# **UW** Integrative Health

Department of Family Medicine and Community Health

# **Heart Health**

# **Overview**

This overview explores how Integrative Whole Health can support prevention and treatment of cardiovascular disease. Each of us may have different reasons why heart health is important in terms of our Mission, Aspiration, Purpose (MAP), and we all have different preferences around how we can keep our hearts healthy. Risk factor profiles vary from person to person and can be addressed in a variety of ways.

What are some of our options? Every aspect of self-care influences cardiovascular disease. This includes Nutrition (e.g., eating a Mediterranean or DASH Diet), Mind and Emotion s (e.g., stress management approaches), Recharge (optimizing sleep), and Physical Activity (e.g., coming up with a personalized activity plan). It also includes Surroundings (pollution levels, work environment), Personal Development (growing and learning), relationships (Family, Friends and Co-workers), and Spirit and Soul (living with meaning and purpose). Beyond self-care, professional care is also important; it includes conventional care, such as medications and procedures, as well as complementary and integrative health (CIH) approaches like mind-body techniques, acupuncture, and taking dietary supplements.<sup>1,2</sup>

Note that this overview focuses primarily on reducing risk related to cardiovascular disease (CVD). In addition, there are specific Integrative Whole Health tools focusing on some of the most common risk factors that contribute to heart disease: <u>hypertension</u>, <u>lipid disorders</u>, <u>achieving a healthy weight</u>, and <u>diabetes</u>. There are also resources that go into more detail about <u>congestive heart failure (CHF)</u> and <u>arrhythmias</u>. Many of the suggestions offered in this overview are also applicable not only for coronary artery disease, but also for peripheral arterial disease and stroke. The narrative below illustrates how Whole Health for the heart could look, informed by the latest research we have.

# **Meet the Patient**

Charles is a 53-year-old man who has been seen in the same primary clinic for many years. He has met with a specially trained volunteer at his clinic to review his Personal Health Inventory (PHI). He has been considering working on a few different areas of his self-care, and now he will be seeing his primary care provider (who is newly trained in an Integrative Health Approach) to discuss how he can reach some of his goals.

Charles' problem list includes the following:

- Anxiety
- Dyslipidemia
- Gastroesophageal reflux disease (GERD)
- Hypertension
- Insomnia (sleeps less than 5-6 hours nightly)
- Obesity
- Posttraumatic stress disorder (PTSD)

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

- Statin intolerance (myalgias with simvastatin and pravastatin)
- Tobacco use (he has smoked a pack a day for 33 years) Family history of coronary artery disease. His father died of a myocardial infarction at age 57. His mother has longstanding hypertension, and his sister had a three-vessel coronary artery bypass graft at age 60.
- Present medications include:
  - Lisinopril 20 mg
  - Aspirin 81 mg
  - Omeprazole 20 mg
  - Zolpidem 5 mg at bedtime
  - Trazodone 100 mg at bedtime

Clinical Data: Charles is 5' 11" tall and weighs 234 pounds. His waist circumference is 43 inches (about 109 cm). His body mass index (BMI) is 32.6. His blood pressure is 152/88. His pulse is 88 and regular.

A review of his most recent lab results is remarkable for the following:

- Low-density lipoprotein (LDL) = 174
- High-density lipoprotein (HDL) = 38
- Triglycerides (TG) = 175
- Renal function is normal
- Fasting blood sugar (FBS) = 118

# **Personal Health Inventory**

Various members of the team review <u>Charles' PHI</u> (Personal Health Inventor). The medical assistant reads it before she takes him to the exam room to check his vital signs. So does his provider, and the nurse who will be calling to check in with him in a few weeks about how he is doing. A few things come up as the team reviews the PHI and talks with Charles:

- **Vitality Signs.** On his Personal Health Inventory (PHI), Charles rates himself a 2 out of 5 for his overall physical well-being. He also gives himself a 2 out of 5 for overall mental and emotional well-being and a 3 out of 5 when he rates his overall life.
- When asked **what matters most** to him, he responds that family matters and he wants to be happier in his marriage. Living a long life is also important.
- **Physical Activity:** Charles rates himself at 2 and would like to be at least at 4. He writes that he was once a good athlete, but now he has little interest in and no energy for fitness activities.
- **Recharge**: For years, he has had trouble getting restorative sleep. Even when he sleeps for more than six hours without waking, which is rare, he does not feel rested in the morning and is tired most of the day.
- **Nutrition**: Charles says he eats whatever is easy and at hand, often grabbing fast food at his job. He and his family rarely eat together. His wife does most of the meal planning.
- **Personal Development**: Charles is an assistant manager at a fast food restaurant. He enjoys the responsibility of his position and sometimes wishes he could take some night courses in business.

- Family, Friends, and Co-workers: He rates himself a 3 and would like the arguments with his wife to stop.
- **Spirit and Soul:** Charles scored himself at 2. He says he had more of a sense of purpose as a young man than he has now. He has not been to church in a few months.
- **Surroundings:** He likes where he lives and is proud of his home. Not a lot of noise or air pollution.
- **Mind and Emotions:** Charles gives himself a 3, saying "it is what it is" and "not much" could make things better. He has never tried any specific stress management or mind-body practices. Watching football on TV is the main way he relaxes.
- **Professional Care:** Charles admits he does not like coming to his medical appointments; he finds them frustrating. "Every person I see tells me the same thing —quit smoking, change your diet, start exercising... It's all BS. No offense—I really appreciate the staff here. I know you're all trying to help me, but I am still scared I am going to have a heart attack just like my dad. I am getting really close to the age he was when he died."

As the team explores all this with Charles, it is important for them to consider potential shared goals. The clinical team wants to lower Charles' cardiac risk, and of course medications will be discussed. Ultimately, Charles shares this goal too, but he might benefit from a different perspective. Over the years, talking about risk factors has not really taken him very far in terms of engaging him with his own care. He mentions that, since talking about his PHI a few weeks ago with his primary care physician, he is willing to consider focusing on Physical Activity and Mind and Emotions. He is curious what the clinical team thinks about this. His other team members heartily agree, and they help him start to create a Personal Health Plan (PHP).

