High Blood Pressure

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Blood pressure is the measurement of systolic pressure (maximum pressure during one heartbeat) over diastolic pressure (minimum pressure between heartbeats). After the landmark SPRINT trial, published in 2015, found that lower blood pressure significantly reduced the risk of cardiovascular outcomes and death, the threshold for high blood pressure (hypertension) was lowered from 140/90 mm Hg to 130/80 mm Hg.

Natural interventions such as quercetin, coenzyme Q10, magnesium, and bioactive whey peptides, along with dietary and lifestyle changes, can help lower blood pressure.

What is Healthy Blood Pressure?

Healthy blood pressure is less than 120/80 mm Hg, and Life Extension recommends an optimal target of 115/75 mm Hg. Observational evidence suggests the risk of cardiovascular disease *doubles* for each increment of 20 mm Hg systolic and 10 mm Hg diastolic above 115/75 mm Hg.

Adding one or more blood pressure-lowering medications may be appropriate if dietary and lifestyle changes alone are insufficient to bring blood pressure into the healthy range.

People with diabetes, pre-existing cardiovascular or kidney disease, or who are over age 80 should be particularly careful with blood pressure-lowering medication. Always consult a doctor before implementing any changes to your daily regimen.

Note: High blood pressure is not the only risk factor for cardiovascular events. People interested in reducing their cardiovascular risks should follow these blood pressure-lowering strategies, and also read the Life Extension Magazine article titled "How to Circumvent 17 Independent Heart Attack Risk Factors."

Dietary and Lifestyle Changes–The First Step in Controlling Blood Pressure

For otherwise healthy people with blood pressure above 120/80 mm Hg, dietary and lifestyle changes are often sufficient to bring blood pressure into a healthy range.

- Follow a healthy diet (eg, Dietary Approaches to Stop Hypertension [DASH] and Mediterranean diets)
- Reduce caloric intake
- Reduce sodium intake and consume sufficient dietary potassium
- Weight loss
- Regular exercise
- Limit alcohol consumption
- Limit use of non-steroidal anti-inflammatory drugs (NSAIDs)
- Get tested for sleep apnea, as it can increase the risk of high blood pressure
- Manage stress

Note: Using an **at-home blood pressure monitor** to regularly monitor blood pressure throughout the day is an effective way to track effectiveness of dietary and lifestyle changes and other interventions for blood pressure.

Medications to Help Lower Blood Pressure

If diet and lifestyle changes alone do not sufficiently lower blood pressure, blood pressure medication may be appropriate. Consult a qualified healthcare provider before beginning medical treatment for high blood pressure.

- First-line recommendation
  - Angiotensin II receptor blockers (particularly telmisartan)
  - Angiotensin-converting enzyme inhibitors
- Second-line recommendation
  - Thiazide diuretics
- Third-line recommendation
  - Calcium channel blockers

Simultaneous use of more than one blood pressure medication, called combination therapy, may be appropriate for people in whom a single drug fails to control blood pressure.

Note: Beta-blockers are generally *not* recommended as first-line therapy for blood pressure reduction except in those with an indication for beta-blocker therapy such as recent heart attack or heart failure.

What Natural Interventions May Help Lower Blood Pressure?

- **Quercetin**. Quercetin, a plant flavonoid shown to effectively lower blood pressure, is linked to lower cardiovascular risk. It is believed to act as an angiotensin receptor blocker.
- **Myricetin**. Myricetin is a flavonoid like quercetin, which also appears to act as an angiotensin receptor blocker. Myricetin may lower blood pressure in diabetics with hypertension.
- **Stevioside**. Stevioside, an extract from the Stevia plant commonly used as a sweetener in the United States, can also act as a calcium channel blocker to reduce blood pressure.
- **Melatonin**. Melatonin helps relax blood vessels and inhibit the sympathetic nervous system, both of which can reduce blood pressure. A meta-analysis indicated melatonin supplementation was effective at lowering nocturnal blood pressure.
- **Fish oil**. Fish oils and omega-3 fatty acids are associated with lower cardiovascular risk. Fish oil supplements have been shown to lower blood pressure in numerous clinical studies.
- **Coenzyme Q10**. Coenzyme Q10 has strong antihypertensive and cardioprotective effects, which may be due to its protection of various vasodilators.
- **Magnesium**. Magnesium supplementation can lower blood pressure in people with hypertension. It can improve endothelial function and act as a calcium channel blocker and vasodilator.
- Other natural interventions include **whey protein peptides**, **grape polyphenols**, **pomegranate**, **olive leaf extract**, **celery seed extract**, and **hesperidin**.

Introduction

Life Extension has long warned that **blood pressure** exceeding **115/75** mm Hg can be deadly.[1-4] A large study published in 2015 helped corroborate our contention, but also pointed out some important caveats that aging individuals should be aware of before embarking on an aggressive blood-pressure-lowering regimen.

The SPRINT trial results were published November 9th, 2015 in the *NewEngland Journal of Medicine*.[5]

This randomized controlled trial that enrolled over 9,300 subjects showed that non-diabetics at increased cardiovascular risk can substantially **reduce** their risk of cardiovascular events and death by lowering their blood pressure to levels below what were clinical standards at that time.

One group of SPRINT trial participants was intensively treated with blood-pressure-lowering medications to a target systolic blood pressure of less than 120 mm Hg. The other group received medications with a treatment goal of achieving systolic blood pressure of less than 140 mm Hg. The intensively treated subjects took, on average, one additional blood pressure medication compared with the standard treatment group.

The trial was scheduled to last for 5 years, but was stopped after a median of only 3.3 years of follow up because subjects who underwent more intensive blood pressure lowering had a dramatic **25%** risk reduction for a composite of cardiovascular outcomes and a **27%** lower risk of death from any cause compared with the standard-treatment group.

But while the intensive treatment led to better cardiovascular and overall outcomes, it did increase the risk of kidney problems. As readers of Life Extension publications are aware, aggressive blood-pressure-lowering treatment has the potential to cause side effects, such as impaired kidney function.[6,7] We have long recommended regular blood testing to assess kidney function, as well as overall health; this strategy is particularly important for people who undergo aggressive blood-pressure-lowering treatment. By periodically testing one's **glomerular filtration rate**, **creatinine**, and **cystatin-C**, declining kidney function can be identified in time to initiate preventive measures.

Subsequent to publication of the SPRINT trial results, major shifts have occurred in the conventional interpretation of blood pressure levels. In late 2017, a consortium of prominent medical organizations focused on heart and vascular health released updated guidelines overhauling the definition of high blood pressure.[8] The most significant change was that the threshold for overt Stage 1 hypertension dropped from 140/90 mm Hg to 130/80 mm Hg. This change caused millions of additional Americans to suddenly be classified as having high blood pressure.

While we at Life Extension applaud the new guidelines for increasing awareness of the dangers of blood pressure levels previously described only as "prehypertension," it is disconcerting that it took these major medical organizations this long to lower blood pressure thresholds. Life Extension has advocated a target blood pressure for most people of 120/80 mm Hg for many years, with an optimal level of 115/75 mm Hg for many people.

This protocol outlines a ***systematic approach*** to blood pressure control that combines natural interventions—such as **quercetin**, **myricetin and myricitrin**, **stevioside**, and **melatonin**—and lifestyle strategies with prescription antihypertensive drugs. When coupled with consistent **at-home blood pressure monitoring** and periodic **blood testing** to assess kidney function, this approach can help achieve a target blood pressure of **115/75 mm Hg** while minimizing risk.

