

Integrative Approaches to Hypertension

Hypertension (HTN) is the most prevalent vascular disease in the world; an estimated 1 billion adults have it.¹ Cardiovascular disease (CVD) risk increases exponentially as blood pressure (BP) increases², so it is important to consider BP management as a part of overall heart health. There are many different ways to address blood pressure within Integrative Health framework. Recognizing that detailed guidelines for medical management are widely available, this tool will briefly summarize the latest professional care guidelines for HTN management and then focus in greater detail on research findings related to self-care options and complementary and integrative health (CIH) approaches. There are many options to manage BP that can be woven into Personal Health Plans (PHPs).

Blood Pressure Guidelines

The American College of Cardiology (ACC) and American Heart Association (AHA) Guidelines for 2019, which focus on prevention of heart disease in general, emphasize the following, which are consistent in many ways with an Integrative Health approach³:

- The "most important way" to prevent CVD and other heart problems is through "...a healthy lifestyle throughout life."
- Team-based care is an effective strategy for prevention. The guidelines suggest that "Clinicians should evaluate the social determinants of health that affect individuals to inform treatment decisions." This ties in closely with "Me" at the center of the Circle of Health tailoring care to each individual based on their context. It also links to the "Community" circle, which is inclusive of social determinants and their influence on health and disease.
- Adults from 40-75 being evaluated for CVD prevention should have their 10-year risk calculated and be assessed for other risk-enhancing factors to determine whether medications should be started.
- All adults should consume a healthy diet (as described in the Food and Drink section, below). A healthy weight is key to preventing heart disease.
- As outlined in the Moving the Body section below, it is good to engage in 150 minutes weekly of moderate-intensity or 75 minutes weekly of vigorous-intensity activity.
- Treat people with type 2 diabetes with lifestyle changes, and start with metformin (or other diabetes medications when needed) if medications are indicated. Always check on tobacco use; do not typically use aspirin. Treat lipid problems with statins.
- Nonpharmacological interventions are recommended for all adults with elevated BP or HTN (in addition to medications, as appropriate).

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Within that framework, then, there are ACC/AHA Guidelines specific to HTN. These focus more on specific BP parameters and, to a large degree, medication guidelines. Highlights include the following⁴:

- Accurate BP measurement is critical. Use an average of measurements from at least two different occasions. Home monitoring is associated with lower BP criteria to guide treatment. Normal BP is defined as <120/<180 mmHg. Categories go up from there; stage 2 HTN is 2140 systolic blood pressure (SBP) or <a href="https://example.com/specifical-com/specifical
- Risk increases in a log-linear fashion. For every 20 mm Hg in SBP from 115 to 180 mm Hg, or for every 10 mm Hg increase in DBP from 75 to 115 mmHg, risk of death from stroke, heart disease, or vascular disease doubles. For 45-year olds without HTN, 40-year risk for eventually developing it is "...93% for African Americans, 92% for Hispanics, 86% for Whites, and 84% for Chinese adults..."
- Think of HTN in the framework of other CVD risk factors, including smoking, diabetes, dyslipidemia, excess weight, poor fitness levels, poor diet, stress, and sleep apnea. Various laboratory tests and other studies may be helpful. (That is, consider the entire person and how BP fits in to the bigger picture.)
- Criteria are given in the guidelines for how to screen for secondary causes, based on the presence of drug resistance, rapid onset, target organ damage, etc.
- Nonpharmacologic interventions are mentioned, including physical activity, limiting alcohol, weight loss, sodium restriction, potassium supplementation.
- Parameters are provided to determine at what level of CVD risk a person should be treated with medications. For example, it is recommended that adults with stage 2 HTN should be evaluated within a month, treated with non-drug therapy and 2 BP medications from different classes, and followed up a month later.
- Many other guidelines are available, based on individual circumstances (race, comorbidities, and others). More details can be found in the <u>ACC/AHA online resources</u>.

Me At The Center

In addition to coronary artery disease, HTN is also associated with higher risks of other heart and vascular diseases, including of heart failure, atrial fibrillation, aortic valve disease, sick sinus syndrome, and abdominal aortic aneurysms.⁵ HTN is associated with non-cardiac comorbidities as well. A 2017 review of 29 articles concluded that hypertension has a significant association with breast cancer, especially for postmenopausal women.⁶ There is also an association, in epidemiologic studies, with renal cancer (2-4 times the risk), colorectal cancer, malignant melanoma, and prostate cancer.⁷ People with depression have an increased risk for HTN (odds ratio 1.3 for men and 1.04 for women), as do people with anxiety (odds ratio 1.3 for men and 1.05 for women).⁸ A diagnosis of PTSD, and the chronicity of PTSD, are closely linked to increased risk of HTN as well.⁹

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While self-monitoring can be an important way to mobilize individual efforts to manage BP, large studies have concluded that it does not improve BP or control unless it is accompanied by cointerventions with medical team members, like pharmacists, providers, or people who can provide education and/or lifestyle counseling.¹⁰

One significant challenge with care of people with HTN is adherence to medications. A review and meta-analysis including over 12,600 people found that 45% of people with HTN alone and 31% of people who had HTN and other health concerns were not taking their medications. Two-thirds of the nonadherence was noted in people of African or Asian descent.

An individual's genetic profile can also have an influence on BP. For example, certain mutations affecting chloride reabsorption by the kidneys can cause a person to have relatively lower BPs. Polymorphisms related to angiotensin-converting enzyme (ACE) can also have an effect, particularly around how weight change affects BP.¹² Race and ethnicity also have an influence. For example, studies indicate that African Americans have more of a BP reduction than Whites when they reduce sodium, increase potassium, or follow a DASH diet.¹³

The next sections review various self-care and therapeutic approaches that can benefit BP. Note the average effects they can have on numbers; most of them lower SBP and DBO by somewhere between 2 and 6 mmHg. Think about how you can provide patients with an array of options, so that they can find the best combination of approaches that works for them. In addition to an appropriate exploration around medications, which should be kept as a high priority, what other options would you feel comfortable discussing with people?

Lifestyle

Changes in lifestyle habits can be effective for lowering BP, particularly in those who are younger and have moderately elevated readings of greater than 140/90.¹⁴ Of course, one of the best things about working with lifestyle changes is that they have multiple benefits; they do not only improve BP readings. Exercising, eating a diet rich in fruits and vegetables, and maintaining appropriate weight also significantly reduce the risk of cancer, diabetes, and stroke

The ACC/AHA guidelines point out that each lifestyle change a person makes can decrease SBP by 4-5 mmHg and DBP by 2-4 mmHg; they also note that a diet low in sodium, and saturated/total fats and high in vegetables, fruits, and grains may decrease SBP by 11 mmHg.¹⁵ The U.S. Preventive Services Task Force has noted that there are small but significant improvements in BP (drops of 1 mmHg or so) associated with people choosing healthy a healthier lifestyle, even without their receiving formal counseling based on risk.¹⁶ That said, more intensive counseling is associated with greater improvements.

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TABLE 1. REVIEW OF LIFESTYLE INFLUENCES ON BLOOD PRESSURE^{2,17-20}

Element	Blood Pressure Re- duction (mmHg)	Notes
Weight loss if Overweight	SBP: 4.4 DBP: 3.6	Data is for people with an average weight loss of 5 kg (11 lb). More weight loss means more improvements. For more information: https://www.nhlbi.nih.gov/health/educational/lose wt/recommen.htm
Physical Activity	SBP: 2.5 DBP: 2.3	This is after 30-40 minutes daily, most days of the week, over 12 weeks or more. Many studies find even greater reductions.
DASH diet	SBP: 5.5 DBP: 3	Blood pressure effects were seen in many studies within just two weeks on the DASH diet. http://www.nhlbi.nih.gov/health/health-topics/top-ics/dash/
Sodium (Na) Restriction	Unitake by 2.3 grams/day led to SBP drop of 3.8. Unit by 4.5 grams/day led to SBP drop of 23 and DBP drop of 9.	Limit salt to less than 2,400 mg/day (1tsp). The body only needs 500 mg (1/4 tsp) daily. For more information on lowering salt in the diet, go to: http://www.nhlbi.nih.gov/files/docs/resources/heart/hbp-salt.pdf
Alcohol Re- striction	SBP: 3.3 DBP: 2.0 Dose dependent	Numbers are based on dropping consumption by an average of 76%. Limit to no more than 2 drinks/day for men and 1 drink/day for women.
Tobacco Cessation	Highly variable	Avoid first and secondhand smoke and all tobacco products.
Vegetarian Diets	SBP: 6.9 DBP: 4.7	Based on 2014 meta-analysis

SBP=Systolic Blood Pressure; DBP=Diastolic Blood Pressure; gm=grams; kg=kilograms. All units are millimeters mercury (mmHg), DASH – Dietary Approaches to Stop Hypertension

Nutrition

A 2018 meta-analysis of prospective studies summarized the research related to 12 different food groups/categories and their effects on relative risk (RR) of someone developing HTN. While noting that higher-quality evidence is needed²¹, they concluded that HTN risk decreased when people ate the following:

- Whole grains, 30 gm/day (RR=0.92)
- Fruits, 100 gm/day (RR=0.97)

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- Nuts, 28 gm/day (RR=0.7)
- Dairy, 200 gm/day (RR=0.95).