### Introduction

Cardiovascular disease remains the leading cause of death worldwide, accounting for 31% of deaths.<sup>3</sup> It is the leading cause of death for American men and women from most racial and ethnic groups<sup>4</sup>.<sup>5</sup> Each year, about one in every four adult deaths in the U.S. is due to CVD. This equates to one death every 37 seconds. It is also a major cause of disability.<sup>6</sup>

Our understanding of how arterial disease (atherosclerosis) occurs continues to evolve.<sup>7</sup> We know it is an active and complex process. Inflammation is an important factor; anything that can be done to reduce chronic inflammation can potentially help. Irregularities in blood flow, chemical irritants, and various chronic disease cause damage to the inner layer of the arteries. There is then an accumulation of plaque, which is made of fatty substances, cholesterol, cell waste products, calcium, and fibrin (which promotes clotting). White blood cells receive signals to move into an artery's wall, but the process of clearing out the plaque goes wrong for various reasons. The white cells accumulate in the artery wall as lipid-dense foam cells,<sup>8</sup> which release compounds that increase the odds that the artery wall will rupture. Pieces of the plaque can then break off and cause blockages themselves, and when a plaque ruptures, it can trigger the formation of blood clots.

We are just beginning to explore how microRNAs, non-coding RNA molecules, can influence cell signaling and function in cardiac tissue and might become the focus of preventive and therapeutic approaches.<sup>9</sup> Nutrition, among other factors, strongly influence their effects.<sup>10</sup>





#### The Dance Between Risk Factor Management and Personalized Care

There are numerous risk factors for CVD. While some, including age and family history, may not be changed, many others can be.<sup>4</sup> Charles has many of the risk factors we tend to focus on most, including hypertension, dyslipidemia, smoking, physical inactivity, poor dietary habits, and diabetes (or at least indications that he is insulin resistant and will soon meet diabetes criteria). Nearly 80 million U.S. adults have high blood pressure,<sup>11</sup> but fewer than 50% have their blood pressure under control,<sup>12</sup>. Uncontrolled hypertension is behind 62% of strokes and 49% of ischemic cardiac events.<sup>13</sup>

An Integrative Whole Health approach tailors risk factor reduction to each individual's needs and preferences, building a personal health plan (PHP) around what really matters to him or her. This allows for greater opportunity for patient engagement, which is absolutely necessary if heart disease (or any health condition) is to be optimally prevented or managed. Charles' clinical team can help him pinpoint one area (or a few) where he would like to start making changes. Other changes will likely arise as he starts to see some initial success.

Overall, a healthy lifestyle makes a significant difference when it comes to cardiovascular disease risk. Healthy levels of physical activity and alcohol, combined with not smoking and a healthy diet, decrease CVD risk by 66%. Stroke risk is lowered by 60%, and heart failure risk drops by 69%.<sup>14</sup> Findings from the Nurses' Health Study suggest that consistently following a healthy lifestyle could prevent 82% of coronary events<sup>15</sup>; similarly, for the men in the Health Professionals follow up study, 62% of events could have been avoided. <sup>15</sup> A 2012 trial found that lifestyle management had a beneficial effect on some risk factors even in patients who were already optimally medically managed.<sup>16</sup>

Beyond individual behavior change, social determinants of health, such as poverty, illiteracy, urbanization, pollution, maternal nutrition, and policy approaches also play a foundational role<sup>17</sup> (and tie into the Circle of Health—particularly the community piece—in a variety of ways).

#### **Self-Care**

Fascinating research has emerged in recent years identifying a surprisingly large number of self-care factors that can help promote heart health. As you consider approaches to take with people like Charles, there are a number of options for each of the areas of self-care in the Circle of Health.

#### **Physical Activity**

"Exercise is good for you" is not new news for our patients. Charles knows this, and most people do. The key is how to translate that knowledge into practice. It starts by actively engaging each patient in creating their PHP.

A sedentary lifestyle is associated with multiple cardiovascular risk factors, including higher blood pressure, unhealthy weight gain, increased cholesterol levels, and impaired glucose metabolism.<sup>18,19</sup> On the other hand, regular physical activity lessens risk for coronary artery

disease, heart attack, heart failure, hypertension, obesity, and diabetes. It also reduces cardiovascular and all-cause mortality.<sup>20-23</sup> A 2016 review found that high levels of moderate intensity (60-75 minutes daily) exercise can negate the increased risk of death tied to high amounts of time spent not moving; however, it didn't negate risks linked to "high TV-viewing time,"<sup>24</sup> which seems to have its own negative effects. A 2018 study noted that there are thresholds, in that "sitting" for more than 6-8 hours daily and TV viewing for more than 3-4 hours a day are associated with much greater risk for CDV and all-cause mortality.

Of course, physical activity plays an important role in promoting optimal body weight, but unfortunately, the overall volume of aerobic exercise required to achieve healthy and sustained weight loss is relatively high, so many people lose their motivation to exercise when the pounds do not quickly "melt" away.<sup>25</sup> It is important for health care providers to remind patients that regular exercise provides a variety of health benefits, some of which lessen the risk for CVD, even in the absence of significant weight loss. And, weight loss can be very beneficial. Unfit individuals have 2-3 times the risk of dying compared to other people with the same BMI.<sup>26</sup> People who are overweight or obese can reduce their risk of CVD by getting physically fit.<sup>27</sup> In fact, regular physical activity reduces the risk of heart attack, heart failure, hypertension, obesity, and diabetes mellitus across all BMI categories.<sup>28,29</sup>

A combination of aerobic exercise and weight/resistance training is recommended for most people, though the majority of research for prevention of CVD has focused on aerobic activity. For example, results from the Honolulu Heart Program, a prospective cohort trial involving 700+ elderly men, revealed a significantly reduced mortality rate among those who walked over 2 miles each day at baseline, compared with those who walked only one mile per day, over a period of 12 years (23.8% vs. 40.5%).<sup>30</sup> Men who walked less than 0.25 mile per day had double the risk of CVD compared with men who walked greater than 1.5 miles per day (5.1% versus 2.5%).

The INTERHEART study, a case-control trial in 52 countries involving over nearly 30,000 people, showed that 4 or more hours of regular, moderately intense exercise per week reduced heart attack risk by 12.2%.<sup>31</sup> There are data suggesting that walking briskly for a total of only 3 or more hours a week is associated with reduced risk for acute coronary events in women, equivalent to the effects seen with more vigorous exercise.<sup>32</sup> Yet another study showed that walking for as little as 1 hour per week can reduce the risk for CVD.<sup>33</sup> A 2019 review found that people with existing heart disease had a 14% risk reduction, and people with no heart disease had a 7% reduction, for every 500 MET-min per week increase in physical activity they had.<sup>34</sup> (500 MET-minutes is roughly equivalent to 150 minutes of moderate intensity aerobic exercise, a common recommendation for weekly physical activity.) A number of tables of METs for different activities are available <u>online</u> and in journal articles.<sup>35</sup>

How little can someone exercise each day and still obtain health benefits? According to a prospective cohort study involving over 400,000 men and women, the answer is 15 minutes.<sup>36</sup> Study participants experienced a 14% reduced risk of death and a median 3-year longer life expectancy over 8 years of follow-up compared with sedentary individuals; each additional 15 minutes of physical activity per day further reduced mortality rates in people of all ages, including those with pre-existing CVD.