Growing Body of Evidence for Benefits of Lower Blood Pressure Targets

The table below shows the blood pressure categorization thresholds based on the 2017 consortium guidelines.[8]

Blood Pressure Category	Systolic mm Hg (upper #)		Diastolic mm Hg (lower #)
Normal	Less than 120	*and*	Less than 80
Elevated	120 – 129	*and*	Less than 80
High Blood Pressure (Hypertension) Stage 1	130 – 139	*or*	80 - 89
High Blood Pressure (Hypertension) Stage 2	At least 140	*or*	At least 90
Hypertensive Crisis	Higher than 180	*and/or*	Higher than 120

We at Life Extension agree that "normal" blood pressure levels are below 120/80—with an optimal target being 115/75 for most adults up to age 80. According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure, cardiovascular disease risk ***doubles*** for each increment of 20 mm Hg systolic and 10 mm Hg diastolic above 115/75 mm Hg.[3] These findings become even more concerning when considering the staggering prevalence of higher-than-normal blood pressure: up to **half** of adults worldwide have blood pressure levels ranging from 120/80 to 139/89 mm Hg.[9]

A recent meta-analysis of observational studies showed that blood pressure in this range correlates with a nearly 20% increased risk of declining kidney function; the association was especially strong in older individuals.[10]

In 2006, an analysis of 8,960 middle-aged adults in the Atherosclerosis Risk in Communities (ARIC) study demonstrated that individuals with blood pressure levels ranging from 120/80 to 139/89 mm Hg had about double the risk of cardiovascular disease compared with people whose blood pressure was *below* 120/80 mm Hg.[1]

A meta-analysis of 61 prospective trials evaluated the relationship between blood pressure and cardiovascular-related mortality rates for one million individuals with no known history of cardiovascular disease. Researchers noted that at least down to 115/75 mm Hg, there is no threshold where lower blood pressure is not directly associated with lower mortality rates due to cardiovascular events. In addition, among people 40 to 69 years old, each 20 mm Hg difference in systolic blood pressure was associated with at least a **twofold** difference in overall mortality due to stroke, ischemic heart disease, or other cardiovascular events.[2]

With the publication of the SPRINT trial results, the evidence base supporting more aggressive blood pressure treatment targets in select populations continues to broaden. In late 2016, *Life Extension Magazine* published a comprehensive analysis of the SPRINT trial and an overview of the shortcomings of conventional views regarding blood pressure in an article titled "Lower Blood Pressure Empowers Longer Life."

IS LOWER BLOOD PRESSURE ALWAYS BETTER?

The concept that "lower is always better" in the context of aggressive blood pressure reduction can be a recipe for disaster, in particular for elderly, frail patients.

Often told is the story of the young intern fresh from medical school graduation starting their residency. The intern aggressively treats their older patients to achieve rapid blood pressure reduction, yet is dismayed when their kidney function and cognitive abilities deteriorate rapidly.

Wiser, more experienced physicians know that older patients with pronounced pre-existing vascular disease and other medical problems often require higher blood pressure to perfuse critical organs like the heart, kidneys, and brain. These patients require a higher *perfusion pressure* to allow blood to reach critical organs and tissues throughout the body.[11]

Some older patients simply do not tolerate aggressive blood pressure reduction to a predefined value, which requires careful monitoring of kidney function and blood tests for BUN (blood urea nitrogen), creatinine, cystatin-C, and electrolytes like potassium and sodium, as well as assessment of cognitive function. These tests are necessary to facilitate appropriate titration of antihypertensive medication to a blood pressure tolerated by these patients.

Life Extension's Protocol for Optimal Blood Pressure Control

For decades, Life Extension has suggested that for most otherwise healthy adults up to age 80, an optimal target blood pressure is **115/75** mm Hg. Some adults with pre-existing cardiovascular disease, diabetes, or significant kidney disease may not tolerate aggressive blood pressure control, and caution must be used when lowering blood pressure in all aging adults, paying careful attention to heart function[202-205] as well as renal and cognitive function. In patients with diabetes, aggressive blood pressure control may lead to *worse* outcomes based upon the current research data. Baseline blood pressure and health status must be taken into account during the implementation of this protocol:

- Those whose baseline blood pressure exceeds 120/80 mm Hg and are otherwise healthy should begin by implementing phase 1 of this protocol, which consists of dietary and lifestyle changes as well as targeted dietary supplementation, for a 3-month trial period. If this 3-month trial does not produce consistent blood pressure readings of approximately 115/75 mm Hg, the patient should consider discussing with his or her physician the appropriateness of including one or more blood-pressure-lowering medications into the regimen, as described in phase 2 of this protocol.
- Diabetics whose baseline blood pressure exceeds 120/80 mm Hg should implement phase 1 of this protocol (diet and lifestyle changes along with targeted natural interventions), but should carefully weigh the risks and benefits of blood-pressure-lowering drug treatment. A large clinical trial conducted by the ACCORD Study Group showed that, in diabetics, intensive antihypertensive drug treatment targeting a systolic blood pressure of less than 120 mm Hg did not reduce fatal and nonfatal cardiovascular events compared with less-intensive treatment targeting a systolic blood pressure of less than 140 mm Hg, although there was a non-significant trend toward benefit in some participants. A 2016 analysis of data on more than 73,000 subjects from 49 clinical trials investigated the link between blood pressure levels and treatment outcomes in diabetics. **The research team found that antihypertensive treatment in diabetics whose systolic blood pressure was *under* 140 mm Hg led to *worse* outcomes. Specifically, diabetics whose blood pressure was under 140 at baseline experienced a 15% increased risk of cardiovascular death as a result of further blood-pressure-lowering treatment, with no observed benefit.**[12-14]
- People who have significant pre-existing cardiovascular or kidney disease (including previous kidney transplant) and individuals over the age of 80 may not tolerate aggressive blood-pressure-lowering drug therapy, and may need a slow, steady, individualized approach.
- Evidence for an "ideal" blood pressure target for people over age 80 is unclear at the present time since mixed results have been observed.[2,15-17] This adds to the critical importance of protecting one's inner arterial lining (**endothelium**) throughout life. A number of strategies for protecting arterial health and preserving endothelial function are described in Life Extension's Atherosclerosis and Cardiovascular Disease protocol.
- Anyone already on a physician-supervised plan to lower their blood pres program or altering their plan.

When High Blood Pressure Requires Urgent Care – Hypertensive Crisis

A hypertensive crisis is an extreme and sudden increase in blood pressure that can lead to a stroke and/or damage to other organs. Any blood pressure reading of 180/120 mm Hg or higher is worrisome, considered a hypertensive crisis, and necessitates immediate evaluation and treatment. If your blood pressure reading is this high, do not rely on the diet, lifestyle and supplementation recommendations described here—seek immediate medical attention.

Phase 1: Diet and Lifestyle Changes and Targeted Natural Interventions

The initial phase of Life Extension's systematic strategy for blood pressure control involves diet and lifestyle changes combined with targeted natural interventions. Blood pressure readings should be taken twice daily for at least 3 days prior to embarking on this regimen, and the average blood pressure should be recorded. After initiating the phase 1 regimen, blood pressure should be monitored and recorded twice daily. The recommendations described here should be continued indefinitely,[18] even if medications are required to maintain blood pressure in the target range of 115/75 to 120/80 mm Hg.