There were also foods that increased relative risk of developing HTN:

- Red meat, 100 gm/day (RR=1.14)
- Processed meat, 50 gm/day (RR=1.12)
- Sugar-sweetened beverages, 250 ml/day (RR=1.07)

Of note, BP reduction through changes in diet seem to be even more significant in the elderly.

Vegetarian Diets

Fruits and vegetables are high in electrolytes, polyphenols, and other compounds that can favorably affect BP. Findings from a several meta-analyses point to lower BP levels associated with following a vegetarian diet^{17,18}, as noted in Table 1, above.

Dietary Approaches to Stop Hypertension (DASH)

A 2016 review and meta-analysis focused on the relative effects of a variety of dietary patterns on BP. Diets like the DASH diet, Nordic diet, and Mediterranean diet significantly lowered SBP by an average of 4.3 mmHg and DBP by 2.4 mmHg.²² The Mediterranean diet seems to have more limited effects (SBP and DBP reductions of about 2 mmHg) compared to the DASH Diet. A 2019 meta-analysis of 67 trials that looked at these diets as well as a variety of others concluded, "The DASH, Mediterranean, low-carbohydrate, Paleolithic, high-protein, low glycemic index, low-sodium, and low-fat dietary approaches were significantly more effective in lowering SBP (-8.73 to -2.32 mmHg) and DBP (-4.85 to -1.27 mmHg) compared to the control diet."²³ Of all these, DASH was ranked the most effective dietary approach of all.

In actuality, the DASH diet shares a lot of recommendations in common with the Mediterranean diet. It consists of foods that are:

- High in fruits and vegetables
- Low in dairy, animal meat, and saturated fat
- High in nuts, seeds, and beans
- Low in snacks and sweets.

The DASH diet also emphasizes a reduction in sodium intake and avoidance of sugar-sweetened beverages.

The DASH diet is low in saturated fat, cholesterol, and simple sugars, which can worsen inflammation and increase the risk of diabetes and heart disease. It incorporates protein more from plant versus animal sources.

In those with high BP, the DASH diet on average lowers the SBP 11.6 points and the DBP 5.3 points.²⁴ It also lowers homocysteine levels,²⁵ has a positive effect on bone strength,²⁶ and raises HDL by 21%-33%.²⁷ Although the DASH diet is an effective intervention and generally considered to represent a satisfying way to eat, program adherence is not always optimal.²⁸

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The "DASH Diet" tool has more detailed information.

Sodium restriction

Considerable debate continues about what are healthy upper limits for sodium intake.²⁹ The body only needs 500 mg daily for optimal functioning (1/4 tsp). Table 1, above, highlights reductions in BP that occur based on amounts of sodium people cut out of their diets. Reducing sodium is beneficial to African Americans as well as (though less for) Whites, and it is beneficial for both men and women.¹⁷ Reducing sodium intake can also prevent HTN from ever occurring (relative risk reduction of 20%). It can also reduce BP even more when it is combined with medications versus when people take medications only.³⁰

Direct patients to take the salt shaker off the table and avoid salt-rich foods. Foods that tend to be high in salt include canned soups, broths, frozen dinners, chips, lunch meats, salad dressings, pizza, packaged mixes, and foods eaten away from home.

For more information on a low-salt diet, refer to "Implementing Recommendations for Dietary Salt Reduction."

Increased Potassium Intake

Data from individual trials have been inconsistent, but several meta-analyses now support a relationship between potassium (K) intake and better BP readings in people who have HTN; potassium does not clearly affect BPs in people with normal BP levels. Potassium is best-obtained through the diet, and a DASH diet offers a good amount. High-potassium foods include avocados, acorn squash, apricots, bananas, broccoli, cucumbers, eggplant, grapefruit, leafy greens, mushrooms, oranges, peas, prunes, pumpkins, salmon, spinach, sweet potatoes, tomato juice, white beans, and zucchini. Milk and yogurt are also high in potassium. The DASH diet provides 4.7 gm of K per day.

Potassium has more of a favorable effect for people with high sodium intake. It also has a more substantial effect in Black people. It is suggested that people keep the ratio of K to sodium that they eat in the range of 4 or 5 to 1.¹⁵ If people have poor kidney function, they should keep potassium intake from their diets below 4.7 gm/day (perhaps lower for more severe chronic kidney disease).³² Many BP medications can raise or lower potassium levels.

Magnesium

Magnesium (Mg) also plays a role in BP management.³³ According to some trials, Mg can decrease SBP by 3-4 and DBP by 2.5 mm Hg, on average. The improvements are greater when a person's intake over 370 mg/day. The optimal dose of an Mg supplement seems to be 500-1,000 mg/day, and chelating it with amino acids like taurine seems to enhance its effect and improve its tolerability.³⁴

Omega-3 Polyunsaturated fatty acids

Eating foods containing omega-3 has been associated with lower BPs. Omega-3's may work by many mechanisms, including release of nitric oxide, increasing vasodilator prostanoids, reducing insulin resistance, and stimulating the parasympathetic nervous system.³⁵ In people with untreated HTN, taking an average of 4 gm (a high dose) of omega-3s led to reductions of SBP

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by 4.5 and DBP by 3.1 mmHg.³⁶ Omega-3s are likely to be more beneficial for reducing the risk of heart disease through their anti-platelet and anti-inflammatory effects than by their effect on BP.

Fish oil consists of two essential fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). Evidence suggests that DHA has more of a hypotensive effect than EPA.³⁷ Patients can use fish oil at a dose of 1 gram daily to reduce the risk of heart disease, particularly if they already have had a documented heart attack.^{38,39} A 2014 review of randomized controlled trials using both EPA and DHA, however, found the combination results in reduced SBP, with higher intakes (greater than or equal to 2 gm daily) needed to reduce DBP more.⁴⁰ Nuts and flaxseed oil, as omega-3 sources, have not been studied to the same extent as fish oil.³⁶

Olive Oil

Intake of extra-virgin olive oil has been found to be associated with lower SBP and DBP readings, in people eating a Mediterranean diet.⁴¹ Identical twins with HTN, treated with 500 or 1,000 mg of olive leaf extract daily for 8 weeks, had a decrease of SBP of 3 and DBP of 1 mmHg taking the lower dose and 11 and 4 mmHg taking the higher dose.⁴²

Milk peptides

Compared with carbohydrate, dietary protein intake has been linked to reductions in SBP and DBP of 1.8 and 1.2 mmHg, respectively. This seems true for both vegetable and animal proteins.⁴³ Certain fish like sardines, tuna, mackerel, and bonito have been found to have ACE inhibition activity.⁴⁴

Epidemiological studies have shown an association of lower BP with calcium (Ca) consumption. This may be related to the Ca content in milk, as well as milk-derived proteins or peptides. It appears that when milk is fermented by specific bacterial strains (such as *Lactobacillus helveticus*), peptides are formed that have an inhibitory effect on the ACE system, leading to a blood-pressure-lowering effect. 46

Pasteurization destroys the bacteria that activate these beneficial peptides. To obtain the blood-pressure-lowering effects of dairy, one would have to drink unpasteurized milk, which is not available in many areas, for various reasons. An alternative is to eat yogurt, which includes many of the bacteria that break down the milk proteins (e.g., casein and whey) into the beneficial peptides. Which types of yogurt contain the needed bacteria (*L. helveticus*) to create these ACE-inhibiting peptides is still being elucidated.

A 2016 trial (the Whey2Go Trial) found that consuming 56 gm/day of unhydrolyzed milk proteins—whey protein—for 8 weeks lowered 24-hour ambulatory blood pressures (SBP down by 3.9, DBP by 2.5 mmHg), in addition to improving vascular reactivity and various laboratory findings.⁴⁷

There are supplement companies marketing these peptides as a "natural" ACE inhibitor. There is limited benefit of using this type of remedy over ACE inhibitor medications, which are readily available.