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

As little as 15 minutes of walking a day can reduce the risk of death from a cardiovascular event by 14% and add, on average, 3 years of life.

If someone already has CVD, we know that cardiac rehabilitation can have significant benefits on morbidity, risk factor modification, and mortality.<sup>37</sup> However, it is underutilized; keep that option in mind. Cardiac rehabilitation also decreases anxiety and depression in people who have had myocardial infarctions (MIs).<sup>38</sup> How much overall benefit there is for exercise after percutaneous coronary interventions in people with coronary heart disease remains unclear.<sup>39</sup>

#### Tai Chi

While tai chi has shown promising health benefits in a number of studies,<sup>40</sup> A 2014 Cochrane review focused on tai chi concluded that evidence supporting it for the primary prevention of CVD is limited.<sup>41,42</sup> A 2015 Cochrane review reached the same conclusion for qi gong.<sup>41</sup> A few small studies have shown promise:

- A 2019 study that followed 120 older adults for over 6 years found that tai chi was both a suitable exercise for older individuals and that it could help regulate blood pressure, benefit heart and lung function, and reduce the incidence of cardio- and cerebrovascular disease.<sup>43</sup>
- A 2017 review focused on stroke and stroke prevention noted "significant, but not robust" benefits of tai chi/qi gong for elevated blood pressures, fasting glucose, and BMI compared with people who did other forms of exercise.<sup>44</sup>
- One 2018 review of 13 studies found that tai chi improved aerobic endurance and psychosocial well-being among coronary heart disease patients.<sup>45</sup>
- A 2015 study found that doing qi gong for 12 weeks improved heart rate variability (which correlates to better heart health) compared to controls.<sup>46</sup> Tai chi has been shown to offer cardiovascular benefits, improve balance, and increase muscle strength, all without impairing arterial compliance.<sup>47</sup> Regular tai chi practice is also associated with reduced anxiety and stress, lowered heart rate and blood pressure, and improved sleep.<sup>48</sup>
- Data support tai chi in patients who have had stroke, to improve overall physical function<sup>49</sup> (walking speed, balance, and lower body strength).

Check out "Physical Activity," Chapter 5 of the <u>Passport to Whole Health</u> for more information about Tai Chi—what it is, safety information, and a summary of research findings for noncardiac indications.

#### Yoga

A number of promising studies have begun to emerge showing that yoga has health benefits. However, data is less clear-cut when it comes to its use specifically related to preventing or treating heart disease. A 2015 study concluded that yoga programs may lead to significant improvements in exercise capacity and quality of life in people with chronic disease,<sup>50</sup> but a 2018 study reported that research regarding the use of yoga in chronic disease care is inconclusive.<sup>51</sup> A 2015 systematic review concluded that "weak recommendations can be made for the ancillary use of yoga" for people with coronary heart disease, heart failure, and cardiac dysrhythmia.<sup>52</sup> Other research findings of note include the following:  A 2016 review that pooled data from the American College of Cardiology and American Heart Association compared effectiveness of different forms of lifestyle modifications. Yoga had one of the largest 10-year cardiovascular disease risk reductions of all the modifications studied, with even more of a protective effect than walking and following a Mediterranean diet which were also (not surprisingly) quite effective.<sup>53</sup>

- A 2016 review concluded that yoga can be considered a safe and effective intervention for reducing waist circumference and blood pressure in people with metabolic syndrome if they are not exercising in other ways; however, no specific recommendations can be made for or against its use in general by people with metabolic syndrome.<sup>54</sup>
- A 2014 Cochrane review noted that evidence for yoga's use in preventing heart disease is limited. There is some evidence of favorable effects on HDL, triglycerides, and diastolic blood pressure, but studies are small and short term.<sup>55</sup>
- Yoga-based cardiac rehabilitation in "optimally medicated post-MI patients" over 12 weeks improved heart rate variability compared to standard care.<sup>56</sup>
- Yoga has been found, in a review of 15 studies, to reduce inflammatory biomarkers like Creactive protein.<sup>57</sup>
- Pranayama breathing exercises were found, in a review of 13 trials, to have acute and chronic blood pressure lowering effects, though study quality was poor.<sup>58</sup>

#### **More Information**

The "Physical Activity," Chapter 5 of the "<u>Passport to Whole Health</u>" and the "<u>Yoga</u>" Integrative Whole Health tool offer additional information about yoga. For more information on incorporating Physical Activity into a Personal Health Plan, check out the "<u>Physical Activity</u>" Integrative Whole Health overview.

# **Back to Charles**

A good starting point with Charles might be working to convince him that as little as 15 minutes a day of moderate intensity exercise, such as a brisk walk, perhaps outside with his wife (perhaps for the good their relationship) or a friend, could provide him with measurable health benefits. Once he starts, he very well may experience improved energy levels that would encourage him to be a little more active each day. For more guidance on how to tailor movement recommendations to individual needs, refer to "<u>Prescribing Movement</u>" Integrative Whole Health tool.

#### Surroundings

A stressful, cluttered, unsafe, or unhealthy environment can contribute to CVD risk. Changes in climate conditions in Beijing are connected to a 50% increase in CVD mortality for men and 27% increase for women, and improvements in air quality in Finland, England, Wales, and Poland have been linked to mortality drops.<sup>59</sup> Studies in identical twins also indicate that CVD outcomes are associated with a person's living environment.

In addition, myocardial infarctions (MIs) occur more frequently, and are larger, when they

happen in the morning hours (especially from 3 to 6 a.m.).<sup>60</sup> Blood pressure, HDL, and LDL all increase in winter versus summer,<sup>61</sup> and people are much more likely to die from CVD in the winter and on days with larger temperature variations.<sup>62</sup> People who live at high altitude have less hypertension and better lipid profiles.<sup>63,64</sup> While some environmental factors that increase risk are not easy to change, others may be. Some examples include the following<sup>59</sup>:

