the cornerstones in the treatment of arterial hypertension (AH). Current American and European guidelines recommend people to ingest fruit, vegetables, whole grains, and low-fat dairy products as well as to decrease the consumption of red meat, sugar, and trans fats. This review aimed to summarize available evidence on dietary patterns associated with lower blood pressure (BP). Research has shown that the Dietary Approach to Stop Hypertension (DASH) diet can lower BP equally effectively or even more significantly than some antihypertensive drugs. The Mediterranean diet also leads to a considerable reduction in BP. Vegans and vegetarians have been shown to have a lower prevalence of AH than omnivores. Caloric restriction may decrease BP in normotensive, prehypertensive, and hypertensive populations. Blood pressure can also be lowered by certain nutraceuticals (such as beetroot juice, magnesium, vitamin C, catechin-rich beverages, or soy isoflavones). Diet effects on BP are mediated by body weight loss, amelioration of inflammation, increased insulin sensitivity, and antihypertensive properties of some individual nutrients. There is robust evidence that vegetarian and vegan diets have the ability to reduce BP. The presence of the so-called floor effect makes these diets usable in normo- and prehypertensive people at high risk of developing AH. However, the dietary and nutraceutical approach to BP lowering cannot substitute drug treatment when the latter is needed.

Correspondence to:
Arrigo F. G. Cicero, MD, PhD, Atherosclerosis and Hypertension Research Group, Department of Medical and Surgical Sciences, Sant'Orsola-Malpighi University Hospital, U.O. Medicina Interna Borghi, Via Albertoni 15, 40 138 Bologna, Italy, phone: +39 512142224, email: arrigo.cicero@unibo.it
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Introduction Lifestyle modification is a cornerstone of antihypertensive treatment. The diet represents a significant, modifiable environmental factor, which can influence people's health and the course of diseases.[1]

The modern era of a diet as a therapeutic measure started in the late 1930s when Walter Kempner suggested using the rice-based diet as a kind of treatment in the patient with renal failure and congestive heart failure. He showed that this intervention led to a decrease of the heart size evaluated on chest X-ray, normalization of electrocardiography results, and improved retinal condition. Kempner obtained similar results in the cohort of hypertensive patients: the diet based on rice and fruit helped them decrease blood pressure (BP), total cholesterol levels, and heart size. Sadly, these findings did not receive enough attention from the scientific community.[2]

Nowadays, a nutrition style is considered as a valuable tool of medicine, including cardiology. According to a recent, large meta-analysis[3] (17 230 patients), BP is lowered most effectively by the DASH (Dietary Approach to Stop Hypertension) diet, the paleolithic diet, and the low-carbohydrate diet (the third most potent diet for systolic BP [SBP] lowering) or the Mediterranean diet (the third most potent diet for diastolic BP [DBP] lowering). Another meta-analysis[4] published in 2020 revealed the most consistent evidence for the BP-lowering effect of the Mediterranean diet.

How current guidelines address the diet

Guidelines for the prevention, detection, evaluation, and management of high BP in adults, issued by the American College of Cardiology / American Heart Association in 2017, recommend a heart-healthy diet like the DASH diet,[5] previously named a "combination diet."[6] The DASH dietary pattern is rich in fruit, vegetables, whole grains, and low-fat dairy products, whereas its recommended content of saturated and total fats is quite low. The DASH diet can help lower SBP by 11 mm Hg, and DBP by 3 mm Hg.[7,8]

As indicated by the guidelines for the management of arterial hypertension (AH), conceived by the European Society of Cardiology / European Society of Hypertension in 2018, hypertensive patients need to adopt a healthy, balanced diet based on vegetables, fruit, legumes, low-fat dairy products, whole grains, fish, and olive oil.[9] There is also a need to decrease the consumption of red meat and products containing saturated fatty acids.[10-12] In general, such a pattern fits the characteristics of the Mediterranean diet, which may reduce the number of cardiovascular events and all-cause mortality.[10-13] The Mediterranean diet also decreases ambulatory BP and blood glucose levels and results in favorable alterations in lipid levels.[14] Regarding beverages, the abovementioned guidelines reported on some cardiovascular benefits of coffee and tea,[15-17] whereas it was suggested that the consumption of sugar-sweetened soft drinks should be markedly limited.[18]

On May 6, 2020, the International Society of Hypertension issued *Global Hypertension Practice Guidelines*,[19] which recommend people to eat whole grains, fruit, vegetables, polyunsaturated fats, and dairy products and to limit foods high in sugar, saturated fats, and trans fats at the same time (similarly to the DASH diet). These guidelines highlighted that BP can be lowered by vegetable sources of nitrates like beetroot and leafy vegetables. Foods rich in calcium, magnesium, and potassium (avocados, nuts, seeds, legumes, and tofu) can also offer some antihypertensive benefits.[19] General nutritional recommendations of the main guidelines on AH are summarized in TABLE 1.