For people whose blood pressure exceeds 120/80 mm Hg, these dietary and lifestyle changes and natural interventions may be tried for 3 months before medications are considered.

The Importance of At-Home Blood Pressure Monitoring

Monitoring blood pressure outside of the doctor's office is emerging as a standard of care for high blood pressure, as it helps to more accurately diagnose and track treatment efficacy.[19] Everyone who has been diagnosed with high blood pressure should have an **at-home monitor** in order to ensure that any intervention they are undertaking is working to help keep their blood pressure readings around 115/75 throughout the day.

The importance of regular at-home blood pressure monitoring cannot be overstated. In fact, monitoring your blood pressure at home may help you control your blood pressure, possibly obviating the need to increase medication dosage. In a randomized controlled trial, 136 participants with uncontrolled high blood pressure were assigned to at-home blood pressure monitoring or usual care; their medication regimen was not modified. Those who regularly monitored their blood pressure at home saw significant reductions in systolic and diastolic blood pressure compared with those who did not self-monitor. At the end of the two-month trial, **32.4%** of the self-monitoring group had blood pressure of less than 130/80 mm Hg, while only ***half*** as many participants—16.2%—who did not self-monitor saw their blood pressure fall below this level.[20] Several other studies have found similar benefits associated with at-home blood pressure monitoring.[21-24]

Dietary and Lifestyle Changes

Healthy Diet (DASH- or Mediterranean-Type Dietary Pattern). The Dietary Approaches to Stop Hypertension (DASH) diet is high in fruits, vegetables, nuts, and low-fat dairy products, and emphasizes fish and chicken over red meat. DASH is low in saturated fat, cholesterol, sugar, and refined carbohydrates,[25-27] and is especially high in fiber (31 g/day) and potassium (4.7

g/day), factors that likely contribute to its efficacy for treating hypertension.[28] A sodium-restricted DASH diet may be particularly effective.[29] Research has shown that the DASH diet, when combined with a weekly cognitive-behavioral weight loss intervention and supervised exercise sessions 3 times per week, helped reduce systolic blood pressure by 16.1 mm Hg and reduce weight by 19.2 lbs in overweight men and women with above-normal blood pressure.[30]

The Mediterranean dietary pattern emphasizes similar foods, and may include moderate amounts of wine with dinner. This dietary pattern has a robust research record associating greater adherence with reduced risk of cardiovascular disease, diabetes, neurodegenerative disease, cancer, and death from all causes, as well as with lower blood pressure.[31-35]

Caloric Restriction. Caloric restriction is the long-term reduction of dietary calories while still consuming adequate amounts of essential nutrients. Caloric restriction studies have demonstrated benefit for blood pressure, diabetes, metabolic syndrome, heart disease, and possibly for the prevention of cancer. Clinical studies generally restrict calorie intake by 10–30% compared with normal energy consumption. Studies of long-term caloric restriction in many species have demonstrated that it extends life and retards age-related diseases.[36,37]

Caloric restriction's benefits are mediated through multiple physiologic pathways, including AMPK activation, reduction of inflammation, improved insulin sensitivity and nitric oxide metabolism, angiotensin-blocking effects, and reversal of age- and obesity-related changes in the nervous system.[38-43] Even modest weight loss induced by caloric restriction results in improvement in arterial stiffness superior to that achieved by resistance training exercise.[44]

During a two-year clinical caloric restriction trial in which participants consumed 1750–2100 calories per day, an impressive reduction in blood pressure ensued: systolic blood pressure dropped by 25% and diastolic blood pressure dropped by 22%.[45] In a two-year randomized controlled trial of less than 25% caloric restriction, multiple cardiovascular risk parameters improved more in the caloric restriction group, including reductions in systolic and diastolic blood pressure.[46] A study of non-drug interventions compared a low-salt diet, calorie restriction, and exercise for an average of 23 months in 825 subjects with high blood pressure. Caloric restriction lowered systolic blood pressure by 6.6 mm Hg, on average. Among the caloric restriction group, there was a 17% chance of a blood pressure reduction of 10 mm Hg systolic and 5 mm Hg diastolic.[47]

Reduce Sodium Intake and Maintain Sufficient Dietary Potassium. Higher salt (sodium) intake is associated with higher blood pressure and greater risk of cardiovascular disease. Limiting salt intake lowers blood pressure[29] and cardiovascular risk, and salt reduction is part of standard dietary advice for blood pressure treatment.[48] Similarly, evidence from observational studies and clinical trials consistently indicates that high levels of dietary potassium are associated with lower blood pressure.[49,50] The DASH diet, Mediterranean diet, and vegetables, fruits, legumes, whole grains, and nuts all contain a healthy balance of sodium and potassium.

Weight Loss. A reduction of systolic blood pressure by 5–20 mm Hg accompanying weight loss has been observed in several studies.[51] Weight loss may also allow a decrease in the required dose of blood pressure medications.[48] Weight loss has been found to be especially important in adults under the age of 65. For adults over 65, weight had less impact on systolic blood pressure.[52] Refer to the Weight Loss protocol for an overview of a comprehensive approach to attaining a healthy weight.

Exercise. Regular exercise has been associated with average reductions in blood pressure of 3.2–3.8 mm Hg (systolic) and 2.6–3.5 mm Hg (diastolic) in thousands of subjects across many studies.[53-55] Even something as simple as breaking up prolonged sitting with light intensity walking was associated in one study with lower blood pressure (-3 mm Hg systolic and -3 mm Hg diastolic).[56]

Limit Alcohol Intake. In adults ages 20–84 without high blood pressure, the National Health and Nutrition Examination Survey (NHANES) showed that alcohol consumption above two drinks per day in men and one drink per day in women was associated with higher systolic blood pressure in both men and women.[57] The good news is that limiting alcohol consumption to less than two drinks per day for men and less than one drink per day for women can reduce systolic blood pressure by 2–4 mm Hg.[58]

Limit Use of NSAIDs. Nonsteroidal anti-inflammatory drugs (NSAIDs), especially ibuprofen, have been shown to increase blood pressure in people with hypertension.[59] People with high blood pressure who take NSAIDs have an elevated risk of developing chronic kidney disease. Researchers found that those with high blood pressure who had been taking NSAIDs for at least three months were 32% more likely to have chronic kidney disease than those who didn't take NSAIDs, and those who used NSAIDs more than once a day had a 23% greater risk of developing chronic kidney disease than people who didn't.[60] Other medications that can have an effect on blood pressure include some tricyclic and other types of antidepressants, older high-dose oral contraceptives, migraine medications, and cold remedies (eg, pseudoephedrine).[4]

Get Tested for Sleep Apnea. Symptoms of obstructive sleep apnea include snoring and choking, gasping, or silent breathing pauses during sleep. Sleep apnea is a major underappreciated risk factor for high blood pressure. Rates of sleep apnea have greatly increased over the past two decades and are now estimated to occur in 26% of adults between the ages of 30 and 70 years old.[61] Sleep apnea causes a sudden drop in blood oxygen, which can lead to an increase in blood pressure.[62] A meta-analysis of randomized controlled trials found that continuous positive airway pressure (CPAP), a treatment for sleep apnea, helped to decrease blood pressure in individuals with sleep apnea and resistant hypertension by nearly 5 mm Hg systolic and 3 mm Hg diastolic.[63]

Manage Stress. Acute stress can cause short-lived blood pressure spikes, and effectively managing stress may improve blood pressure and overall health. The body's stress response results in release of the hormones cortisol and epinephrine, which elevate heart rate and cause blood vessel constriction, raising blood pressure.[64] A meta-analysis found that individuals who had stronger responses to acute psychological stress were 21% more likely to develop hypertension.[65]Many strategies for reducing stress are described in Life Extension's Stress Management protocol.