- **Spend time outside.** Living closer to vegetation is linked to lower levels of CVD, stress, diabetes, and stroke.<sup>65,66</sup> It is also is linked to lower blood pressures, improved heart rate variability, and a reduction in cardiovascular mortality.<sup>67</sup> Further, it is also tied to better general health, more social support, and higher levels of physical activity.<sup>65,68</sup> Time spent outdoors is inversely related to CVD mortality.<sup>69</sup> In the Nurses' Health Study, women living in the greenest areas had 12% lower mortality rates.<sup>70</sup> Decrease in tree canopy near one's home has been linked to increase mortality risk as well.<sup>71</sup> In some studies, CVD risks are increased by lack of sunlight to *the same degree* as they are increased by smoking.<sup>69</sup> This may be associated with skin production of vitamin D and the observation that blood pressure increases with distance from the equator and levels of ultraviolet (UV) B radiation.<sup>72</sup> However, UV A exposure also decreases blood pressure, perhaps due to nitric oxide (NO) release.<sup>73</sup>
- Live in a "good" neighborhood. Of course, this is not always controllable, but people who live in disadvantaged neighborhoods have up to a 3 times higher incidence of CVD, after controlling for multiple other social and other risk factors.<sup>74</sup> Many factors, ranging from food quality, to smoking prevalence, obesity levels, stress, and social integration, may play a role.
- Avoid air pollution as much as possible. Again, not always controllable, but an estimated 55,000 to 200,000 premature deaths in the U.S. each year have been attributed to it.<sup>59</sup> Many of the deaths seem to be linked to individual risk. Smokers, people with diabetes, and those with existing CVD seem to be especially vulnerable. Better baseline health decreases susceptibility, but pollutants may cause endothelial injury even in young, healthy people.<sup>75</sup> People who live near roadways also have higher levels of risk.<sup>76-78</sup>
- **Reduce environmental noise.** 46% of the U.S. population is exposed to high noise levels, which induces stress, impairs sleep, raises heart rate and blood pressure, and elevates CVD risk.<sup>79</sup> Living near an airport can increase risk.<sup>80</sup> Music that is pleasant to the listener, however, especially when the listener is given a choice of music, appears to reduce anxiety in those with CVD and may have beneficial effects on blood pressure, pulse rate, and quality of sleep.<sup>81</sup>
- **Do not smoke or spend time near smokers.** People who smoke die an average of 13-14 years sooner than nonsmokers. Each year 443,000 Americans die because of smoking, and still, around 16% of Americans are smokers.<sup>82</sup> Smokers have 2 times the risk of heart disease and 10 times the risk of peripheral vascular disease compared to nonsmokers.<sup>83</sup> Smoking seems to increase risk of heart disease independently from other risk factors.
- **Do not take antibiotics unnecessarily.** A recent study including over 36,000 women found that prolonged antibiotic exposure in middle or older adulthood was linked to CVD risk (this was not the case with young adulthood use).<sup>84</sup> It is thought that this is linked to effects on the microbiome, which is discussed in more detail in the Nutrition section of this overview.

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

# **Back to Charles**

Asking Charles about his surroundings may offer a number of insights into how his PHP can support his heart (and overall) health. If Charles lives on a highly traveled street or in a neighborhood ringed by industry, he might benefit from simple, relatively inexpensive interventions, such as using an ambient noise machine at night or installing high-efficiency particulate air (HEPA) filters in the air ducts of his home. For more ideas, go to the <u>"Surroundings"</u> Integrative Whole Health overview.

#### **Personal Development**

**Work life.** Charles seems to derive some sense of personal value from his work life, and it would be worthwhile to explore this realm further to be sure it is as healthy an environment for him as possible.

Working long hours (more than 55 hours per week on average) increases risk of stroke, according to a recent meta-analysis.<sup>85</sup> While some studies indicate an increase in CHD risk as well, the connection is less clear. For more information on the relationship between work patterns and health, review the "<u>Healthy Work Habits: Avoiding Workaholism</u>" Integrative Whole Health tool. Perceived job insecurity has long been proposed as a potential, though modest, source of cardiovascular risk,<sup>86</sup> while data associating the impact of job stress on CVD risk, such as that coming from high job demands combined with low control, is more robust.<sup>87-90</sup> Studies exploring any association of CVD with "job strain" (for example, high job demands combined with low control) suggest a significant increased risk for CVD.<sup>90,91</sup> Of note, INTERHEART investigators found that job stress, almost anywhere in the world, was associated with a doubling of the odds of heart attack.<sup>92</sup> On the other hand, positive factors present at work and home, such as supportive co-workers and family members, act as buffers against CVD risk.<sup>93,94</sup>

There is some good news, though—behavioral interventions may mitigate the CVD risk associated with various forms of job stress. One review of seven prospective cohort trials involving over 100,000 study participants found that an overall healthy lifestyle could reduce CVD risk among people with significant job strain by about 50%.<sup>87</sup> Thus, even if Charles' work life is less than fulfilling, he will likely benefit from eating a healthy diet and following other lifestyle habits that can help offset the effects of job strain on his heart.

**Finances and education.** Not surprisingly, financial concerns and socioeconomic status (SES) have also been associated with increased CVD risk.<sup>95,96</sup> Less affluent communities have higher rates of angina, MI, and heart failure.<sup>97</sup> Of note, CVD was considered a rich person's disease in the 1930s and 1940s, but that has changed with the advent of the standard American diet.<sup>98</sup> In the Whitehall study, men with the lowest SES had 2.7 times the risk of dying in the next 10 years of heart disease compared to those who were in the wealthiest group.<sup>99</sup> There is a strong independent association between income and heart disease.<sup>100</sup> Unfortunately, for those with fewer resources, we do not do as well offering support with prevention and management of CVD.<sup>101</sup>

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

Education is also closely linked to CVD risk. Entering an organization with a college degree is linked to lower CVD incidence and mortality.<sup>98</sup>

**Outlook and personality.** One's outlook on life and expectations for the future can play a role in promoting heart health, too. Specifically, positive well-being—including positive emotions, optimism, and life satisfaction—are protective against CVD and lower one's risk of mortality. <sup>102</sup>

Study authors have reported that optimistic persons have improved vascular health, reduced heart attack risk, and lessened cardiovascular mortality relative to pessimistic people.<sup>103,104</sup> People with CVD who are optimistic about their treatment and recovery experience better long-term survival and functional status than patients with similar disease but lower expectations.<sup>105</sup> The relationship between optimism, a characteristic that many experts believe can be learned, and possible improved CVD outcomes has become an intense focus of study.<sup>105</sup> Many experts believe that optimism, even if absent initially, can be cultivated.

Recent studies have linked poor CVD outcomes to Type D personality traits. The Type D (distressed) personality, is "a normal personality construct" defined by higher likelihood of negative affectivity—having a wider range of negative emotions and more negative perspectives about oneself and one's surroundings than most people.<sup>106</sup> Type D people respond well to cardiac rehabilitation programs, which include physical activity as well as psychological interventions and counseling.<sup>107</sup>

Regular volunteer work is also associated with enhanced self-rated health<sup>108-110</sup> and reduced mortality risk.<sup>108,111,112</sup> In one study of older adults, those who volunteered in support of worthy causes for at least 200 hours per year reduced their risk of hypertension by 40% over a four-year period.<sup>113</sup>

The <u>"Personal Development"</u> Integrative Whole Health overview has additional detailed information on these and other areas of personal development.