Dietary patterns associated with lower blood pressure

The Dietary Approach to Stop Hypertension The main characteristics of the DASH diet include large amounts of fruit, juices, vegetables, nuts, seeds, and legumes; preference of skimmed milk over full-fat dairy products; a smaller amount of meat (beef, pork, and poultry) together with a higher intake of fish as compared with the usual American diet. The DASH plan also postulates a marked decrease in intake of fats, oils, salad dressings, and sweets.[8]

A comparison of the DASH diet and the typical American diet showed that the former resulted in lower SBP at every sodium level analyzed (low, intermediate, and high) and lowered DBP at intermediate and high sodium levels. The numerical difference in mean systolic BP, observed between the typical American diet with a high sodium intake and the DASH diet with a low sodium intake, was a mean value of 7.1 mm Hg in normotensive participants, and 11.5 mm Hg in hypertensive subjects.[6] Thus, in the latter group, the effect was equal to or even more significant than the effect of an antihypertensive drug.[20-21]

Moreover, the DASH Collaborative Research Group showed that transition from the typical American diet to the DASH diet reduced SBP by 5.5 mm Hg and DBP by 3 mm Hg in 8 weeks, which was a larger decrease than that observed for the control diet. In the subpopulation with baseline AH, the combination diet had an even more prominent effect than the control diet: SBP decreased by 11.4 mm Hg and DBP by 5.5 mm Hg.[8]

The Mediterranean diet The Mediterranean diet is based on the typical dietary pattern observed in people living in Greece and southern Italy. It includes a variety of fruit, vegetables, legumes, cereals, dairy products (cheese, yogurt), olive oil, and low-to-moderate amounts of wine, whereas meat consumption is somewhat limited and represented mostly by poultry.[22,23] The PREDIMED trial (Prevención con Dieta Mediterránea; including 7447 patients at high cardiovascular risk) compared the Mediterranean diet, supplemented with extra-virgin olive oil or mixed nuts, with the control low-fat diet.[13] Both diets led to a significant reduction in ambulatory BP at 1 year. Compared with the control diet, SBP was lowered by 2.3 mm Hg (95% CI, –4.0 to –0.5) and 2.6 mm Hg (95% CI, –4.3 to –0.9) in the groups supplemented with olive oil and nuts, respectively, and DBP was lowered by 1.2 mm Hg (95% CI, –2.2 to –0.2) in the olive-oil group and increased by 0.7 mm Hg (95% CI, –0.4 to 1.7) in the group receiving nuts. Patients were not subjected to any caloric restriction, sodium intake reduction, or increased physical activity.[14] The Mediterranean diet supplemented with nuts was shown to decrease endothelin-1 levels and downregulate endothelin receptors A and B, which mediates its vasopressor effect.[24] Psaltopoulou et al[25] proved that following the Mediterranean diet was inversely related to BP levels in 20 343 Greek volunteers, aged 20 to 86 years, in a general population study. The authors also found an inverse relationship between olive oil consumption and BP, whereas cereal intake was positively related to BP.

Vegetarian and vegan diets The CARDIA study (Coronary Artery Risk Development in Young Adults; including 4304 individuals) demonstrated that the intake of whole and refined grains, fruit, vegetables, nuts, and legumes were inversely related to AH independently of age, sex, race, energy intake, and risk factors for cardiovascular disease. On the contrary, risk of AH was

TABLE 1 Nutritional recommendations of the main guidelines on arterial hypertension