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Soy Protein

A double-blinded study showed that 40 gm of soy protein (the amount in one soy burger or two glasses of soy milk) lowered SBP by 7.9 mmHg and DBP by 5.3 mmHg in people with HTN.⁴⁸ Obtaining all protein from one food source is not ideal. There is some concern that high amounts of soy protein may increase the risk of bladder cancer, but protein from a variety of plant sources such as nuts, beans, and vegetables appears to be safe and beneficial.

Dark chocolate

The cacao bean (*Theobroma cacao*) is rich in polyphenols such as procyanidins that have beneficial influences on arterial walls. A 2018 meta-analysis found that for the highest versus lowest category of chocolate consumption, the risk ratio of CVD dropped to 0.77.⁴⁹ A 2017 Cochrane review concluded that "flavanol-rich chocolate and cocoa products cause a small (2 mmHg) BP-lowering effect in mainly healthy adults in the short term." There may be differential effects; that is, effects may be greater in people with prehypertension compared to people with lower pressures.⁵⁰

Many brands of commercial chocolate are processed under conditions that destroy flavonoids, so look for "gourmet" chocolate that has at least 70% cocoa.⁵¹ The daily "dose: is 10-30 gm daily of dark chocolate (about 1/4 of a regular sized chocolate bar).

Garlic

A 2015 meta-analysis found that garlic had significant BP-lowering effects. ⁵² It brought SBPs down by 6.7 mmHg on average, and DBPs were reduced an average of 4.8 mmHg. A 2016 review found that for people with BP \geq 140/90, reductions were even greater (SBP 8.7 and DBP 6.1 mmHg, on average). ⁵³

Beet Root (Beets)

Beet roots reduce BP through their effects on the nitrate/nitrite/nitric oxide pathways and can be considered a safe way to help control BP as part of an overall healthy diet.⁵⁴ Beets contain high levels of nitrate, and consuming them leads to dose-dependent effect of BP that can last for 24 hours.⁵⁵ After 4 weeks of consumption, mean reductions in BP were (for 24-hour ambulatory monitoring) a notable 7.7 mmHg SBP and 5.2 mmHg DBP.³⁶

Coffee

A 2018 meta-analysis found that coffee consumption is inversely related to HTN, in a dose-response manner, noting that up to a point, risk of HTN dropped by 2% for each cup of coffee consumed daily. Some studies have questioned whether HTN risk might increase slightly if a person drinks more than 3 cups daily.⁵⁶ A review of green coffee extract supplementation (dose <400 mg) found benefits for SBP and DBP of 3.1 and 2.2 mmHg, respectively.⁵⁷

Tea

Consuming 2-6 cups daily of either green or black tea over 1-6 months BPs, with more benefit when consumption was ongoing for longer than 12 weeks.⁵⁸ For green tea, the effect is higher (SBP, 2.1 and DBP 1.7 mm Hg) than for black tea (1.4 and 1.1 mm Hg).

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Hibiscus tea, 2-4 cups daily for 2-8 weeks, also significantly reduces BP, including in people who are taking medications.⁵⁹

Other Foods and Food Groups^{17,60}

- **Carbohydrates**. Carbohydrates' connection to BP are unclear, in terms of both how much of them are eaten and also the types of carbohydrates one eats.
- Copper and zinc. Copper and zinc levels do not seem to be independently associated with HTN.⁶¹
- **Fats**. Saturated fat does not affect BP, though it may have other effects on heart health. Monounsaturated fats modestly lower BP, but their benefits to heart health occur primarily through other means
- **Fiber.** While fiber clearly has beneficial effects on lipids, it is not clear how much it directly effects BP. A 2005 study estimated that supplementing with 40-50 gm daily of a mixed fiber leads to a BP reduction of about 7.5/5.5 mm Hg.⁶²
- **Probiotics.** As has been the case with the microbiome and so many physiological processes and illnesses, there is a connection between BP and the gut microbiome. This is still being explored, but we know, for example, that various gut microorganism metabolites can alter gut function. Increased salt intake has a harmful effect on the microbiome. Probiotics may improve BP to a modest degree, particularly if it is elevated at baseline. One meta-analysis reported a change of 3.1 mmHg in SBP and 1.1 in DBP in people who drank a fermented milk product. 64
- **Vitamin C.** The benefits of increasing vitamin C are unclear, according to some researchers, but one meta-analysis focusing on supplementing with 500 mg/day over 8 weeks found a SBP reduction of 4.8 mmHg, with no DBP effect. People with low blood levels of vitamin C have a greater likelihood of being hypertensive. Vitamin C may also make some drugs, like amlodipine, more effective.
- Vitamin D. Vitamin D studies have somewhat complex findings. In general, BP effects seem to be limited. A meta-analysis found that effects depend on level of supplementation and population subgroup. Non-overweight patients, people over 50, and people taking ≥800 IU/day for <6 months seem to have the best results. People who take calcium supplements along with vitamin D actually show increases in BP in some studies⁶⁸, but calcium does seem to be beneficial for pregnant women because it reduces pre-eclampsia, pre-term birth, and overall complications.⁶⁹

Physical Activity

Movement and physical activity benefit many aspects of health, beyond contributing to healthy BP levels. Whether patients are using exercise to lower BP, lose weight or improve aerobic capacity, appropriate exertion and persistence are keys to success. Tying in why activity matters to a person (its link to Mission, Aspiration, Purpose, or MAP) is a key aspect of Integrative Health care. It can take one to three months to see positive effects from increasing physical activity. If people do not exert themselves within safe parameters and do not maintain their activity levels over time, there may be little beneficial change.

A 2019 network meta-analysis of 391 trials compared the effect of exercise interventions to those of medications and concluded, "Assuming equally reliable estimates, the SBP-lowering

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effect of exercise among hypertensive populations appears similar to that of commonly used antihypertensive medications." A review of 16 studies concluded (in addition to benefits for many other risk factors) exercising over a period of \geq 12 weeks reduced SBP by an average of 2.5 and DBP by an average of 2.3 mmHg.²⁰

Physical fitness guidelines vary, but personalizing an activity plan for each patient can be a useful approach. More information can be found in the "Physical Activity" overview.

In people with HTN, as with most adults, the recommendations are to complement aerobic exercise with muscle-strengthening activities that are moderate or high intensity and involve all major muscle groups on two or more days a week. It is clear in the research that endurance (aerobic), resistance, and isometric resistance training all lower systolic and diastolic BPs.⁷¹ One trial focused on non-White adults found that dynamic resistance training has an equivalent or even greater benefit on BP compared to aerobic exercise.⁷² A 2018 meta-analysis concluded that high-intensity interval training and moderate-intensity continuous training had similar beneficial effects.⁷³

An easy tool to help understand how to obtain 50%-85% maximal oxygen uptake, which is recommended in many guidelines, is the perceived exertion scale, shown in Figure 1.



Figure 1. Perceived Exertion Scale. 74

Perceived exertion. On a scale from 1-20, with 20 being the point of exhaustion, encourage patients to aim for 14 and work up to this as a maximum over a 25-minute period of time. At this level of exertion, a person should be able to talk but not sing. Exercise should occur on most

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days of the week. If a person does not have time for structured exercise each day, they can be encouraged to use stairs, walk briskly to lunch, or bike to work.

Yoga. A 2019 systematic review and meta-analysis in *Mayo Clinic Proceedings* concluded, based on data from 3,517 hypertensive adults, that practicing yoga an average of 5 sessions weekly for between 30-90 minutes per session, for 6-20 weeks (depending on the study) led to moderate reductions in SBP of 5 mm Hg and DBP of 3.9 mmHg.⁷⁵ Another review concluded that benefits overall were actually in the range of 10 mmHg for SBP and 8 mmHg DBP.⁷⁶ Of course, whatever the BP numbers indicate, yoga has other benefits as well. (The "<u>Yoga</u>" Integrative Health tool has more details.)

Tai chi. Tai chi also seems to lower BP. A 2020 meta-analysis concluded that in a group of over 3,200 middle-aged adults, practicing an average of 4 times a week for 45-60 minutes, led to significant BP reductions.⁷⁷ Interestingly, studies in English found an average SBP drop of 10.4 mmHg, and DBP drop of 4 mmHg; Chinese studies reported decreases that were double those. The evidence for tai chi is reviewed in detail in Chapter 5 of the <u>Passport to Whole Health</u>.

Other specific activities, such as dance therapy, also show promise for reducing BP, but more research is needed.⁷⁸

Recharge

Sleep quality has an effect on BP. Short sleep duration and poor sleep quality can both lead to substantial increases in BP. Normally, people should have a decrease in SBP and DBP of about 10%20% while sleeping. If the sympathetic nervous system remains active, this does not occur. Obstructive sleep apnea (OSA) can lead to acute BP increases; people with moderate to severe OSA had 3.2 times the odds of developing hypertension. The "Recharge" overview has a number of suggestions about how to help a person improve their sleep.