#### **Nutrition**

Focusing on nutrition can have a profound benefit for CVD; diet favorably affects many CVD risk factors, including hypertension, lipid disorders, insulin resistance, and obesity. Appropriate weight loss among overweight patients improves all of the conditions related to metabolic syndrome.<sup>114</sup>. Over two-thirds of American adults are overweight or obese,<sup>115</sup> which places them at significantly increased risk for CVD. This means weight loss is a particularly important focus when it comes to Nutrition for heart health.<sup>116</sup>

#### **Healthy Eating Patterns**

While specific foods and nutrients have roles to play with respect to CVD risk, overall patterns of eating are also the subject of a great deal of research.<sup>117,118</sup> A small number of dietary patterns have emerged as both healthy and potentially satisfying to the people eating them. These include the **DASH** (Dietary Approaches to Stop Hypertension) **Diet** and the **Mediterranean diet**.

Both programs encourage eating foods that may beneficially affect cholesterol and reduce inflammation and the development of atherosclerosis. These include vegetables, fruit, whole grains, and nuts. Intake of saturated fat and red and processed meat is limited. For more information, check out the <u>"Choosing a Diet"</u> Integrative Whole Health tool.

**The Portfolio Diet** has also gained attention in recent years, thanks to some favorable research findings. This plant-based diet, primarily focuses on incorporating various foods (many are high in plant sterols and stanols) known to improve lipid profiles. It has been found to have marked favorable effects on HDL, LDL, apolipoprotein B, blood pressure, CRP, and overall 10-year CVD risk, when combined with the National Cholesterol Education Program (NCEP) Step 2 diet. Combining the two was significantly more beneficial than the NCEP diet alone.<sup>119</sup>

**Intermittent fasting (IF)**, limiting caloric intake at specific intervals, also has benefits. It has been found to improve blood pressure, resting heart rate, lipid levels, insulin resistance, and inflammation that can drive atherosclerosis. It also improves heart rate variability by modulating parasympathetic tone.<sup>120</sup> A number of approaches to IF have been studied, including alternative-day fasting and decreasing intake of carbohydrates by a certain percentage over 2 years' time.

**Plant-Based Diets** have significant benefits as well.<sup>121</sup> Vegetarian and vegan diets, are associated with lower levels of obesity and hypertension.<sup>122,123</sup> A large European study followed nearly 45,000 people over 11.6 years and found that vegetarians had lower mean BMIs, lower systolic pressures, and a 32% lower risk of developing heart disease.<sup>124</sup> These diets are known to reverse angiographic findings of CVD as well.<sup>125</sup> Focusing on consumption of plan-based over animal-based proteins is worth recommending.

#### Carbohydrates

#### **Glycemic Index and Load**

Carbohydrates come in different forms, with different chemical structures and particle sizes. Foods contain varying amounts of fiber, and they induce distinct plasma glucose and insulin responses. Glycemic index and glycemic load are measures of how a given food affects blood glucose levels. Regular eating of high glycemic load foods, such as processed carbohydrates, stimulates insulin secretion, promotes insulin resistance and induces the release of proinflammatory mediators.<sup>126,127</sup>

Prospective cohort studies examining the association between glycemic index, glycemic load, and CVD risk have produced inconsistent results, though most suggest an increased risk of CVD with high glycemic diets.<sup>128</sup> One large prospective cohort study of over 53,000 people found that replacing foods high in saturated fat with high glycemic index carbohydrate foods increased CVD risk.<sup>129</sup> In contrast, following a low glycemic load diet that adheres to the principles of the Mediterranean diet reduces the risk for type 2 diabetes by about 20%.<sup>130</sup> Thus, the quality and type of carbohydrates eaten are important when considering CV risk. For more information, check out the "<u>Managing Carbohydrates for Better Health</u>" handout.

#### Fiber

Eating plenty of high-fiber foods improves insulin sensitivity and reduces cholesterol absorption (and thus lipid levels), through the binding of bile acids.<sup>131,132</sup> High-fiber diets rich in leafy green vegetables, fruits, oats, beans, peas, and psyllium are associated with a reduced risk of CVD, including heart attacks.<sup>133,134</sup> Viscous fiber (for example, from oats and barley) has significant LDL cholesterol lowering effects.<sup>135,136</sup> A 2019 review found "significantly lower body weight, systolic blood pressure, and total cholesterol when comparing groups with high versus low intakes of dietary fiber." Risk reduction was greatest when daily intake was 25-29 gm, but there was a dose response curve; higher intakes may be even more beneficial.<sup>137</sup>

#### Fats

Sterols and stanols are fats found in a variety of fruits, vegetables, nuts, seeds, cereals, and legumes (such as peas, beans, lentils). They significantly reduce gut cholesterol absorption.<sup>138</sup> <sup>139</sup> Other foods high in stanols and sterols include avocado, olive oil, soybeans, and leafy green vegetables.

The type of fat ingested is more important than total fat intake. Fats that are solid at room temperature (including coconut and palm oils) negatively affect CVD risk factors. Liquid oils are recommended in many guidelines, because overall they have beneficial effects on lipids and lipoproteins.<sup>121</sup> Omega-3s have small beneficial effects on blood pressure, but otherwise, dietary fat seems to have relatively minor effects—favorable or not—on blood pressures.<sup>140</sup>

**Olive oil** contains predominantly monounsaturated fats and has well-documented cardioprotective properties. Its cardioprotective properties have been attributed to its high oleic acid content, and its polyphenols also contribute to its benefits.<sup>141</sup> Low-quality olive oils lose their antioxidant and anti-inflammatory capacities because they contain fewer polyphenols. Polyphenols offer cardioprotective effects,<sup>142</sup> and recent data show healthy levels may improve arterial stiffness.<sup>143</sup> Very high-quality extra virgin olive oil contains added natural anti-inflammatory capacity through the compound oleocanthal, whose activity has been likened to ibuprofen.<sup>144</sup>

**Other oils.** A recent expert review of the literature concluded the following about specific oils:<sup>121</sup>

- **Canola oil**, as a liquid oil, is a reasonable source of fat, but when processed, it loses its beneficial polyphenols.
- **Coconut oil**, rich in saturated fatty acids, is not recommended. There are many sweeping claims about benefits, but these claims have little support from research findings.
- **Sunflower oil** is rich in mono- and polyunsaturated fats and, as such, seems to be a reasonable option.
- Palm oil increases heart disease risk and should be avoided.