Source of guidelines	Recommendations
American College of Cardiology / American Heart Association (2017)	A heart-healthy diet, such as the Dietary Approach to Stop Hypertension (DASH) diet, which facilitates achieving the desirable weight
European Society of Cardiology / European Society of Hypertension (2018)	A healthy, balanced diet containing vegetables, legumes, fresh fruit, low-fat dairy products, whole grains, fish, and unsaturated fatty acids (especially olive oil); low consumption of red meat and saturated fatty acids
International Society of Hypertension (2020)	A diet rich in whole grains, fruit, vegetables, polyunsaturated fats, and dairy products; low consumption of foods high in sugar, saturated fats, and trans fats

positively associated with red and processed meat intake.[26] However, low-fat, rich in fruit and / or vegetables (≥6 servings) and grain (≥6 servings) dietary intervention of the Women's Health Initiative Dietary Modification trial (including 48 835 postmenopausal women) showed no association with sustained reduction in the BP level.[27]

A cross-sectional analysis of the European Prospective Investigation into Cancer and Nutrition-Oxford study (EPIC-Oxford; 11 004 participants) revealed that vegans had a lower prevalence of AH than meat eaters, fish eaters, and vegetarians. The age-adjusted prevalence of self-reported AH varied from 5.8% and 7.7% in vegans to 15% and 12.1% in meat eaters (in men and women, respectively). However, the differences were nonsignificant after adjustment for age and body mass index (BMI).[28]

The NutriNet-Santé study showed a negative relationship between fruit and vegetable intake and SBP in both sexes.[29] The INTERMAP study (International Study on Macro / Micronutrients and BP) demonstrated a significant inverse relation of vegetable protein intake and BP.[30] The INTERMAP subanalysis for the United States (2195 individuals) showed a significant, linear, inverse relationship between raw vegetable intake and BP. The authors analyzed the most frequently eaten raw vegetables and found out that intake of each of the following vegetables: tomatoes, carrots, and scallions, had a significant inverse relationship with either SBP or DBP. An inverse relationship between intake of cooked vegetables and BP was also confirmed. The analysis for each vegetable showed that intake of cooked celery, peas, scallions, and tomatoes was inversely related to either SBP or DBP. The relation between intake of raw vegetables and BP was stronger than between intake of cooked vegetables and BP.[31]

A large meta-analysis (118 518 individuals; 2 936 359 person-years of follow-up) showed a positive association between meat (including poultry and processed meat) and seafood consumption and the risk of AH. This effect was independent of fruit, vegetable, and whole grain intake.[32] The issue of seafood consumption is rather controversial, because other studies showed its positive influence on BP.[33,34]

A comparison of BP among raw food vegans leading a sedentary lifestyle, endurance athletes following the Western diet, and sedentary individuals on the Western diet showed that BP was significantly lower in the vegan group (mean [SD], 104 [15] / 62 [11] mm Hg compared with 122 [13] / 72 [9] mm Hg in BMI-matched runners and 132 [14] / 79 [8] mm Hg in sedentary subjects). Interestingly, a mean (SD) BMI of endurance athletes was slightly lower than that of vegans (21.1 [1.6] kg/m^2 vs 21.3 [3.1] kg/m^2), which underlines the fact that the antihypertensive effect of the vegan diet is mediated not only by weight.[35]

In a cross-sectional study by Liu et al,[36] the vegan group had a significantly lower mean SBP and DBP (by 3.87 mm Hg and 2.48 mm Hg, respectively) than the omnivore group. Such regularity was also found in patients with proteinuria: vegans had lower SBP (–2.73 mm Hg) and DBP (–2.54 mm Hg) than nonvegans. Of note, the vegan and lacto-ovo-vegetarian subgroups were characterized by a healthier lifestyle than the omnivore subgroup (namely, a lower prevalence of smoking, alcohol consumption, and betel nut chewing as well as a higher rate of regular physical activity). The lacto-ovo-vegetarian subgroup had significantly lower mean DBP compared with the omnivore group.[36]

The Adventist Health Study 2[37] showed that people consuming meat, fish, and dairy products less than once a month had a lower prevalence of AH than omnivores (odds ratio [OR], 0.37; 95% CI, 0.19–0.74). Lacto-ovo–vegetarians also had a lower risk of AH (OR, 0.57; 95% CI, 0.36–0.92). After adjustment for BMI, these ORs lost their statistical significance. The authors suggested that the antihypertensive effect of the vegetarian diet was mostly mediated by weight loss.[37]