Surroundings

BP increases based on external factors. There is an association between noise exposure and more clinically severe HTN symptoms.⁸¹ People with fewer resources and those with established CVD seem more susceptible to the effects of environmental stressors on their BPs.⁸² A 2017 review found that forest bathing (Shinrin-yoku) significantly reduces BP, while a person is in the forest environment.⁸³ It remains to be determined if there are long-term effects, or how this affects normotensive people versus those with HTN.

Personal Development

Education level is tied to better outcomes for people with HTN. A study of 223 patients with HTN found that education level was independently associated with risk.⁸⁴

Spirit and Soul

A 2019 review of 79 studies could not draw conclusions about the effect of religion on HTN.⁸⁵ However, religion and/or spirituality coping was associated with lower risk of HTN in the Black Women's Health Study.⁸⁶

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Mind and Emotions

A 2017 meta-analysis, while noting a great deal of variability among studies, concluded that psychosocial stress is associated with an increased risk of HTN (odds ratio of 2.40), and people with HTN experienced more stress compared to those with normal pressures (odds ratio 2.69).⁸⁷ Working with individuals around their specific stressors to individualize therapeutic approaches has the potential to increase their chances of success. Multiple factors can have an impact, ranging from urbanization, workplace stress, and lack of social connection.⁸⁸

Emotions such as anxiety, hostility, and anger can influence the hypothalamic-pituitary axis, stimulating the sympathetic nervous system and resulting in the release of neurotransmitters and hormones that elevate BP. If the mind is constantly experiencing such emotions, the body may be bathed in these compounds with resultant elevations in BP and cardiovascular risk; being less emotionally reactive contributes to lower BP levels. Conversely, emotional dampening (alexithymia) can also have negative BP effects. As with so many aspects of our health, finding emotional balance is beneficial when it comes to BP.

Stress is as important a risk factor for development of CVD as truncal obesity and HTN. When a detailed list of risk factors were compiled from data coming from 52 countries, stress was only behind smoking in terms of factors that contribute most to CVD risk.⁹¹

In 20%-30% of people, stress increases susceptibility to the effects of salt on their BPs. ⁹² Low-stress resilience at age 18 was correlated with increased risk of HTN in a sample of over 93,000 men, with risk being higher for those who had a higher body mass index (BMI). ⁹³ A 2018 study of stress management in the workplace found that employees with HTN did much better with their SBPs (but not DBPs) with an average drop of 7.5 mmHg when they used stress management techniques. Measures of depressive rumination and emotional exhaustion improved in parallel with reductions in BP. ⁹⁴

Mind-Body Tools to Lower Blood Pressure

There are a number of ways to reduce stress and thereby potentially prevent or treat HTN. Decisions about which mind-body tools to use must be based on individual preference, accessibility, and clinician experience about what might be the best fi' for any given person. Less research is available for Guided Imagery and Clinical Hypnosis, as compared to meditation, breathing exercises, and biofeedback. A Cochrane review concluded there was insufficient evidence to guide practice around using Guided Imagery in pregnancy⁹⁵, and a 2016 meta-analysis reported that there is a trend toward BP benefit with music interventions.⁹⁶

Meditation

In general, meditation seems to have significant favorable effects BP. A 2017 review of 19 studies found that SBP improved by 2.5 mmHg for transcendental meditation and an average of 3.8 mmHg for other types of meditation interventions; the latter did not meet statistical significance.⁹⁷

Transcendental Meditation™ (TM), in which a person focuses on a word or mantra for 20 minutes a day for 16 weeks, was found to improve markers of the metabolic syndrome including

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HTN in individuals with known heart disease. ⁹⁸ A 2017 review found that regular practice may reduce SBP by 4 and DBP by 2 mmHg, respectively. ⁹⁹

Mindful awareness meditation has shown similar benefits.¹⁰⁰ Mindfulness-based stress reduction (MBSR), which includes body-scanning and gentle yoga postures alongside other meditation techniques, resulted in BP being successfully lowered in the clinic setting, but it did not result in reduced ambulatory BP readings.^{101,102} In people with cancer, those who took an MBSR course had decreased BP at 6- and 12-month follow-ups.¹⁰⁰ In a study of people with prehypertension, SBP, but not DBP, was significantly lowered (4.8 mmHg).¹⁰¹

Breathing Exercises

Taking deep breaths helps to balance autonomic nervous system activity and BP, while enhancing heart rate variability (HRV). Deep abdominal breathing stimulates the vagus nerve that travels through the diaphragm and stimulates the parasympathetic nervous system, leading to the relaxation response. When sympathetic tone is elevated, there is desensitization of the arterial and cardiopulmonary baroreceptors and BP can increase.

Slowing the breathing rate to less than 10 breaths/minute (ideal is 5-6 breaths/min) enhances baroreceptor sensitivity, lowering BP and increasing HRV. Slow breathing (8 breaths/minute) was found to lower baroreflex sensitivity in 60 people with HTN. ¹⁰³ A stepwise-paced breathing procedure reduced SBP by an average of 8 mmHg, and DBP by an average of 5 mm Hg. ¹⁰⁴ A 2019 meta-analysis of 17 studies found that device-guided slow breathing (breathing meets biofeedback) decreased SBP by 5.6 and DBP by 3 mmHg. ¹⁰⁵ In older adults, "slow-loaded breathing" — slow breathing accompanied by inspiratory muscle training—helped reduce resting BP even for older people who had isolated systolic HTN. ¹⁰⁶ A study of alternate-nostril yoga breathing also found reduced BP in the short-term. ¹⁰⁷

The "Breathing" Integrative Health tool has additional information about breath-based techniques.

Biofeedback

For well over 20 years, studies have indicated that biofeedback-assisted relaxation improves BP, even several months after treatment. A review of studies evaluating a biofeedback device designed to lower BP by modulating respiratory rate found that after eight weeks of treatment, there was an average drop of 14 mmHg SBP and 8 mmHg DBP. The more the biofeedback device was used, the greater the drop. The recommended dose is 15 minutes of use each day with at least 45 minutes of slow breathing per week. Examples of biofeedback devices designed for personal use include the following (none of these is officially sponsored or endorsed by VA):

- RESPeRate® (about \$100). A device that uses sound and a respiration monitor one wears around the chest to slow breathing down. Goal is 5-6 breaths per minute. http://www.re-sperate.com/
- EmWave® and EmWave2® Products (~\$100 phone, \$225 laptop or desktop version). Bluetooth model for smartphones is now available. http://www.heartmath.com/
- Unyte[™] products (about \$200 device cost, then \$5/month; lifetime use \$350). Biofeedback-guided meditation training software. https://unyte.com/collections/subscriptions.

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• A number of other devices are also available online if one does a web search for "stress management devices."

Similar results can be obtained using a simple breathing exercise. The key is to slow the breath to 6 breaths per minute, or one "in and out" breath every 10 seconds. Exhalation should be about twice as long as inhalation. Breathe in for a count of 3-4 and breathe out for a count of 6-7 and to take at least 60-80 intentional, slow breaths daily.

The "<u>Heart Rate Variability and Arrhythmias</u>" tool has additional information about biofeedback and heart health.

Acupuncture

A 2018 Cochrane review looking at 22 trials with 1,744 people noted poor methodological quality because of high risk of bias due to lack of blinding, concluding that "there was no evidence for a sustained BP lowering effect of acupuncture." Low-quality evidence showed a short-term effect on pressures for 1-24 hours. Similarly, a 2018 meta-analysis found "...there is inadequate high-quality evidence that acupuncture therapy is useful in treating HTN" but did note that pooled results indicated that acupuncture plus medications had greater effects on BP than medications alone. A 2019 review concurred that more studies are needed, finding that in 15 reviews, acupuncture was more effective in treating BPs than sham acupuncture, when both were used along with Western medicine.

Dietary Supplements

Note: Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

A number of dietary supplements have been used to manage HTN. Whether or not a clinician chooses to recommend them, it is important to have enough familiarity with them to guide patients and answer their questions about various products' efficacy and safety. Note that beets, garlic, chocolate, green and black tea, hibiscus tea, and coffee are discussed in the Food and Drink section, above.

Most supplements used for HTN increase nitric oxide levels.³⁶ Some—including cocoa, fish oil, and garlic—also increase angiotensin converting enzyme (ACE) inhibition. Olive oil, garlic, and olive leaf extract also seem to block calcium channels. Many other mechanisms of action have been posited as well.