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative



#### Omega-3 Fats

Omega-3 polyunsaturated fatty acids are shunted into phospholipid pathways versus becoming triglycerides. They appear to reduce triglyceride and LDL levels, and they may have benefits for arrhythmias. In addition, they appear to reduce markers of inflammation, endothelial dysfunction, and platelet aggregation<sup>145</sup>; they also improve heart rate variability.<sup>146</sup> They have less of an effect on blood pressure or insulin signaling, <sup>147</sup> and they don't seem to be helpful for treating or preventing atrial fibrillation <sup>148,149</sup> or heart failure.<sup>150,151</sup> A 2014 meta-analysis found they have significant benefits for CVD outcomes,<sup>152</sup> as have a number of other studies.

Omega-3s may be an important reason for the benefits of fish consumption; for every 20-gm increase in fish consumption each day, risk of coronary death decreases by 7%.<sup>153</sup> Eating omega-3s from fish seems to have more of a benefit than taking supplements.<sup>154</sup> While an American Heart Association science advisory concluded that omega-3 supplementation in heart disease is reasonable, the degree of benefit they have remains unclear.<sup>154</sup>

#### **Saturated Fat**

Since the early 1980s, Americans have been advised to reduce total and saturated fat intake to support heart health. In recent years, that message has changed. Now the goal is to keep dietary fat intake moderate, with a focus on primarily eating unsaturated versus saturated fat. Clinical, epidemiological, and mechanistic studies consistently show that substituting mono- and polyunsaturated fat for saturated fat reduces CVD risk.<sup>155-157</sup> Diets low in saturated fat appear to protect against CVD,<sup>158</sup> but some studies have led to questions about the appropriateness of demonizing saturated fat, with results suggesting no association between saturated fat intake and coronary artery disease, stroke, or incident CVD.<sup>159</sup> Some experts believe that the influence of dietary fats on CVD risk has been overstated, and that the real culprit behind CVD risk today is the plethora of highly processed, manufactured foods on store shelves, including processed meats.<sup>160,161</sup>

#### **Trans Fats**

One issue that does not invite debate is the health risks associated with eating trans fats, which are produced by heating and hydrogenating liquid vegetable oils, making them more stable and giving them added shelf life (examples are snack and processed foods and margarines). The process also makes them suitable for repeated heating without degradation and thus theoretically ideal for frying fast foods. Unfortunately, trans fats have been implicated in atherosclerosis<sup>162</sup> and are associated with an increased risk for CVD,<sup>163</sup> presumably due to adverse effects on inflammatory processes and lipid levels.

#### Specific foods, nutrients, and beverages

An extensive analysis explored which foods and nutrients had the strongest causal relationships when it comes to either causing or preventing heart disease, based on all the latest research findings (and the relative samples sizes and quality of various studies).<sup>164</sup> Researchers placed food groups into two classes:

- 1. Strongest evidence of harm: unprocessed red meat, processed meats, sugarsweetened beverages, high glycemic load, and trans fats
- 2. Strongest evidence of benefit/preventive effect: fruits, vegetables, beans/legumes, nuts/seeds, whole greens fish, yogurt, fiber, seafood omega-3s, and potassium

What follows is an alphabetical list of some of the key foods or food additives that could be part of the discussion around Nutrition for a PHP.

**Added sugars** (e.g., table sugar and high fructose corn syrup) promote atherogenesis and increase CVD risk.<sup>165,166</sup> Free sugars have marked negative effects on lipid panels,<sup>147</sup> and an estimated 20.2% of the nearly 200,000 diet-related deaths that occurred in 2012 were attributed to sugar-sweetened beverage consumption.<sup>167</sup>

**Alcohol.** A 2018 literature review concluded that "Research has shown some benefits of alcohol consumption, however, there is not sufficient high-quality evidence to recommend specific alcoholic beverages for CV risk reduction. There is also some risk of falls, certain cancers, and liver disease." Starting to drink alcohol to prevent CVD is not recommended; it is perhaps best to consume alcohol with meals if one does consume it.<sup>147</sup>

**Berries.** Anthocyanadins, one of the subclasses of flavonoids, have antioxidant properties. They act as free radical scavengers, regulate nitric oxide production, support artery wall function, and modulate blood glucose levels.<sup>168</sup> In the Nurses' Health Study, the quintile of women who consumed the most anthocyanidin had a hazard ratio for heart disease of 0.68.<sup>169</sup> These compounds are found in blueberries, strawberries, raspberries, and other red- and bluecolored fruits, as well as red radishes, cabbage, and eggplant.

**Coffee and tea.** Coffee, once widely considered unhealthy, is now being found in large analyses to have a dose-response protective benefit; habitual consumption is linked to lower risks of all-cause and CVD mortality.<sup>170,171</sup> Some experts believe that regular coffee drinking may help protect against development of atrial fibrillation.<sup>172</sup> Tea also seems to have a beneficial effect. A large Chinese study found that consumption of any type of tea (green, black, etc.) was tied to a 10% reduction in major cardiac events.<sup>173</sup> A Japanese study found that consuming 5 or more cups of green tea daily decreased all-cause mortality by 12% in men and 23% in women.<sup>174</sup> Caution may be needed for people on beta blockers, as one investigation found that regular green tea consumption may interfere with the blood-pressure-lowering effects of nadolol.<sup>175</sup>

**Dairy products**, while showing potential benefits in some observational trials (and some sponsored by industry interests), are not clearly beneficial for CVD.<sup>147</sup> They seem to negatively affect lipid profiles, but not blood pressure.<sup>176</sup>

**Energy drinks** are best avoided. They elevate blood pressure, clotting risk, and risk of cardiac arrhythmias.<sup>177</sup>

**Eggs.** Eggs are the major source of dietary cholesterol in most people's diets. The 2015 Dietary Guidelines Advisory Committee's concluded that evidence does *not* show a link

School of Medicin and Public Health

SITY OF WISCONSIN-MADISON

between dietary cholesterol intake and cholesterol levels<sup>178</sup>; however, the 2015-2020 Dietary Guidelines for Americans recommended minimizing cholesterol-containing foods in the diet. Studies have indicated a link between dietary cholesterol and CVD risk.<sup>179</sup> A meta-analysis of 17 studies found that for every additional 100 mg/day of dietary cholesterol consumed, total cholesterol increased an average of 2.17 mg/dl, and LDL an average of 1.93 mg/dl (with individual responses varying greatly).<sup>180</sup>

**Fermented foods and seaweed** show promise in observational studies, but more research on their benefits is needed.<sup>147</sup>

**Garlic,** both as a food and as a supplement, seems to have a significant benefit for systolic blood pressure control. Findings for diastolic blood pressure and lipids are not as clearly supportive.