A meta-analysis of 7 controlled trials (including 311 individuals) revealed that the vegetarian diet was related to a significant decrease of mean SBP by 4.8 mm Hg (95% CI, –6.6 to –3.1) and DBP by 2.2 mm Hg (95% CI, –3.5 to –1) compared with the omnivorous diets. The results of a meta-analysis of 32 observational studies (21 604 individuals) were even more optimistic: mean SBP in vegetarians was lower by 6.9 mm Hg (95% CI,

–9.1 to –4.7) and mean DBP by 4.7 mm Hg (95% CI, –6.3 to –3.1) than in omnivores.[38]

A meta-analysis by Lopez et al[39] (including 983 subjects) did not show any difference in BP between vegans and controls in total, but a subgroup analysis of patients with baseline SBP higher than or equal to 130 mm Hg demonstrated that the vegan diet led to a significant decrease in SBP (–4.1 mm Hg; 95% CI, –8.14 to –0.06) and DBP (–4.01 mm Hg; 95% CI, –5.97 to –2.05).[39]

In a prospective study (4109 individuals), vegetarians had a 34% lower risk of AH (OR, 0.66; 95% CI, 0.5–0.87) than omnivores after adjustment for age and sex. After further adjustment for C-reactive protein levels, waist circumference, and fasting glucose levels, the risk remained lower (OR, 0.72; 95% CI, 0.55–0.86).[40]

Therefore, in general, it is likely that plant-based diets can help prevent and treat AH. A vegetarian / vegan style of nutrition probably reduces BP owing to the favorable effects of high fiber content,[41] a special amino acid ratio (prevalence of glutamic acid),[42] abundance of vitamins (A, C, and E),[43] antioxidants (lutein and β-cryptoxanthin),[41] polyunsaturated fatty acids,[44-46] and minerals (phosphorus, calcium, magnesium,[47,48] and potassium in particular, which was shown to lower BP[49,50]). Apart from that, transition from animal- to plant-based food can alter the gut microbiota,[51] decreasing production of its toxic metabolites (p-cresol sulfate, indoxyl sulfate, and trimethylamine N-oxide).[52-54]

It still remains to be elucidated which subtype of the vegetarian diet (vegan, lacto-vegetarian, lacto-ovo–vegetarian, or pesco-vegetarian) is the best choice. There is also an issue of vitamin deficiency: for instance, vitamin B_{12} deficit, which is common in vegans, may decrease the cardiovascular benefit of the vegetarian diet.[55]

Energy restriction The prevalence of obesity in the world nearly tripled between 1975 and 2018.[56] Increased body weight and obesity are independent risk factors for AH.[57] Caloric restriction was shown to lower SBP and DBP compared with a standard diet in normotensive, prehypertensive, and hypertensive populations.[58-66] Nevertheless, the MONET study (Montreal Ottawa New Emerging Team) did not find any BP changes after 6 months of caloric restriction.[67]

Cross-sectional studies comparing nonfasters with people practicing caloric restriction showed a significantly lower BP in the latter group.[68-70] In general, total energy intake in fasters was about one-third lower than that of people following the Western diet.[68]

Medically supervised water-only fasting (2 to 3 days on fruit and vegetables, 10 to 11 days of fasting, 6 to 7 days of refeeding on the vegan diet) resulted in normotension in almost 90% of in hypertensive patients. The mean reduction in BP was 37 / 13 mm Hg and the greatest reduction was 60 / 17 mm Hg (in patients with AH stage 3). Participants who were taking antihypertensive drugs at baseline (6.3%) discontinued their use.[71]

De Toledo et al[72] described a program of fasting (3 l of noncaloric beverages, 250 ml of freshly squeezed fruit or vegetable juice, 250 ml of vegetable soup; total caloric intake, 200–250 kcal), which was prescribed for 5, 10, 15, or 20 days together with mild exercise. Mean SBP in the entire cohort (1422 individuals) decreased from 131.6 (0.7) mm Hg to 120.7 (0.4) mm Hg and mean DBP, from 83.7 (0.4) mm Hg to 77.9 (0.3) mm Hg. The effect depended on program duration and did not show any sex differences. The authors did not notice any hypotensive complications.[72]

In general, caloric restriction can lower both SBP and DBP regardless of sex, ethnicity, BMI, presence of metabolic syndrome, or diabetes. The BP-lowering effect may persist beyond the end of the fasting period. The greatest decrease occurs in patients with the highest baseline BP level. Importantly, it means that such diet is not likely to provoke hypotension (the so-called floor effect).[73]

There are many unanswered questions in the field of caloric restriction and BP: the preference between routine everyday caloric restriction and intermittent or periodic fasting; the optimal ratio of protein, carbohydrates, and fats in the diet; or the best duration of the restriction period. Finally, the long-term effect of these diets on hypertension and the related cardiovascular risk remains to be elucidated.