Some important research findings related to dietary supplements and HTN include the following:

Coenzyme Q10 (CoQ10). Also known as ubiquinone, CoQ10 is found in every cell in the
human body and is used in the mitochondria to facilitate energy production. It works by an
array of mechanisms, including through being a free radical scavenger, regenerating other
vitamins and antioxidants, and supporting oxidative phosphorylation in the mitochondria. A
2009 Cochrane review found that treatment in people with pressures >140/90 led to decreases of SBP by an average of 11 and DBP 7 mmHg after four weeks of taking 100 mg

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daily.¹¹⁴ *However*, a 2016 follow up Cochrane review found nonsignificant changes of 3.7 and 2.0 mmHg.¹¹⁵ CoQ10 should be taken with a meal that includes some fat, to enhance absorption; it has a good safety profile. It seems to be beneficial when used with drugs that can deplete levels of CoQ10, such as statins, tricyclic antidepressants, and metformin.

- **L-Arginine.** Taken orally, the amino acid L-arginine, at doses ranging from 4-24 gm daily over 2-12 weeks, lowered SBP by 5.4 and DBP by 2.7 mmHg.¹¹⁶ The beneficial effect is probably maximal after 4 weeks.
- **Lycopene.** Lycopene, a carotenoid found in red-toned foods like tomatoes, seems to have additive effects to medications for BP treatment.¹¹⁷ SBP reduction was an average of 5.6 mmHg in people who took 10-50 mg/day for 4-12 weeks.¹¹⁷
- Melatonin. Long-acting forms of melatonin seem to improve sleep in people with HTN taking beta-blockers, and melatonin seems to cause a decrease in nighttime BPs (SBP 6.1 and DBP 3.5 mmHg.)
- Multivitamin, multimineral supplements (MVMMs). A large meta-analysis found that taking MVMMs might decrease SBP and DBP by 1.3 and 0.7 mmHg, respectively.¹¹⁸
- **Pycnogenol.** Pycnogenol, a bark extract from French maritime pine, allowed for a reduction by half of antihypertensive medications in one study. 119
- Resveratrol. Resveratrol is a polyphenol found in grapes. Doses of ≥150 mg daily of grape seed extract reduced SBP by 1.5 mmHg but did not significantly affect DBP.¹²⁰
- Others. Preliminary data suggest that black sesame, pomegranate juice, hawthorn, vitamin B6, alpha-lipoic acid, carnitines, and taurine may have "slight but significant" effects on BP. More trials are needed.¹²¹

In Conclusion

As you work with people to help them reduce their cardiac risk, blood pressure will necessarily be an important focus. Consider it within the larger picture of a person's overall health. Keep in mind the latest recommendations, tailor a plan to each individual patient, and stay aware of how all the different areas of self-care can help keep BP in range. Keep asking yourself what combination of medications, lifestyle changes, and other approaches will work best for any given person. Doing so has the power to lengthen— and improve —their lives.

Resource Links

- <u>ACC/AHA online resources</u>: https://www.heart.org/en/health-topics/high-blood-pressure/high-blood-pressure-toolkit-resources
- "Implementing Yoga": https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/handout intro to yoga.pdf
- "Physical Activity": https://www.fammed.wisc.edu/integrative/resources/modules/physical-activity-movement-flexibility/
- "Recharge": https://wholehealth.wisc.edu/self-care/recharge/

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- <u>"Breathing"</u>: https://www.fammed.wisc.edu/files/webfm-uploads/documents/outreach/im/tool-breathing.pdf
- "Heart Rate Variability and Arrhythmias": https://www.fammed.wisc.edu/files/webfm-up-loads/documents/outreach/im/tool-HRV-arrhythmias.pdf
- <u>Passport to Whole Health</u>: https://www.va.gov/WHOLEHEALTHLIBRARY/docs/Passport to WholeHealth FY2020 508.pdf

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References

- 1. Arnett DK, Claas SA. Omics of blood pressure and hypertension. *Circ Res.* May 11 2018;122(10):1409-1419. doi:10.1161/circresaha.118.311342
- 2. Ozemek C, Laddu DR, Arena R, Lavie CJ. The role of diet for prevention and management of hypertension. *Curr Opin Cardiol*. Jul 2018;33(4):388-393. doi:10.1097/hco.0000000000000532
- 3. American College of Cardiology Foundation and American Heart Association. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: Executive Summary. Accessed July 21, 2020, https://healthmetrics.heart.org/wp-content/uploads/2019/04/2019-ACCAHA-Guideline-on-the-Primary-Prevention-of-Cardiovascular-Disease-Executive-Summary.pdf
- 4. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA. Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. *J Am Coll Cardiol.* 2018;71:e127-e248.
- 5. Kokubo Y, Matsumoto C. Hypertension is a risk factor for several types of heart disease: review of prospective studies. *Adv Exp Med Biol.* 2017;956:419-426. doi:10.1007/5584 2016 99
- 6. Han H, Guo W, Shi W, et al. Hypertension and breast cancer risk: a systematic review and metaanalysis. *Sci Rep*. Mar 20 2017;7:44877. doi:10.1038/srep44877
- 7. Radišauskas R, Kuzmickienė I, Milinavičienė E, Everatt R. Hypertension, serum lipids and cancer risk: A review of epidemiological evidence. *Medicina (Kaunas)*. 2016;52(2):89-98. doi:10.1016/j.medici.2016.03.002
- 8. Sandström YK, Ljunggren G, Wändell P, Wahlström L, Carlsson AC. Psychiatric comorbidities in patients with hypertension--a study of registered diagnoses 2009-2013 in the total population in Stockholm County, Sweden. *J Hypertens*. Mar 2016;34(3):414-20; discussion 420. doi:10.1097/hjh.0000000000000824
- 9. Howard JT, Sosnov JA, Janak JC, et al. Associations of initial injury severity and posttraumatic stress disorder diagnoses with long-term hypertension risk after combat injury. *Hypertension*. May 2018;71(5):824-832. doi:10.1161/hypertensionaha.117.10496
- Tucker KL, Sheppard JP, Stevens R, et al. Self-monitoring of blood pressure in hypertension: A systematic review and individual patient data meta-analysis. *PLoS Med*. Sep 2017;14(9):e1002389. doi:10.1371/journal.pmed.1002389



- 11. Abegaz TM, Shehab A, Gebreyohannes EA, Bhagavathula AS, Elnour AA. Nonadherence to antihypertensive drugs: A systematic review and meta-analysis. *Medicine (Baltimore)*. Jan 2017;96(4):e5641. doi:10.1097/md.000000000005641
- 12. Kostis JB, Wilson AC, Hooper WC, et al. Association of angiotensin-converting enzyme DD genotype with blood pressure sensitivity to weight loss. *Am Heart J*. Oct 2002;144(4):625-9. doi:10.1067/mhj.2002.123570
- 13. Morris RC, Jr., Sebastian A, Forman A, Tanaka M, Schmidlin O. Normotensive salt sensitivity: effects of race and dietary potassium. *Hypertension*. Jan 1999;33(1):18-23. doi:10.1161/01.hyp.33.1.18
- 14. Nicolson DJ, Dickinson HO, Campbell F, Mason JM. Lifestyle interventions or drugs for patients with essential hypertension: a systematic review. *J Hypertens*. Nov 2004;22(11):2043-8.
- 15. Whelton PK, He J. Potassium in preventing and treating high blood pressure. *Semin Nephrol*. Sep 1999;19(5):494-9.
- 16. Patnode CD, Henderson JT, Thompson JH, Senger CA, Fortmann SP, Whitlock EP. Behavioral counseling and pharmacotherapy interventions for tobacco cessation in adults, including pregnant women: a review of reviews for the U.S. Preventive Services Task Force. *Ann Intern Med.* Oct 20 2015;163(8):608-21. doi:10.7326/m15-0171
- 17. Appel LJ. The effects of dietary factors on blood pressure. *Cardiol Clin*. May 2017;35(2):197-212. doi:10.1016/j.ccl.2016.12.002
- 18. Yokoyama Y, Nishimura K, Barnard ND, et al. Vegetarian diets and blood pressure: a meta-analysis. *JAMA Intern Med*. Apr 2014;174(4):577-87. doi:10.1001/jamainternmed.2013.14547
- 19. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. Nov 2003;42(5):878-84. doi:10.1161/01.Hyp.0000094221.86888.Ae
- 20. Ostman C, Smart NA, Morcos D, Duller A, Ridley W, Jewiss D. The effect of exercise training on clinical outcomes in patients with the metabolic syndrome: a systematic review and meta-analysis. *Cardiovasc Diabetol*. Aug 30 2017;16(1):110. doi:10.1186/s12933-017-0590-y
- 21. Schwingshackl L, Schwedhelm C, Hoffmann G, et al. Food groups and risk of hypertension: a systematic review and dose-response meta-analysis of prospective studies. *Adv Nutr.* Nov 2017;8(6):793-803. doi:10.3945/an.117.017178
- 22. Ndanuko RN, Tapsell LC, Charlton KE, Neale EP, Batterham MJ. Dietary patterns and blood pressure in adults: a systematic review and meta-analysis of randomized controlled trials. *Adv Nutr.* Jan 2016;7(1):76-89. doi:10.3945/an.115.009753
- 23. Schwingshackl L, Chaimani A, Schwedhelm C, et al. Comparative effects of different dietary approaches on blood pressure in hypertensive and pre-hypertensive patients: A systematic review and network meta-analysis. *Crit Rev Food Sci Nutr.* 2019;59(16):2674-2687. doi:10.1080/10408398.2018.1463967
- Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med. Apr 17 1997;336(16):1117-24. doi:10.1056/nejm199704173361601
- 25. Appel LJ, Miller ER, 3rd, Jee SH, et al. Effect of dietary patterns on serum homocysteine: results of a randomized, controlled feeding study. *Circulation*. Aug 22 2000;102(8):852-7.
- 26. Lin PH, Ginty F, Appel LJ, et al. The DASH diet and sodium reduction improve markers of bone turnover and calcium metabolism in adults. *J Nutr*. Oct 2003;133(10):3130-6.
- 27. Crawford P, Paden SL, Park MK. Clinical inquiries: What is the dietary treatment for low HDL cholesterol? *J Fam Pract*. Dec 2006;55(12):1076-8.
- 28. Kwan MW, Wong MC, Wang HH, et al. Compliance with the Dietary Approaches to Stop Hypertension (DASH) diet: a systematic review. *PLoS One*. 2013;8(10):e78412. doi:10.1371/journal.pone.0078412