**Green Leafy Vegetables** reduce arterial stiffness and blood pressure, most likely because they are a source of nitrates. However, their benefits only last for a few days, so regular consumption is important.<sup>181</sup> They also contain lutein, a powerful antioxidant and anti-inflammatory carotenoid. For every 1 oz consumed a day (about one-fifth of a serving) there is a 13% risk reduction for developing type 2 diabetes.<sup>182</sup> Three servings a day combined with a low-carbohydrate diet reduces CVD risk by 24%. <sup>183</sup>

**Legumes**, as an excellent source of fiber and protein, are linked to improved lipid profiles and less insulin resistance, as well as better blood pressures and body weight.<sup>184</sup>

**Mushrooms.** Mushroom consumption, while not clearly linked to decreased CVD mortality, is associated with improvement in many risk factors, such as metabolic syndrome, obesity, and type 2 diabetes.<sup>147,185</sup>

**Nuts.** Four servings of nuts a week decrease type 2 diabetes risk by 13%.<sup>186</sup> A pooled review of 25 studies found that LDL levels dropped an average of 7.4% with 2.4 oz of daily nut consumption, independent of the type of nut consumed.<sup>187</sup> Several reviews have found an inverse association between eating nuts and CVD risk, with each daily serving resulting in a relative risk reduction for fatal and nonfatal cardiac events of 0.72; there was a dose response effect.<sup>188</sup> Nuts are calorie-dense, so care must be taken around the amount eaten on a regular basis. Interestingly, though, there is not a strong association between nut consumption and weight gain in most studies.<sup>189</sup>

**Red Meat.** Eating 100 gm a day of unprocessed meat is associated with a 15% increase in risk of cardiovascular death. Eating 50 gm a day of processed meat is linked to risk increases of 24% for cardiovascular mortality, 13% for stroke, and 32% for type 2 diabetes.<sup>190</sup>

**Salt.** The 1988 Intersalt Study found that higher urinary sodium excretion was correlated with higher blood pressures.<sup>191</sup> A 2001 study that looked at three tiers of sodium intake for people who were on the DASH diet found that lower-sodium diets were linked to lower pressures.<sup>192</sup> A 2014 meta-analysis found a J-curve relationship between salt intake and mortality; too much or too little can have a negative impact on blood pressure.<sup>193</sup>

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

School of Medicin and Public Health

WISCONSIN-MADISO



# **Back to Charles**

There are an almost bewildering array of options Charles can consider when it comes to Food and Drink and heart health. It is perhaps easiest to choose one simple change and proceed with it, adding additional changes over time. Charles should take the lead in deciding which changes he would like to make, with guidance from his care team members.

#### Recharge

Sleep and rest have substantial effects on heart health. Insomnia, regardless of etiology, is associated with increased CV morbidity and mortality, hypertension, and heart failure.<sup>194,195</sup> Some studies show an association between insomnia and subsequent development of hypertension and dyslipidemia.<sup>196,197</sup> Chronic sleep loss accelerates age-related chronic cardiometabolic changes and increases their severity.<sup>198</sup> Extremes of sleep duration, either very short (for example, less than or equal to 5-6 hours) or very long (greater than or equal to 10 hours), are associated with increased risk of hypertension, coronary artery disease, and CVD.<sup>199,200</sup>

Long work hours and short sleep duration contribute independently to the risk of CVD in men.<sup>201,202</sup> A prospective study based on data from the Whitehall study revealed that working more than 55 hours per week was related to sleep disturbances, including shortened sleeping hours and difficulty falling asleep.<sup>203</sup>

Normal sleep physiology involves a combined reduction in sympathetic tone and an increase in parasympathetic nervous system activity, resulting in decreases in heart rate, stroke volume, blood pressure, and myocardial workload. Sleep-disordered breathing may affect as many as 10% of adults and 50%-75% of people with CHF.<sup>204</sup> The overall prevalence of obstructive sleep apnea (OSA)—in those who have CVD or are risk for it—is estimated to be 30%-60%.<sup>205</sup> Untreated, these maladies contribute to an increased risk of hypertension, heart disease, dysrhythmias, and stroke.<sup>206-208</sup> The hyper-aroused state associated with PTSD may also be related to sleep-disordered breathing (SDB), which is more prevalent among those with PTSD than the general population.<sup>209</sup> Sleep disorders may also have a role in the association between depressive symptoms and cardiovascular mortality.<sup>210</sup>

# **Back to Charles**

It is unclear why Charles is not experiencing fully restorative sleep, but any number of factors could be at play including PTSD, stress, caffeine use, or a sleep disorder. An evaluation by a sleep specialist might be helpful. If SDB is present, management may not only improve the restorative nature of his sleep, but also reduce his CVD risk.



School of Medicine and Public Health

#### Family, Friends, and Co-Workers

Relationships have a powerful influence on heart health. Poor social relationships have been found in a large meta-analysis to be associated with a 29% increased risk of CVD and a 32% increased risk of stroke.<sup>211</sup> The behaviors of those around us can also influence our cardiac risk. If a person has a friend who becomes obese, they have a 57% chance of becoming obese during the same time period.<sup>212</sup> Having at least one obese friend increases obesity risk by 171%.<sup>213</sup> Friends who smoke also influence smoking likelihood. Social stress is linked to oxidative stress, resistance to glucocorticoids, and increased expression of genes that promote inflammation.<sup>214</sup>

Results from both animal<sup>215,216</sup> and human studies<sup>217</sup> point to a strong influence of social relationships on risk for CVD. Marital problems,<sup>218</sup> the death of a spouse or child,<sup>219,220</sup> and care for a sick spouse at home<sup>221</sup> also have been linked to an increased risk of CVD. Having more social capital—people whom you can turn to for various types of support—has been correlated with better levels of adherence to a healthy lifestyle in people with heart disease.<sup>222</sup>

A 2018 meta-analysis found that Pet Therapy is linked to improvements in heart rate, anxiety, and stress, but not clearly with changes in blood pressure.<sup>223</sup> Owning a pet seems to decrease mortality risk in people with established CVD, but other connections between pet ownership and heard disease risk are less clear.<sup>224</sup>

**Loneliness.** Social isolation and loneliness are common sources of chronic stress in adults,<sup>225</sup> and people with CVD or other chronic health conditions have a significantly worse prognosis if they also experience social isolation or loneliness; the magnitude of risk is comparable to that associated with smoking tobacco. <sup>32,217,226,227</sup>