Other dietary patterns The paleolithic diet (the dietary pattern of preagricultural hunter-gatherers, including lean meat, fruit, vegetables, and nuts) led to a significant SBP reduction by 3.1 (2.9) mm Hg.[74]

A meta-analysis by Ge et al[75] (21 942 subjects) showed that the Atkins diet reduced SBP by 5.1 mm Hg and DBP by 3.3 mm Hg compared with the usual nutrition style. The DASH diet showed a weaker result: a decrease by 4.7 mm Hg and 2.9 mm Hg for SBP and DBP, respectively.[75]

A summary of BP-lowering effects of selected, most commonly studied diets is presented in TABLE 2.

Impact of single nutrients on blood pressure

Salt Excessive sodium consumption (>5 g of sodium daily) is associated with a rise in SBP with age,[76] whereas sodium restriction has a BP-lowering effect.[77-79] A meta-analysis showed that a reduction of approximately 1.75 g of sodium intake per day (4.4 g of salt daily) was associated with a mean reduction of SBP by 4.2 mm Hg and DBP by 2.1 mm Hg. In people with AH, the effect was even more significant

TABLE 2 Quantitative blood pressure–lowering effects of selected dietary patterns

Diet	BP-lowering effect
Dietary Approach to Stop Hypertension (DASH)	–11 mm Hg in SBP and –3 mm Hg in DBP compared with the control group[7,8] –5.5 mm Hg in SBP and –3 mm Hg in DBP in normotensive patients; –11.4 mm Hg in SBP and –5.5 mm Hg n DBP in the hypertensive population compared with controls[8]
Mediterranean	–2.5 mm Hg in SBP and –1.3 mm Hg in DBP compared with the control diet[13]
Vegetarian	–4.8 mm in SBP and –2.2 mm Hg in DBP compared with the omnivorous diets[38] –4.1 mm Hg in SBP and–4.01 mm Hg in DBP in patients with baseline SBP ≥130 mm Hg[39]
Severe energy restriction	A mean reduction of 37 / 13 mm Hg in BP; the greatest reduction of 60 / 17 mm Hg (in patients with arterial hypertension stage 3)[71] –9.9 mm Hg in SBP and –5.8 mm Hg in DBP[72]
Paleolithic	–3.1 mm Hg in SBP compared with the control group[74]
Atkins	–5.1 mm Hg in SBP and –3.3 mm Hg in DBP[75]

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure

(–5.4 mm Hg / –2.8 mm Hg).[80] It has been noted that the antihypertensive effect of sodium restriction is more pronounced in people of African descent, in older patients, and those with diabetes, metabolic syndrome, or chronic kidney disease.[81] Limiting salt intake is simple, but it may influence BP so potently that it leads to a reduction in the number or dose of necessary BP-lowering drugs.[82,83]

The European Society of Cardiology / European Society of Hypertension guidelines on the treatment of AH[9] recommend limiting sodium intake to approximately 2 g per day (approximately 5 g of salt daily) in the general population, including all hypertensive patients. These guidelines also reported that salt hidden in processed foods accounts for as much as 80% of the overall salt consumption, so the adherence to a salt-restricting regimen may be difficult.[9]

In the NutriNet-Santé study (8670 participants), salt intake was not associated with SBP in either sex, although it was higher in hypertensive individuals compared with those normotensive. Nevertheless, SBP significantly increased in parallel with the dietary sodium-to-potassium ratio, so this ratio may be more relevant than sodium intake itself.[29]

Regarding successful implementation and adherence, it is better to introduce changes in the overall dietary pattern.[77] The United States Department of Health and Human Services defines dietary patterns as "the quantities, proportions, variety, or combinations of different foods and beverages in diets, and the frequency with which they are habitually consumed."[78] The effects of individual nutrients are challenging to analyze, because people do not consume single foods or their components only.[84] However, there is some evidence on antihypertensive effects of certain nutrients.