- 29. Graudal N, Jürgens G. Conflicting evidence on health effects associated with salt reduction calls for a redesign of the salt dietary guidelines. *Prog Cardiovasc Dis.* May-Jun 2018;61(1):20-26. doi:10.1016/j.pcad.2018.04.008
- Appel LJ, Espeland MA, Easter L, Wilson AC, Folmar S, Lacy CR. Effects of reduced sodium intake on hypertension control in older individuals: results from the Trial of Nonpharmacologic Interventions in the Elderly (TONE). *Arch Intern Med*. Mar 12 2001;161(5):685-93. doi:10.1001/archinte.161.5.685
- 31. Geleijnse JM, Kok FJ, Grobbee DE. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials. *J Hum Hypertens*. Jul 2003;17(7):471-80. doi:10.1038/sj.jhh.1001575
- 32. K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease. *Am J Kidney Dis.* May 2004;43(5 Suppl 1):S1-290.
- 33. Schutten JC, Joosten MM, de Borst MH, Bakker SJL. Magnesium and blood pressure: a physiology-based approach. *Adv Chronic Kidney Dis*. May 2018;25(3):244-250. doi:10.1053/j.ackd.2017.12.003
- 34. Houston M. The role of magnesium in hypertension and cardiovascular disease. *J Clin Hypertens* (*Greenwich*). Nov 2011;13(11):843-7. doi:10.1111/j.1751-7176.2011.00538.x
- 35. Cicero AF, Ertek S, Borghi C. Omega-3 polyunsaturated fatty acids: their potential role in blood pressure prevention and management. *Curr Vasc Pharmacol*. Jul 2009;7(3):330-7. doi:10.2174/157016109788340659
- 36. Turner JM, Spatz ES. Nutritional supplements for the treatment of hypertension: a practical guide for clinicians. *Curr Cardiol Rep.* Dec 2016;18(12):126. doi:10.1007/s11886-016-0806-x
- 37. Mori TA. Omega-3 fatty acids and hypertension in humans. *Clin Exp Pharmacol Physiol*. Sep 2006;33(9):842-6. doi:10.1111/j.1440-1681.2006.04451.x
- 38. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico. *Lancet*. Aug 7 1999;354(9177):447-55.
- 39. Burr ML, Fehily AM, Gilbert JF, et al. Effects of changes in fat, fish, and fibre intakes on death and myocardial reinfarction: diet and reinfarction trial (DART). *Lancet*. Sep 30 1989;2(8666):757-61.
- 40. Miller PE, Van Elswyk M, Alexander DD. Long-chain omega-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid and blood pressure: a meta-analysis of randomized controlled trials. *Am J Hypertens*. Jul 2014;27(7):885-96. doi:10.1093/aih/hpu024
- 41. Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study. *Am J Clin Nutr*. Oct 2004;80(4):1012-8. doi:10.1093/ajcn/80.4.1012
- 42. Perrinjaquet-Moccetti T, Busjahn A, Schmidlin C, Schmidt A, Bradl B, Aydogan C. Food supplementation with an olive (Olea europaea L.) leaf extract reduces blood pressure in borderline hypertensive monozygotic twins. *Phytother Res.* Sep 2008;22(9):1239-42. doi:10.1002/ptr.2455
- 43. Rebholz CM, Friedman EE, Powers LJ, Arroyave WD, He J, Kelly TN. Dietary protein intake and blood pressure: a meta-analysis of randomized controlled trials. *Am J Epidemiol*. Oct 1 2012;176 Suppl 7:S27-43. doi:10.1093/aje/kws245
- 44. Lordan S, Ross RP, Stanton C. Marine bioactives as functional food ingredients: potential to reduce the incidence of chronic diseases. *Mar Drugs*. 2011;9(6):1056-100. doi:10.3390/md9061056
- 45. McCarron DA, Morris CD, Henry HJ, Stanton JL. Blood pressure and nutrient intake in the United States. *Science*. Jun 29 1984;224(4656):1392-8.
- 46. Jauhiainen T, Korpela R. Milk peptides and blood pressure. *J Nutr.* Mar 2007;137(3 Suppl 2):825s-9s
- 47. Fekete AA, Giromini C, Chatzidiakou Y, Givens DI, Lovegrove JA. Whey protein lowers blood pressure and improves endothelial function and lipid biomarkers in adults with prehypertension and



- mild hypertension: results from the chronic Whey2Go randomized controlled trial. *Am J Clin Nutr*. Dec 2016;104(6):1534-1544. doi:10.3945/ajcn.116.137919
- 48. Yang G, Shu XO, Jin F, et al. Longitudinal study of soy food intake and blood pressure among middle-aged and elderly Chinese women. *Am J Clin Nutr*. May 2005;81(5):1012-7.
- 49. Gianfredi V, Salvatori T, Nucci D, Villarini M, Moretti M. Can chocolate consumption reduce cardiocerebrovascular risk? A systematic review and meta-analysis. *Nutrition*. Feb 2018;46:103-114. doi:10.1016/j.nut.2017.09.006
- 50. Ried K, Fakler P, Stocks NP. Effect of cocoa on blood pressure. *Cochrane Database Syst Rev.* Apr 25 2017;4(4):Cd008893. doi:10.1002/14651858.CD008893.pub3
- 51. Nahas R. Complementary and alternative medicine approaches to blood pressure reduction: An evidence-based review. *Can Fam Physician*. Nov 2008;54(11):1529-33.
- 52. Xiong XJ, Wang PQ, Li SJ, Li XK, Zhang YQ, Wang J. Garlic for hypertension: a systematic review and meta-analysis of randomized controlled trials. *Phytomedicine*. Mar 15 2015;22(3):352-61. doi:10.1016/j.phymed.2014.12.013
- 53. Ried K. Garlic lowers blood pressure in hypertensive individuals, regulates serum cholesterol, and stimulates immunity: an updated meta-analysis and review. *J Nutr*. Feb 2016;146(2):389s-396s. doi:10.3945/jn.114.202192
- 54. Bonilla Ocampo DA, Paipilla AF, Marín E, Vargas-Molina S, Petro JL, Pérez-Idárraga A. Dietary nitrate from beetroot juice for hypertension: a systematic review. *Biomolecules*. Nov 2 2018;8(4)doi:10.3390/biom8040134
- 55. Hobbs DA, Kaffa N, George TW, Methven L, Lovegrove JA. Blood pressure-lowering effects of beetroot juice and novel beetroot-enriched bread products in normotensive male subjects. *Br J Nutr.* Dec 14 2012;108(11):2066-74. doi:10.1017/s0007114512000190
- 56. Zhang Z, Hu G, Caballero B, Appel L, Chen L. Habitual coffee consumption and risk of hypertension: a systematic review and meta-analysis of prospective observational studies. *Am J Clin Nutr.* Jun 2011;93(6):1212-9. doi:10.3945/ajcn.110.004044
- 57. Han B, Nazary-Vannani A, Talaei S, et al. The effect of green coffee extract supplementation on blood pressure: A systematic review and meta-analysis of randomized controlled trials. *Phytother Res.* Nov 2019;33(11):2918-2926. doi:10.1002/ptr.6481
- 58. Liu G, Mi XN, Zheng XX, Xu YL, Lu J, Huang XH. Effects of tea intake on blood pressure: a metaanalysis of randomised controlled trials. *Br J Nutr*. Oct 14 2014;112(7):1043-54. doi:10.1017/s0007114514001731
- 59. Wahabi HA, Alansary LA, Al-Sabban AH, Glasziuo P. The effectiveness of Hibiscus sabdariffa in the treatment of hypertension: a systematic review. *Phytomedicine*. Feb 2010;17(2):83-6. doi:10.1016/j.phymed.2009.092
- 60. Borghi C, Cicero AF. Nutraceuticals with a clinically detectable blood pressure-lowering effect: a review of available randomized clinical trials and their meta-analyses. *Br J Clin Pharmacol*. Jan 2017;83(1):163-171, doi:10.1111/bcp.12902
- 61. Yao J, Hu P, Zhang D. Associations between copper and zinc and risk of hypertension in US adults. *Biol Trace Elem Res.* Dec 2018;186(2):346-353. doi:10.1007/s12011-018-1320-3
- 62. Houston MC. Nutraceuticals, vitamins, antioxidants, and minerals in the prevention and treatment of hypertension. *Prog Cardiovasc Dis.* May-Jun 2005;47(6):396-449. doi:10.1016/j.pcad.2005.01.004
- 63. Jama HA, Kaye DM, Marques FZ. The gut microbiota and blood pressure in experimental models. *Curr Opin Nephrol Hypertens*. Mar 2019;28(2):97-104. doi:10.1097/mnh.0000000000000476
- 64. Dong JY, Szeto IM, Makinen K, et al. Effect of probiotic fermented milk on blood pressure: a meta-analysis of randomised controlled trials. *Br J Nutr*. Oct 2013;110(7):1188-94. doi:10.1017/s0007114513001712
- 65. Juraschek SP, Guallar E, Appel LJ, Miller ER, 3rd. Effects of vitamin C supplementation on blood pressure: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*. May 2012;95(5):1079-88. doi:10.3945/ajcn.111.027995