Targeted Natural Interventions

Quercetin. Quercetin is a type of plant pigment called a flavonoid. Many fruits and vegetables contain quercetin. Studies over the last few decades have found that quercetin intake is linked to reduced cardiovascular disease. More recently, intervention studies in animals and humans have shown that quercetin supplementation lowers blood pressure.[66] Quercetin is thought to lower blood pressure through multiple mechanisms, including functioning as an angiotensin receptor blocker (ARB). In fact, a 2015 study showed quercetin achieved a similar estimated receptor docking score for the angiotensin receptor as some pharmaceutical ARBs, including irbesartan and losartan.[67]

The blood-pressure-lowering capacity of quercetin has been observed in several clinical trials. For example, a trial in 93 overweight or obese individuals showed 150 mg of supplemental quercetin daily for six weeks reduced systolic blood pressure by 2.6 mm Hg.[68] In a separate randomized controlled trial, 49 men consumed 150 mg of quercetin or a placebo each day for eight weeks. Subjects who took quercetin experienced a 5.7 mm Hg reduction in 4-hour postprandial (after-meal) blood pressure, while placebo recipients' blood pressure did not change significantly.[69] A 2015 randomized controlled trial found that in hypertensive subjects six weeks of treatment with 162 mg of quercetin daily lowered 24-hour ambulatory blood pressure by 3.6 mm Hg compared with placebo.[70] Other trials that used different quercetin doses and treatment durations have also shown that this flavonoid effectively lowers blood pressure.[71,72]

Myricetin and myricitrin. Like quercetin, myricetin is a flavonoid present in vegetables, fruits, nuts, berries, tea, and red wine.[73,74] And also as with quercetin, it appears that myricetin functions as an angiotensin receptor blocker (ARB).[67] Preclinical studies have shown that myricetin attenuates the rise in blood pressure in response to hypertensive stimuli in animals.[75,76] Myricitrin, also a naturally occurring flavonoid, is converted to myricetin by intestinal flora.[77] Both myricetin and myricitrin have anti-inflammatory properties,[78,79] and myricitrin has shown anxiolytic properties in a preclinical study.[80]

In an uncontrolled 2014 pilot clinical study on diabetics with normal blood pressure, 600 mg of the myricitrin-containing herb *Eugenia punicifolia* daily for three months led to an 11 mm Hg reduction in systolic blood pressure, and a 6 mm Hg reduction in diastolic blood pressure.[81]

Stevioside. A glycoside derived from the leaves of *Stevia rebaudiana,* stevioside is commonly known in the United States as a sweetener. In South America and Asia, extracts of the Stevia plant have been used traditionally to control blood sugar levels.[82,83] Preclinical evidence has shown that stevioside may help control blood pressure by functioning as a calcium channel blocker. Blocking calcium channels is how some medications like verapamil lower blood pressure.[84-86]

A 2015 meta-analysis of data from published studies found stevioside reduced blood pressure by nearly 12 mm Hg (for diastolic pressure) when used for more than one year. Overall, studies in this analysis that used predominantly stevioside as the intervention showed an average reduction of 4.5 mm Hg in systolic blood pressure. The dosage of stevioside used in the studies included in this analysis ranged from 750 to 1,500 mg daily.[87]

Melatonin. Melatonin is well-known and widely used as a natural sleep aid. It is a hormone that the pineal gland releases at night to promote restful sleep and help regulate circadian (day-night) body rhythms.[88]

Melatonin has some other important but underappreciated health benefits: it appears to help control blood pressure by acting within the central nervous system as well as peripheral parts of the body. Peripherally, melatonin helps relax blood vessels and promote vasodilation, which reduces blood pressure. Melatonin can also inhibit the sympathetic nervous system, overstimulation of which can contribute to high blood pressure.[89,90] Uncontrolled nocturnal hypertension is a serious problem that many people may not take into consideration. Elevated nighttime blood pressure contributes to cardiovascular disease and mortality, and is especially prevalent in people with sleep apnea.[91-93]

In a 2011 meta-analysis of data from seven studies (221 subjects in total), 2–3 mg of controlled release melatonin at bedtime reduced nocturnal systolic blood pressure by 6 mm Hg, and nocturnal diastolic pressure by 3.5 mm Hg.[94]

Fish Oil. A 2002 review of 36 different trials that used fish oil supplements to treat hypertension found that fish oil reduced both systolic and diastolic blood pressure. The median dose of fish oil used in these trials was 3.7 g per day.[95] In 2014, a rigorous analysis of 70 randomized controlled trials found that fish oil supplements reduced both systolic and diastolic blood pressure, with the strongest effects in those with untreated hypertension; fish oil also successfully lowered blood pressure in individuals without hypertension. Amounts over 2000 mg were required to lower diastolic blood pressure.[96]

Omega-3 fatty acids and fish oils are among the most important cardioprotective nutrients. Higher fish intake is associated with lower rates of heart failure, sudden cardiac death, ischemic stroke, myocardial infarction, and death from any cause in those with

coronary heart disease. The omega-3 fat eicosapentaenoic acid (EPA) in fish oil exerts these protective effects by inhibiting inflammation, improving signaling across cell membranes, and regulating membrane ion channels to prevent fatal arrhythmias.[97-100]

Coenzyme Q10. An in-depth review examined randomized controlled trials that used coenzyme Q10 (CoQ10) supplementation, for a minimum of three weeks, to treat primary hypertension. Treatment with CoQ10 resulted in an average decrease in systolic blood pressure of 11 mm Hg and an average decrease in diastolic blood pressure of 7 mm Hg.[101] CoQ10's antihypertensive effects may be a result of nitric oxide-dependent vasodilation and protection of nitric oxide from free radical-mediated degradation; CoQ10 may also boost production and increase tissue sensitivity of prostacyclin, a potent vasodilator that prevents blood clotting.[102] CoQ10 supplementation has demonstrated efficacy for decreasing risk of major cardiovascular events and death from cardiovascular and all causes; improving endothelial function, an important concern in high blood pressure, including in statin-treated diabetics; and increasing activity of the free radical modulating enzyme superoxide dismutase.[103-106] In a five-year randomized trial of 443 elderly individuals, CoQ10 combined with selenium reduced cardiovascular mortality by half compared with placebo.[107]

Magnesium. Magnesium supplementation dose-dependently lowers blood pressure in hypertensives.[108] Based on data from epidemiologic and observational studies, individuals with high blood pressure have lower intakes of magnesium than those with normal blood pressure, and low magnesium intake is associated with greater risk of having and dying from heart disease. Magnesium intake of 500–1000 mg per day is associated with lower systolic and diastolic blood pressure. Magnesium also appears to increase the effectiveness of all classes of anti-hypertensive medications. Magnesium's effectiveness is attributable to its ability to improve endothelial function, act as a natural calcium channel blocker and vasodilator, and possible anti-inflammatory activity.[109-113]