Nuts (walnuts, almonds, and hazelnuts) A substudy of the Walnuts and Healthy Aging study (305 patients at low cardiovascular risk) was dedicated to the effects of walnut intake (30–60 g/d) on BP in the elderly visited outside hospitals and other care places. At 2-year follow-up, the decrease of mean office SBP was –4.6 mm Hg (95% CI, –7.4 to –1.8 mm Hg) in the walnut group vs –0.6 mm Hg (95% CI, –3.4 to 2.2 mm Hg) in the control group (the difference did not reach the significance level; $P = 0.051$). No changes in DBP were observed. The effect of nut supplementation was most prominent in patients of the upper tertile of baseline 24-hour ambulatory SBP: they showed a significant SBP decrease of 8.5 mm Hg (95% CI, –12 to –5 mm Hg). The walnut group was characterized by a less common need for antihypertensive drugs uptitration than the control group.[85] The authors explained this favorable effect by the chemical composition of walnuts (unsaturated fatty acids, α-linolenic acid in particular, fiber, arginine, tocopherols, folate, potassium, magnesium, calcium, selenium, phytosterols, and polyphenols)[85-87] and their ability to improve endothelial function.[88]

Olive oil Olive oil, extra virgin olive oil in particular, is a well-known component of heart-healthy diets. In an in-depth meta-analysis (6651 individuals), Zamora-Zamora et al[89] concluded that intake of extra virgin olive oil (10–50 ml/d for at least 3 months) can reduce DBP (by –1.44 mm Hg; 95% CI, –1.89 to –1). The difference in SBP did not reach statistical significance. Interestingly, olive oil in capsules did not have such a favorable influence on BP.[89] Other studies showed much more impressive results. For instance, Venturini et al[90] demonstrated that intake of extra virgin olive oil led to an SBP decrease of 5 mm Hg and a DBP decrease of 14 mm Hg in patients with metabolic syndrome.[90]

The following mechanisms can mediate the antihypertensive effect of olive oil: the ability of its polyphenols to increase the bioavailability of NO[91]; reduction of oxidative stress and inflammation (oxidized low-density lipoproteins can activate the renin–angiotensin system)[92]; counteracting the endothelial dysfunction[93,94]; and inhibition of angiotensin-converting enzymes and blockade of angiotensin II receptor binding.[95]

Kiwi fruits There are also reports on beneficial antihypertensive effects of kiwi fruits (intake of 3 of them daily was associated with lower SBP and DBP [–3.6 mm Hg and –1.9 mm Hg, respectively] compared with 1 apple a day).[96]

Nutraceuticals Based on the results of some meta-analyses of randomized clinical trials,[97] the European Hypertension Society has recently published a statement on the possible use of some nutraceuticals to support the reduction of BP in low-risk individuals with normal-to-high BP levels. It included beetroot juice, magnesium, vitamin C, and catechin-rich beverages. Soy isoflavones could be suggested in perimenopausal women, resveratrol in insulin-resistant patients, and melatonin in those with nocturnal hypertension. Caution with regard to potassium intake is needed in patients with advanced chronic kidney failure and those receiving potassium-sparing diuretics / antialdosterone agents. The effectiveness of pomegranate juice, hibiscus tea, and sesame has been demonstrated in the Middle Eastern population only.[98,99]

Conclusions An overall healthy diet, aimed at body weight optimization, should be suggested in all subjects at risk of developing AH or in those already hypertensive, regardless of the background antihypertensive treatment.

Take-home messages This review can be summarized with a couple of take-home messages:

- Diet modification seems to be a valuable tool for BP normalization. Its effects are mediated by body weight loss, amelioration of inflammation, increase of insulin sensitivity, and antihypertensive effects of some individual nutrients.
- The most critical obstacles on the way of following dietary recommendations in hypertensive patients include: social and environmental barriers, adherence to the recommended diet, nutritional preferences of family members, palatability of the recommended diet, emotional and psychological factors, and costs.[100]
- There has been robust evidence that vegetarian and vegan diets have the ability to reduce BP. The existence of the so-called floor effect—the lower BP, the lesser decrease—makes these diets usable for normo- and prehypertensive individuals at high risk of developing AH.
- Importantly, the dietary and nutraceutical approach to BP lowering can never substitute drug treatment when the latter is needed.

ARTICLE INFORMATION

CONFLICT OF INTEREST None declared.

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