- 66. Ness AR, Chee D, Elliott P. Vitamin C and blood pressure--an overview. *J Hum Hypertens*. Jun 1997;11(6):343-50. doi:10.1038/sj.jhh.1000423
- 67. Mahajan AS, Babbar R, Kansal N, Agarwal SK, Ray PC. Antihypertensive and antioxidant action of amlodipine and vitamin C in patients of essential hypertension. *J Clin Biochem Nutr*. Mar 2007;40(2):141-7. doi:10.3164/jcbn.40.141
- 68. Golzarand M, Shab-Bidar S, Koochakpoor G, Speakman JR, Djafarian K. Effect of vitamin D3 supplementation on blood pressure in adults: an updated meta-analysis. *Nutr Metab Cardiovasc Dis.* Aug 2016;26(8):663-73. doi:10.1016/j.numecd.2016.04.011
- 69. Hofmeyr GJ, Lawrie TA, Atallah AN, Duley L. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev.* Aug 4 2010;(8):Cd001059. doi:10.1002/14651858.CD001059.pub3
- 70. Naci H, Salcher-Konrad M, Dias S, et al. How does exercise treatment compare with antihypertensive medications? A network meta-analysis of 391 randomised controlled trials assessing exercise and medication effects on systolic blood pressure. *Br J Sports Med.* Jul 2019;53(14):859-869. doi:10.1136/bjsports-2018-099921
- 71. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and metaanalysis. *J Am Heart Assoc*. Feb 1 2013;2(1):e004473. doi:10.1161/jaha.112.004473
- 72. MacDonald HV, Johnson BT, Huedo-Medina TB, et al. Dynamic resistance training as stand-alone antihypertensive lifestyle therapy: a meta-analysis. *J Am Heart Assoc*. Sep 28 2016;5(10)doi:10.1161/jaha.116.003231
- 73. Costa EC, Hay JL, Kehler DS, et al. Effects of high-intensity interval training versus moderate-intensity continuous training on blood pressure in adults with pre- to established hypertension: a systematic review and meta-analysis of randomized trials. *Sports Med.* Sep 2018;48(9):2127-2142. doi:10.1007/s40279-018-0944-y
- 74. Rakel D. Non-Pharmaceutical Therapy for Hypertension: Clinician Handout. Accessed July 23, 2020, http://www.fammed.wisc.edu/sites/default/files//webfm-uploads/documents/outreach/im/module_htm_clinician.pdf
- 75. Wu Y, Johnson BT, Acabchuk RL, et al. Yoga as antihypertensive lifestyle therapy: a systematic review and meta-analysis. *Mayo Clin Proc*. Mar 2019;94(3):432-446. doi:10.1016/j.mayocp.2018.09.023
- 76. Cramer H. The efficacy and safety of yoga in managing hypertension. *Exp Clin Endocrinol Diabetes*. Feb 2016;124(2):65-70. doi:10.1055/s-0035-1565062
- 77. Wu Y, Johnson BT, Chen S, Chen Y, Livingston J, Pescatello LS. Tai Ji Quan as antihypertensive lifestyle therapy: A systematic review and meta-analysis. *Journal of sport and health science*. May 1 2020;doi:10.1016/j.jshs.2020.03.007
- Conceicao LS, Neto MG, do Amaral MA, Martins-Filho PR, Oliveira Carvalho V. Effect of dance therapy on blood pressure and exercise capacity of individuals with hypertension: a systematic review and meta-analysis. *international Journal of Cardiology*. Oct 1 2016;220:553-7. doi:10.1016/j.ijcard.2016.06.182
- 79. Shepherd JT, Mancia G. Reflex control of the human cardiovascular system. *Rev Physiol Biochem Pharmacol.* 1986:105:1-99. doi:10.1007/BFb0034497
- 80. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med*. May 11 2000;342(19):1378-84. doi:10.1056/nejm200005113421901
- 81. Zeeb H, Hegewald J, Schubert M, et al. Traffic noise and hypertension results from a large case-control study. *Environ Res.* Aug 2017;157:110-117. doi:10.1016/j.envres.2017.05.019
- 82. Bruno RM, Di Pilla M, Ancona C, et al. Environmental factors and hypertension. *Curr Pharm Des.* 2017;23(22):3239-3246. doi:10.2174/1381612823666170321162233
- 83. Ideno Y, Hayashi K, Abe Y, et al. Blood pressure-lowering effect of Shinrin-yoku (Forest bathing): a systematic review and meta-analysis. *BMC Complement Altern Med.* Aug 16 2017;17(1):409. doi:10.1186/s12906-017-1912-z