In a meta-analysis of seven studies that enrolled patients with systolic blood pressure over 155 mm Hg who had taken antihypertensive medication for at least six months, magnesium supplementation was shown to significantly lower systolic and diastolic blood pressure, by an average of 18.7 mm Hg and 10.9 mm Hg, respectively.[114] Low serum magnesium is associated with a decline in kidney function and an increased risk of chronic kidney disease.[115] Magnesium status can be assessed using the red blood cell magnesium test.[116]

Whey Protein Peptides. Whey supplementation and the administration of specific dairy peptides has been demonstrated to improve blood pressure, and appears to do so through a mechanism similar to that of ACE-inhibiting medications.[117] While this ACE-inhibitory effect is less powerful than that of prescription drugs, whey protein is generally without side effects, and ACE inhibitors have considerable possible adverse effects, contraindications, and drug interactions.[118,119] Some evidence suggests the blood-pressure-lowering effect of whey and whey peptides is an effect of long-term supplementation rather than short-term whey administration. Whey protein peptides may also improve measures of arterial stiffness, in part as a result of inhibition of the release of the vasoconstrictive molecule endothelin-1.[120-126]

Grape Polyphenols. A thorough analysis of randomized controlled trials found that, compared with controls, grape polyphenol treatment lowered systolic blood pressure, and appeared to have its strongest effects in subjects with metabolic syndrome. There is considerable evidence that this effect is mediated by grape polyphenols' ability to substantially improve endothelial function in both healthy subjects and in those at high cardiovascular risk. This improvement is apparent just 30–60 minutes after ingestion. The endothelial effect of grape polyphenols may be explained by a modulation of nitric oxide metabolism via activation of the PI3K/Akt signaling pathway.[127-129]

In a randomized controlled trial in middle-aged subjects with blood pressures ranging from 120-139/80-89 mm Hg, grape seed extract—a rich source of grape polyphenols—effectively lowered systolic blood pressure by 5.6% and diastolic blood pressure by 4.7%. The observed improvement was nearly double in those with the highest blood pressure, and the grape seed extract group also demonstrated a trend toward improved insulin sensitivity.[130]

Pomegranate Extract. Pomegranate juice and its polyphenolic extract have established cardioprotective benefits that include reduction in systolic and diastolic blood pressure.[131-133] Pomegranate juice naturally inhibits the angiotensin-converting enzyme, mimicking the mechanism of antihypertensive ACE inhibitor drugs.[134,135] Animal studies indicate that pomegranate juice extract also interferes with the hypertensive effect of angiotensin II, a property similar to angiotensin II receptor blocker (ARB) medications, and has a beneficial influence on endothelial nitric oxide.[136,137]

Olive Leaf Extract. A 12-week randomized clinical study compared the blood-pressure-lowering effects of olive leaf extract to the ACE-inhibitor medication captopril in patients with stage I hypertension. Both the olive leaf and the captopril group experienced reductions in systolic and diastolic pressure, with no important difference in the effects of the two compounds. In the olive leaf extract group, systolic and diastolic blood pressure decreased on average by 11.5 mm Hg and 4.8 mm Hg, respectively.[138] This study confirmed results of earlier trials that found olive leaf extract effective for hypertension.[139,140] Olive leaf extract has been shown to increase insulin sensitivity in men at risk of developing metabolic syndrome, a condition often accompanied by high blood pressure.[141] Olive leaf's antihypertensive effect may be attributable to several of the same mechanisms as prescription blood pressure drugs, including calcium-channel blocking, ACE inhibition, and angiotensin II antagonism.[142-145]

Celery Seed Extract. A trial of standardized celery seed extract in 30 patients with mild-to-moderate hypertension found that six weeks of supplementation reduced systolic and diastolic blood pressure by 8.2 and 8.5 mm Hg, respectively.[146] Long-term administration of celery seed extract to hypertensive rats resulted in a substantial reduction in blood pressure.[147] Laboratory studies with celery extract have demonstrated vasodilatory and vasorelaxant activity, which may be mediated by calcium-channel-blocking activity.[148,149]

Hesperidin. The inner peels of sweet orange (*Citrus sinensis*) are a rich source of flavonoids, including hesperidin.[206] Hesperidin and other citrus flavonoids enhance vascular health by improving endothelial function and reducing inflammation.[207,208] In addition, hesperidin's anticoagulant and lipid-regulating properties add to its potential utility in preventing and treating hypertension and other cardiovascular diseases.[209]

In a randomized controlled trial, 64 subjects with type 2 diabetes received either 500 mg of hesperidin per day or placebo for six weeks. Those taking hesperidin had greater reductions in systolic and diastolic blood pressure and inflammatory marker levels compared with placebo.[210] A randomized controlled trial in subjects with metabolic syndrome found that 500 mg of hesperidin for three weeks improved endothelial function and levels of inflammatory markers.[208]

Citrus fruits and their juices have high concentrations of hesperidin.[211] In a controlled clinical trial in healthy individuals, drinking orange juice and taking 500 mg of hesperidin daily for four weeks each resulted in changes in gene expression toward a less inflammatory and less atherosclerosis-promoting profile.[212] In a similar four-week trial, orange juice and supplemental hesperidin were found to have similar positive effects, compared with placebo, on diastolic blood pressure and endothelial function of small blood vessels. This study, in moderately overweight men aged 50–65, suggests hesperidin may be the active compound responsible for oranges' cardioprotective effects.[213] In animal research, hesperidin has been shown to reduce high blood pressure[214] and reverse age-related arterial stiffness.[215]

Hesperidin and its breakdown product, hesperetin, have been found to increase the production of nitric oxide in cells from the inner lining of human blood vessels.[216,217] Nitric oxide from these cells plays a key role in relaxing blood vessel walls and reducing high blood pressure.[218] In the same study, after treatment with hesperidin, human blood vessel cells also produced less endothelin-1, a compound that constricts blood vessels and increases blood pressure, and fewer oxygen free radicals.[216] Hesperidin's ability to raise levels of vessel-dilating nitric oxide has also been demonstrated in animal studies.[219,220] Animal and preclinical research indicates hesperidin may also relax blood vessel walls by altering the function of potassium channels that help regulate muscle contraction in blood vessel walls.[221,222]

Hesperidin, like other plant polyphenols, impacts the health and diversity of the microbial community of the gut. Because the gut microbiome plays a key role in regulating metabolism and inflammation, it is now thought that flavonoids like hesperidin may exert their positive effects on health and disease in part through interactions with gut microbes. The possible links between hesperidin, the gut microbiome, and improved metabolic and cardiovascular health is an exciting and emerging topic in nutrition research.[211,223]

Additional Support. The following natural compounds may be considered for additional cardiovascular and blood pressure support.

- **Calcium and vitamin K.** Calcium plays an important role in regulating the concentration of minerals that are essential to healthy blood pressure, including sodium, potassium, and magnesium. Calcium is also involved in smooth muscle cell contraction in blood vessels.[150] In a review of 40 randomized controlled trials, an average daily calcium dose of 1,200 mg was associated with a modest reduction in systolic (almost 1.9 mm Hg) and diastolic (almost 1.0 mm Hg) blood pressure. In persons with habitually low calcium intake (≤ 800 mg/day), the hypotensive effect was greater.[151]
- Adequate vitamin K intake is crucial during calcium supplementation. Vitamin K prevents calcium deposition in non-bony tissues like the arteries, and protects against atherosclerotic heart disease. Vitamin K comes in several forms: vitamin K2, also known as menaquinone, has shown the greatest association with reduced cardiovascular risk. Vitamin K is also essential for proper blood coagulation and bone health, and is associated with a reduced risk of cancer and death from cancer.[152-156]
- **L-arginine.** An exhaustive analysis of 11 randomized controlled trials found that L-arginine supplementation, in dosages ranging from 4 to 24 g per day, lowered systolic blood pressure by 5.4 mm Hg and diastolic blood pressure by 2.7 mm Hg, measurably more so than placebo.[157]
- **Chlorogenic acid.** A randomized controlled trial in individuals with mild hypertension found that chlorogenic acid, which is abundant in green coffee beans and specially roasted brewed coffees, lowered systolic and diastolic blood pressure by as much as 5.6 mm Hg and 3.9 mm Hg, respectively, compared with placebo.[158] Another clinical trial compared a coffee beverage that was specially treated to enhance chlorogenic acid activity with a control beverage. The chlorogenic acid-enriched coffee resulted in a reduction in blood pressure, while the control beverage had no effect.[159]
- **Hawthorn extract.** Many studies have shown that several species of hawthorn confer cardiovascular benefits. Hawthorn has long been used in Chinese herbal medicine, and it has been used in North America to treat heart problems since

1800. Clinical trials have shown that supplementation with hawthorn and hawthorn extracts improves mild heart failure, hypertension, and elevated blood lipids.[160]

- **Resveratrol.** Resveratrol is a polyphenol found in grapes, wine, Japanese knotweed, and several other plants. It has been extensively studied as a calorie-restriction mimetic because of its ability to influence metabolic pathways similarly to reducing caloric intake. A meta-analysis of six studies found that supplementation with at least 150 mg of resveratrol daily reduced systolic blood pressure by nearly 12 mm Hg while not significantly affecting diastolic blood pressure.[161]

Phase 2: Adding a Drug Regimen

Many people may not be able to lower their blood pressure to the range of 115/75 – 120/80 mm Hg with dietary and lifestyle changes alone (although those who practice caloric restriction may more easily attain this goal). For those whose blood pressure remains elevated, adding a single blood pressure medication, initially at a low dose, can help lower blood pressure. If a single medication is inadequate, then a second and possibly a third can be added, although side effect risk may increase in those who take high doses of multiple blood pressure medications. A trial period of up to one month should be allocated to assess the impact of each drug added to your regimen.

The regimen described may not be appropriate for aging adults with significant pre-existing cardiovascular disease, metabolic disease, renal disease, and/or major cognitive impairment.

This regimen represents Life Extension's suggestions for most adults up to age 80 who have high blood pressure but are otherwise healthy. Please be aware that evidence suggests African American patients may respond better to initial therapy with a calcium channel blocker or a thiazide diuretic (whereas most other patients tend to show a greater response to angiotensin II receptor blockers or angiotensin-converting enzyme inhibitors).[18]

Maintaining optimal blood pressure is a lifelong endeavor and often requires a diligent, frequently individualized approach.

First-Line Recommendation: Angiotensin II Receptor Blocker (ARB) or Angiotensin-Converting Enzyme Inhibitor (ACEI). Angiotensin II is a peptide hormone naturally produced in the body. It exerts broad influence on blood pressure control. Blunting angiotensin II signaling is an established pharmacologic strategy for lowering blood pressure. This can be accomplished with angiotensin II receptor blockers (ARBs) or angiotensin-converting enzyme inhibitors (ACEIs). Both of these drug classes have been studied in large clinical trials.[162,163] ARBs and ACEIs are similarly effective in reducing the risk of cardiovascular disease and stroke when used in the treatment of primary hypertension, but ARBs may be less likely to cause side effects.[164]

- **Angiotensin II receptor blockers.** Life Extension favors initiating therapy with the ARB telmisartan. A little-known side benefit of ARBs is they enhance insulin sensitivity, increase utilization of fat as energy, and improve mitochondrial function. Of all the drugs in this class, telmisartan, first approved to lower blood pressure in 1998,[165] stands out as superior for potential longevity enhancement.[166-168]

  Studies indicate that telmisartan directly stimulates PPAR-gamma (peroxisome proliferator-activated receptor gamma), a key inducer of beneficial metabolic effects.[169-171] PPAR-gamma activating properties have also been reported for other ARB drugs, but telmisartan is at least 10 times more powerful.[169]

  Telmisartan has been shown in preclinical models to reduce weight gain, increase total energy expenditure, and increase expression of key mitochondrial enzymes in skeletal muscle better than a more popular drug in this class (Diovan).[172-177] Also, telmisartan functions by multiple mechanisms to protect against arterial occlusion,[178-180] including increasing beneficial endothelial nitric oxide.[174,181,182] Lastly, several preclinical and lab studies suggest telmisartan may confer meaningful cancer chemopreventive effects.[183-186]

  If you cannot achieve blood pressure readings of 115/75 – 120/80 mm Hg with diet and lifestyle changes and targeted dietary supplementation alone, consult with your personal physician concerning an initial dose of 20 or 40 mg of telmisartan daily; choosing between 20 and 40 mg should be left to the discretion of your physician because individual patient factors will determine which dose is more appropriate for you.

  To read more about telmisartan and its many merits, refer to the March 2015 *Life Extension Magazine* article titled "Best Drug to Treat Hypertension."

- **Angiotensin-converting enzyme inhibitors.** Angiotensin-converting enzyme inhibitors (ACEIs) function differently than ARBs to lower blood pressure, but have similar indications and benefits.[48,118,119] However, as many as 20% of patients prescribed ACEIs will develop a chronic cough, a side effect not associated with ARBs.[187] ACEIs as a class tend to be associated with more adverse effects compared to ARBs. Also, evidence for potential longevity benefits associated with ARBs may not apply to ACEIs.

Second-Line Recommendation: Thiazide Diuretic (Chlorthalidone). Chlorthalidone, a type of thiazide diuretic, can help lower blood pressure by increasing urinary excretion of salt and water. This drug has been used in the treatment of hypertension and for cardiovascular event risk reduction for decades.[188]

If you cannot achieve your target blood pressure within one month of starting your first medication, add a thiazide diuretic to your daily regimen. Start at a low dose, and allow one month after starting the diuretic to see if your blood pressure falls to target range.

Although thiazides have a long record of safe use and a good risk-benefit ratio, these drugs may cause a drop in your blood electrolyte levels (eg, potassium, sodium, and chloride).[189] You can monitor your electrolyte levels by having a routine blood chemistry panel performed periodically after you begin taking a thiazide diuretic.

Third-Line Recommendation: Calcium Channel Blocker. If you cannot achieve your target blood pressure by adhering to good eating habits, getting plenty of exercise, and taking blood-pressure-lowering supplements along with telmisartan and a thiazide diuretic, consider adding a calcium channel blocker.

Calcium channel blockers, such as amlodipine, influence several aspects of cardiovascular physiology, resulting in lowering of blood pressure. A recent systematic review concluded that calcium channel blockers in combination with thiazide diuretics may be a good option for elderly individuals who have isolated systolic hypertension.[190]

Beta-Blockers: Brief Review of Current Evidence

Sympathetic nervous system activity (our “fight or flight” system) tends to increase as we age, and it is thought that this increase may hasten the development of age-related mortality. Prescription drugs called beta-blockers inhibit the action of epinephrine, the main hormone of our sympathetic nervous system. Because of this mechanism, beta-blockers are used for hypertension and have been studied as a means to increase lifespan.