- 84. Di Chiara T, Scaglione A, Corrao S, Argano C, Pinto A, Scaglione R. Education and hypertension: impact on global cardiovascular risk. *Acta Cardiol*. Oct 2017;72(5):507-513. doi:10.1080/00015385.2017.1297626
- 85. Meng Q, Zhang X, Shi R, Liao H, Chen X. Correlation between religion and hypertension. *Intern Emerg Med.* Mar 2019;14(2):209-237. doi:10.1007/s11739-018-1791-4
- 86. Cozier YC, Yu J, Wise LA, et al. Religious and spiritual coping and risk of incident hypertension in the Black Women's Health Study. *Ann Behav Med*. Nov 12 2018;52(12):989-998. doi:10.1093/abm/kay001
- 87. Liu MY, Li N, Li WA, Khan H. Association between psychosocial stress and hypertension: a systematic review and meta-analysis. *Neurol Res.* Jun 2017;39(6):573-580. doi:10.1080/01616412.2017.1317904
- 88. Ushakov AV, Ivanchenko VS, Gagarina AA. Psychological stress in pathogenesis of essential hypertension. *Curr Hypertens Rev.* 2016;12(3):203-214. doi:10.2174/1573402112666161230121622
- 89. Ifeagwazi CM, Egberi HE, Chukwuorji JC. Emotional reactivity and blood pressure elevations: anxiety as a mediator. *Psychol Health Med.* Jun 2018;23(5):585-592. doi:10.1080/13548506.2017.1400670
- 90. McCubbin JA, Loveless JP, Graham JG, et al. Emotional dampening in persons with elevated blood pressure: affect dysregulation and risk for hypertension. *Ann Behav Med*. Feb 2014;47(1):111-9. doi:10.1007/s12160-013-9526-2
- 91. Rosengren A, Hawken S, Ounpuu S, et al. Association of psychosocial risk factors with risk of acute myocardial infarction in 11119 cases and 13648 controls from 52 countries (the INTERHEART study): case-control study. *Lancet*. Sep 11-17 2004;364(9438):953-62. doi:10.1016/s0140-6736(04)17019-0
- 92. Stewart DL, Harshfield GA, Zhu H, Hanevold CD. Stress and salt sensitivity in primary hypertension. *Curr Hypertens Rep.* Feb 2015;17(2):2. doi:10.1007/s11906-014-0513-1
- 93. Crump C, Sundquist J, Winkleby MA, Sundquist K. Low stress resilience in late adolescence and risk of hypertension in adulthood. *Heart*. Apr 2016;102(7):541-7. doi:10.1136/heartjnl-2015-308597
- 94. Clemow LP, Pickering TG, Davidson KW, et al. Stress management in the workplace for employees with hypertension: a randomized controlled trial. *Transl Behav Med.* Sep 8 2018;8(5):761-770. doi:10.1093/tbm/iby018
- 95. Haruna M, Matsuzaki M, Ota E, Shiraishi M, Hanada N, Mori R. Guided imagery for treating hypertension in pregnancy. *Cochrane Database Syst Rev.* Apr 27 2019;4(4):Cd011337. doi:10.1002/14651858.CD011337.pub2
- 96. Kühlmann AY, Etnel JR, Roos-Hesselink JW, Jeekel J, Bogers AJ, Takkenberg JJ. Systematic review and meta-analysis of music interventions in hypertension treatment: a quest for answers. *BMC Cardiovasc Disord*. Apr 19 2016;16:69. doi:10.1186/s12872-016-0244-0
- 97. Shi L, Zhang D, Wang L, Zhuang J, Cook R, Chen L. Meditation and blood pressure: a metaanalysis of randomized clinical trials. *J Hypertens*. Apr 2017;35(4):696-706. doi:10.1097/hjh.000000000001217
- 98. Paul-Labrador M, Polk D, Dwyer JH, et al. Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. *Arch Intern Med.* Jun 12 2006;166(11):1218-24. doi:10.1001/archinte.166.11.1218
- 99. Ooi SL, Giovino M, Pak SC. Transcendental meditation for lowering blood pressure: An overview of systematic reviews and meta-analyses. *Complement Ther Med*. Oct 2017;34:26-34. doi:10.1016/j.ctim.2017.07.008
- 100. Carlson LE, Speca M, Faris P, Patel KD. One year pre-post intervention follow-up of psychological, immune, endocrine and blood pressure outcomes of mindfulness-based stress reduction (MBSR) in breast and prostate cancer outpatients. *Brain Behav Immun*. Nov 2007;21(8):1038-49. doi:10.1016/j.bbi.2007.04.002



- Hughes JW, Fresco DM, Myerscough R, van Dulmen MH, Carlson LE, Josephson R. Randomized controlled trial of mindfulness-based stress reduction for prehypertension. *Psychosom Med*. Oct 2013;75(8):721-8. doi:10.1097/PSY.0b013e3182a3e4e5
- Solano López AL. Effectiveness of the mindfulness-based stress reduction program on blood pressure: a systematic review of literature. Worldviews Evid Based Nurs. Oct 2018;15(5):344-352. doi:10.1111/wvn.12319
- 103. Li C, Chang Q, Zhang J, Chai W. Effects of slow breathing rate on heart rate variability and arterial baroreflex sensitivity in essential hypertension. *Medicine (Baltimore)*. May 2018;97(18):e0639. doi:10.1097/md.000000000010639
- 104. Zhang Z, Wang B, Wu H, Chai X, Wang W, Peng CK. Effects of slow and regular breathing exercise on cardiopulmonary coupling and blood pressure. *Med Biol Eng Comput*. Feb 2017;55(2):327-341. doi:10.1007/s11517-016-1517-6
- 105. Chaddha A, Modaff D, Hooper-Lane C, Feldstein DA. Device and non-device-guided slow breathing to reduce blood pressure: A systematic review and meta-analysis. *Complement Ther Med.* Aug 2019;45:179-184. doi:10.1016/j.ctim.2019.03.005
- 106. Ublosakka-Jones C, Tongdee P, Pachirat O, Jones DA. Slow loaded breathing training improves blood pressure, lung capacity and arm exercise endurance for older people with treated and stable isolated systolic hypertension. *Exp Gerontol*. Jul 15 2018;108:48-53. doi:10.1016/j.exger.2018.03.023
- 107. Telles S, Verma S, Sharma SK, Gupta RK, Balkrishna A. Alternate-nostril yoga breathing reduced blood pressure while increasing performance in a vigilance test. *Med Sci Monit Basic Res.* Dec 29 2017;23:392-398. doi:10.12659/msmbr.906502
- 108. Paran E, Amir M, Yaniv N. Evaluating the response of mild hypertensives to biofeedback-assisted relaxation using a mental stress test. *J Behav Ther Exp Psychiatry*. Jun 1996;27(2):157-67. doi:10.1016/0005-7916(96)00020-1
- 109. Schein MH, Gavish B, Herz M, et al. Treating hypertension with a device that slows and regularises breathing: a randomised, double-blind controlled study. *J Hum Hypertens*. Apr 2001;15(4):271-8. doi:10.1038/si.jhh.1001148
- 110. Meles E, Giannattasio C, Failla M, Gentile G, Capra A, Mancia G. Nonpharmacologic treatment of hypertension by respiratory exercise in the home setting. *Am J Hypertens*. Apr 2004;17(4):370-4. doi:10.1016/j.amjhyper.2003.12.009
- 111. Yang J, Chen J, Yang M, et al. Acupuncture for hypertension. *Cochrane Database Syst Rev.* Nov 14 2018;11:Cd008821. doi:10.1002/14651858.CD008821.pub2
- 112. Chen H, Shen FE, Tan XD, Jiang WB, Gu YH. Efficacy and safety of acupuncture for essential hypertension: A meta-analysis. *Med Sci Monit*. May 8 2018;24:2946-2969. doi:10.12659/msm.909995
- Zhao H, Li D, Li Y, et al. Efficacy and safety of acupuncture for hypertension: An overview of systematic reviews. *Complement Ther Clin Pract*. Feb 2019;34:185-194. doi:10.1016/j.ctcp.2018.12.003
- 114. Ho MJ, Bellusci A, Wright JM. Blood pressure lowering efficacy of coenzyme Q10 for primary hypertension. *Cochrane Database Syst Rev*. 2009;(4):Cd007435. doi:10.1002/14651858.CD007435.pub2
- 115. Ho MJ, Li EC, Wright JM. Blood pressure lowering efficacy of coenzyme Q10 for primary hypertension. *Cochrane Database Syst Rev*. Mar 3 2016;3(3):Cd007435. doi:10.1002/14651858.CD007435.pub3
- 116. Dong JY, Qin LQ, Zhang Z, et al. Effect of oral L-arginine supplementation on blood pressure: a meta-analysis of randomized, double-blind, placebo-controlled trials. *Am Heart J*. Dec 2011;162(6):959-65. doi:10.1016/j.ahj.2011.09.012
- 117. Paran E, Novack V, Engelhard YN, Hazan-Halevy I. The effects of natural antioxidants from tomato extract in treated but uncontrolled hypertensive patients. *Cardiovasc Drugs Ther*. Apr 2009;23(2):145-51. doi:10.1007/s10557-008-6155-2



- 118. Li K, Liu C, Kuang X, Deng Q, Zhao F, Li D. Effects of multivitamin and multimineral supplementation on blood pressure: a meta-analysis of 12 randomized controlled trials. *Nutrients*. Aug 3 2018;10(8)doi:10.3390/nu10081018
- 119. Liu X, Wei J, Tan F, Zhou S, Würthwein G, Rohdewald P. Pycnogenol, French maritime pine bark extract, improves endothelial function of hypertensive patients. *Life Sci.* Jan 2 2004;74(7):855-62. doi:10.1016/j.lfs.2003.07.037
- 120. Feringa HH, Laskey DA, Dickson JE, Coleman CI. The effect of grape seed extract on cardiovascular risk markers: a meta-analysis of randomized controlled trials. *J Am Diet Assoc*. Aug 2011;111(8):1173-81. doi:10.1016/j.jada.2011.05.015
- 121. Sirtori CR, Arnoldi A, Cicero AF. Nutraceuticals for blood pressure control. *Ann Med.* 2015;47(6):447-56. doi:10.3109/07853890.2015.1078905