In a 2013 study, beta-blockers were shown to extend the lifespan of mice and fruit flies. In this study, metoprolol and nebivolol (both beta-blockers) increased the median lifespan of mice by 8.4% and fruit flies by 15–23%.[191]

These changes were not due to calorie restriction or change in activity, as neither the treated mice nor the fruit flies showed changes in food intake or activity level. The authors suggest that the signaling pathway beta-blockers inhibit is a fundamental mechanism that itself regulates an animal’s lifespan.

Mice in the same study that were placed on a calorie-restricted diet had their lifespan extended by 23% (nearly 3 times the extension by beta-blockers). However, beta-blocker treatment doubled the number of liver tumors in the mice, suggesting the compounds were toxic to the liver, even when given at a relatively low dose.

In a more recent animal study, although atenolol (a beta-blocker) changed the mitochondrial membrane fatty acid profile to that of much longer-lived mammals and decreased oxidative stress, lifelong treatment of the mice did not result in any extension of lifespan.[192] The authors concluded that side effects from the drug could have masked the decrease in aging that is usually caused by the change in membrane fatty acid profile.

Beta-blockers used to be considered a first-line treatment for hypertension, but there have recently been some worrisome findings about their use in otherwise healthy adults. The 2014 Evidence-Based Guideline for the Management of High Blood Pressure in Adults (JNC 8) no longer recommends beta-blockers as initial therapy since one study found that the use of beta-blockers resulted in a higher rate of cardiovascular death, myocardial infarction, and especially stroke as compared to use of an ARB.[18]

Also, there is some evidence that some beta-blockers are associated with increased risk of type 2 diabetes. Recent human studies do not support the use of beta-blockers in hypertensive adults who are otherwise healthy.

Table 1: Advantages and Caveats of Common Antihypertensive Drug Classes [48,187,193,194]

Drug Class	Advantages	Caveats
Angiotensin II Receptor Blockers (ARBs) telmisartan, losartan, candesartan, valsartan, fimasartan	Once-daily dose; well tolerated; associated with improved quality of life; reduction in cardiovascular mortality (for telmisartan); indicated in patients who experience coughing from ACEIs; lower risk of swelling (angioedema) compared to ACEIs; considered first-line treatment for patients with hypertension and diabetes, congestive heart failure, chronic kidney disease	Risk of high serum potassium; may cause small increase in serum creatinine in some people via decrease in glomerular filtration rate, but this is usually transient and reversible; should not be used by women who are pregnant or expecting to become pregnant
Angiotensin-converting enzyme inhibitors (ACEIs) benazepril, captopril, enalapril, lisinopril	Indicated in patients with high blood pressure and diabetes, heart failure, chronic kidney disease, or coronary artery disease; may reduce risk of heart attack, stroke, and cardiovascular death in high-risk patients over age 55	Frequent (5–20%) side effect of cough; risk of excessively low blood pressure, excessively high serum potassium; rare risk of swelling (angioedema); should not be used by women who are pregnant or expecting to become pregnant
Beta-Blockers atenololol, metoprolol	Indicated after myocardial infarction and in heart failure and atrial fibrillation patients	Risk of depression, impotence, fatigue, bronchospasm, hypoglycemia, peripheral vascular disease, worsening of lipids, obscuring signs and symptoms of hypoglycemia in diabetics
Calcium Channel Blockers amlodipine, diltiazem, verapamil, nifedipine	Indicated in patients with ischemic heart disease, asthma, kidney disease, peripheral vascular disease, salt sensitivity, and metabolic diseases; tend to be associated with improved quality of life; work independently of sodium consumption	Risk of disturbance of normal heart rhythm; constipation; headache; dizziness; low blood pressure; overgrowth of gums
Thiazide Diuretics hydrochlorothiazide, chlorthalidone, indapamide	Once daily dosing; indicated in congestive heart failure and edema; improve cardiovascular outcomes	Risk of potassium, magnesium, and sodium depletion, and excessive serum calcium levels; cardiac arrhythmias; sexual dysfunction; worsening of lipid and glucose levels

Table 2: Initial Dosages of Common Antihypertensive Drugs		
Class/Drug	**Initial Dose**	**Generic Form Available?**
Angiotensin II Receptor Blockers (ARBs)		
Telmisartan	20 mg per day is lowest, for volume-depleted patients (on diuretics); otherwise 40 mg per day	Yes
Losartan	25 mg per day	Yes
Benicar	20 mg per day	Olmesartan medoxomil, not available
Edarbi	40 mg per day	Azilsartan medoxomil, not available
Irbesartan	75 mg per day	Yes
ACE-Inhibitor		
Lisinopril	5 mg per day	Yes
Diuretic (Thiazide)		
Chlorthalidone	12.5 mg per day	Yes
Beta-Blocker		
Atenolol	25 mg per day	Yes
Calcium Channel Blocker		
Amlodipine	2.5 mg per day	Yes

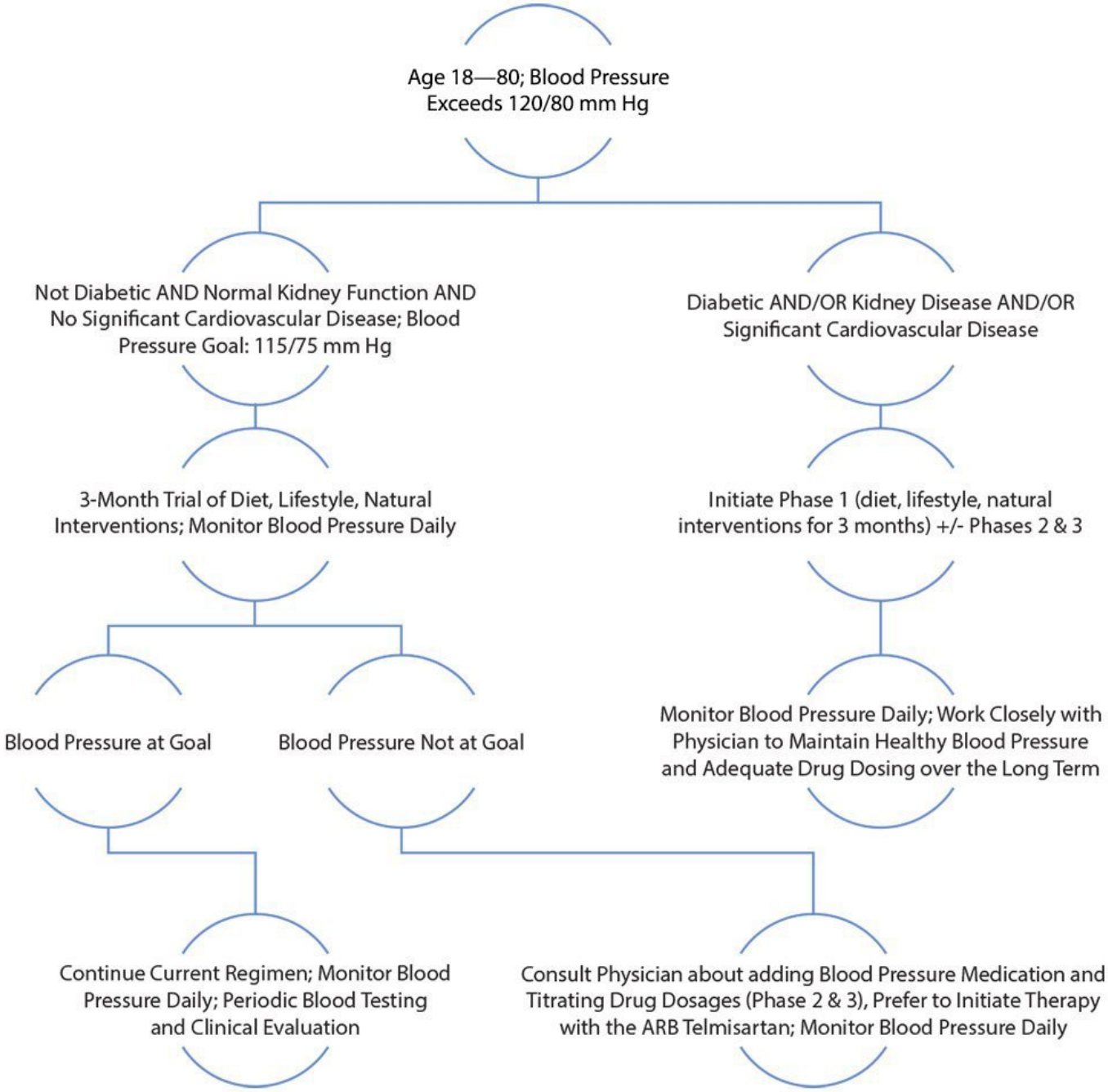
Phase 3: Drug Dosage Titration

There are several approaches to drug and dosage adjustment in the management of high blood pressure. For example, one option is to start with a single medication and then slowly increase the dosage of that medication until the target blood pressure is achieved, side effects limit the dosage, or the maximum recommended dose is reached. In this approach, a second medication may not be added until the dosage limit of the first medication is reached, and the dosage of the second drug is maximized before adding a third.

Another approach, which Life Extension advocates, is to start with a low dose of a single medication, then add a second and third medication before beginning to slowly increase dosages of one drug at a time. This approach may reduce side effects, which may be more likely with higher dosage of a given drug than with lower dosages of multiple drugs.

Overall, decisions to add an additional medication or adjust the dosage of a current medication need to be discussed by the patient and his or her physician. Clinical factors may influence which approach the physician determines to be most appropriate. Many people ultimately require more than one medication to achieve target blood pressure.[195]

Figure 1: Suggested Blood Pressure Management Algorithm



Blood Pressure Medications May Confer Greater Protection if Taken at Bedtime

A number of studies have shown that ***bedtime dosing*** of antihypertensive medication may improve treatment efficacy compared with traditional morning and evening dosage schedules.[196-201]

In one trial that enrolled 661 patients with chronic kidney disease, ambulatory blood pressure was measured at baseline, then tracked for over five years after adjusting the medication schedule according to one of two regimens. In the first group, all antihypertensive drugs were taken upon awakening, while a second group took at least one medication at bedtime. Not only did the second group have lower blood pressure during sleep, but a markedly greater percentage of them gained control over their daytime blood pressure compared with the morning dosing group.[196]

After analyzing the study data, researchers uncovered a dramatic reduction in the risk of cardiovascular events and associated mortality—those taking blood pressure medication at bedtime had only about one-third the risk of those who took all their blood pressure medication in the morning. Moreover, each 5 mm Hg reduction in blood pressure during sleep was tied to a 14% reduction in cardiovascular events during the follow-up period.

In a randomized clinical trial, 204 subjects with high blood pressure were assigned to take a combination of valsartan and hydrochlorothiazide either in the morning or before bed for 12 weeks. Subjects who took their blood pressure medication before bed had better blood pressure control at night than those who took their medication in the morning, and there was no difference in daytime seated blood pressure between the groups. Also, more subjects in the bedtime-dosing group had properly controlled ambulatory blood pressure. The researchers concluded that "…*valsartan/[hydrochlorothiazide] combination should be*

preferably administered at bedtime for treatment of subjects with essential hypertension requiring combination therapy to achieve proper [blood pressure] control."[200]

Several other trials have also shown that bedtime dosing of blood pressure medications offers superior blood pressure control compared with morning dosing.[197-199,201]

Diligent Monitoring to Prevent Treatment-Related Adverse Events

Those who take prescription antihypertensive medications must remain aware of the potential for these drugs to cause kidney dysfunction and electrolyte abnormalities in some people. Also, blood pressure that is too low can cause dizziness, especially upon standing, which may result in fainting and injurious falls. **At-home blood pressure monitoring** is critical, and should be performed **twice daily**, once in the morning and once in the evening.

In order to mitigate the chances of medication-related complications, particularly those related to kidney function, blood tests should be performed regularly to monitor treatment and health status. Changes in medications and medication dosage levels, and changes in overall health status (including urinary and fluid balance symptoms) are indications to repeat testing, bearing in mind that some alterations will manifest rapidly while others may appear gradually. It is important to remember that this applies to all medications, including over-the-counter drugs, not simply to blood pressure medications. For those in stable health, with no change in medication or dosage, testing should be performed every six months at minimum. All changes that could potentially impact kidney function should be closely followed using the indicated laboratory tests.

Important tests for people undertaking strategies to lower blood pressure include:

- Chemistry panel and complete blood count (CBC)
- Cystatin-C
- Orthostatic hypotension evaluation (clinical test)

Blood Pressure Is Not the Only Contributor to Heart Disease

Life Extension has identified at least 17 independent risk factors that increase your likelihood of succumbing to a deadly cardiovascular event. All of these risk factors must be addressed if one's goal is optimal risk reduction.

Although high blood pressure is recognized worldwide as one of the strongest cardiovascular risk factors, focusing only on blood pressure and neglecting the other 16 independent risk factors could be a devastating oversight. These risk factors include:

- Excess LDL
- Excess total cholesterol
- Low HDL
- Excess blood glucose
- Excess homocysteine
- Excess C-reactive protein (CRP)
- Insufficient vitamin D
- Insufficient vitamin K
- Elevated triglycerides
- Low blood EPA and DHA
- Low testosterone (in men)
- Excess estrogen (in men)
- Excess insulin
- Nitric oxide deficit
- Excess fibrinogen
- Elevated levels of oxidized LDL

People interested in maximizing their cardiovascular risk reduction should follow the strategy outlined in this article to control their blood pressure, and also read the Life Extension Magazine article titled "How to Circumvent 17 Independent Heart Attack Risk Factors."

Summary

Life Extension has long suggested that the lower blood pressure achieved by calorie restriction adherents is a critical component of the health and longevity benefits they enjoy. A growing body of evidence supports the benefit of blood pressure lower than 120/80 mm Hg for certain populations.[1-3] The results from the SPRINT trial,[5] published in 2015, lend additional support to a target systolic blood pressure of less than 120 mm Hg as opposed to a more conservative target of less than 140 mm Hg. For decades, Life Extension has advocated a blood pressure goal of **115/75 mm Hg**.

The foundation for Life Extension's approach is the evidence-based diet, lifestyle, and integrative intervention program outlined in this protocol; this aspect of the program should be continued indefinitely for those who want to maximize their health and

longevity through optimal blood pressure control. For those who aren't able to reach a target blood pressure of less than 120/80 mm Hg using these natural measures alone, Life Extension has presented a drug treatment protocol that represents an integration of the most current scientific knowledge, maximizing therapeutic benefit and minimizing the risk of adverse effects.

By working closely with your clinician, regularly monitoring your blood pressure and health status, and taking advantage of the cutting edge information presented here, you can marshal the longevity benefits of optimal blood pressure.

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