One study of men and women aged 50-68 years found that loneliness at study onset predicts cumulative increases in systolic blood pressure at 2, 3, and 4 years of follow-up.<sup>228</sup> The effect of loneliness on blood pressure occurred independent of age, gender, race, CV risk factors, medications, depressive symptoms, or perceived stress. Living alone, as a proxy for social support, is associated with increased mortality among all but the most elderly of patients.<sup>229</sup> A 2018 review concluded that the risks of loneliness for heart disease and stroke exist independently from other commonly treated cardiac risk factors and that decreasing loneliness might indeed be protective.<sup>211</sup>

Data from NHANES III and the National Death Index revealed that a person's degree of social isolation is predictive of their mortality in both men and women, with increasing levels of isolation associated with increased risk of death.<sup>230</sup> Being single and not participating in religious activities predict mortality, regardless of gender. For other variables, gender differences have been seen; lack of group memberships predicts mortality in men, while infrequent social contact predicts mortality more accurately among women. People who feel they have been materially or socially rejected can often be found in the company of other people, yet they feel alone in their minds and with their thoughts; perceived isolation may have more of a health impact than physical isolation.<sup>231,232</sup> Loneliness is linked to atypical reactivity to stress, and a 2018 review noted a connection between loneliness and both blood pressure

increases and inflammation.<sup>233</sup> There is also a suggestion that loneliness may blunt cardiac, immune, and adrenal responses.

# **Back to Charles**

Charles could benefit from individual counseling, and he and his wife could consider marital counseling. In addition, strategizing about ways that they might spend time together when Charles does not have to work could be helpful. Meaningful social relationships outside the home may encourage Charles with stopping smoking and increasing fitness activities, among other behavioral changes, not to mention support adherence with taking his medications. It may be helpful in a variety of ways to encourage Charles to spend time with friends.

#### Spirit and Soul

A 2015 review of all archived studies related to religiosity and spirituality (R/S) and health noted that over 65% of high-quality studies found R/S to have beneficial effects on coronary disease and cardiovascular functioning.<sup>234</sup> A majority of studies show a favorable relationship between R/S and a number of CVD-related measures, including the following: <sup>234,235</sup>

- More active lifestyle
- Healthy dietary practices
- Lower incidence of hypertension
- Reduced psychological stress
- Decreased hostility, depression, and anxiety
- Cardiovascular reactivity
- Incident cardiovascular disease and cardiovascular mortality

Our job in exploring spiritual connection with patients is to help them connect to what they feel results in the most meaning and purpose in their lives.

Most studies suggest an inverse relationship between degree of R/S and smoking as well.<sup>236-238</sup>. How R/S leads to benefits is not fully explained, but social connections, healthy behaviors, stress reduction, and a number of other elements likely play a role.

The "<u>Spiritual Assessment</u>" Integrative Whole Heath tool can help clinicians more fully understand their patients' values and gauge the support systems available to them. Working with chaplains may prove quite helpful. More information on the role of Spirit and Soul in Whole Health is available in the "<u>Spirit and Soul</u>" Integrative Whole Health overview.





# **Back to Charles**

At present we could gather more information about where meaning and purpose fit into Charles' life. Asking him about his Mission/Aspiration/Purpose starts the conversation, and obtaining a more detailed spiritual history might be of benefit for taking the conversation even deeper. If Charles belongs to a religious community, it may be beneficial for him to connect with them. Talking with a chaplain might prove helpful to him.

#### **Mind and Emotions**

Psychosocial factors make important contributions to heart disease risk<sup>239</sup>, as well as to its prevention and treatment. Perhaps the most remarkable finding from the INTERHEART trial,<sup>240</sup> was that psychosocial factors, including stress and depression, were responsible for 32.5% of the population-attributable risk for heart attack across 52 countries. This level of risk was independent of, and only slightly less than, the risk for a lifetime of smoking (35.7%). It was greater than that for hypertension (17.9%) or obesity (20.0%).<sup>241,242</sup> Chronic stress, both early in life and during adulthood, is associated with an excess risk of future coronary artery disease on the order of 40%-60%<sup>232</sup>. The association with stroke is less certain.<sup>243</sup> The message is clear—chronic psychosocial stress is an important CVD risk factor.<sup>244</sup>

#### Stress

People experiencing persistent psychosocial stress have elevated cortisol and catecholamine levels that result in, among other physiologic changes, increases in blood pressure, heart rate, cardiac output, and myocardial electrical impulse conduction, as well sustained proinflammatory cytokine production and endothelial dysfunction. Prolonged exposure to these conditions leads to gradual impairment of cardiovascular function and increased CVD risk.<sup>245</sup> Chronic stressors such as job strain and caregiving, as well as psychological distress from PTSD and depressive and anxiety symptoms, induce a chronic low-grade hypercoagulable state that can further impair CV health.<sup>246-248</sup>

Stress, anger, and depressed mood can act as acute triggers of major cardiac events. In fact, the pooled relative risk of acute coronary syndrome onset being preceded by stress is about 2.5 in case-crossover studies. Stress is also implicated in the prognosis of CVD and in the development of stress-related (Takotsubo) cardiomyopathy, where increased release of catecholamines during periods of intense emotional or physical stress "stuns" the myocardium and causes acute left ventricular dysfunction that can resemble an acute anterior wall MI on ECG.<sup>249,250</sup>

Prospective associations between transient ischemia during mental stress and cardiovascular morbidity and mortality have also been described, independent of CVD severity.<sup>251</sup> A study of patients in the New York area with implantable defibrillators showed that tachy-dysrhythmias increased significantly in the month following the 9/11 attacks, compared with control months.<sup>252</sup> A meta-analysis of five studies compared this data with a control that was based on information

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative from the time period 24 hours before. The pooled relative risk of acute coronary syndrome symptom onset being preceded by a period of anger, stress, or depressed mood was 2.48.<sup>232</sup>

Fortunately, there are many ways to reduce stress, using mind-body approaches and various other self-care techniques. For example, a 2019 review found that regular physical activity, particularly when done as part of a group, counteracts stress' cardiotoxic effects.<sup>253</sup> Additional tools and techniques are described later in this section, as well as in the "<u>Mind and Emotions</u>" Integrative Whole Health overview and tools.

#### **Depression and Anxiety**

A growing body of evidence supports a strong and independent relationship between heart disease and mood-related concerns, such as depression and anxiety and the development of heart disease.<sup>244,254,255</sup> Anxiety and depression are frequent in people with heart failure and contribute to increased mortality.<sup>256</sup> A 2019 meta-analysis found that patients who had an MI had a pooled prevalence of depression of 29%.<sup>257</sup> Treatment outcomes and prognosis are poorer in people with existing coronary heart disease as well.<sup>258</sup> In one large population-based cohort study, women and men with symptoms of anxiety and/or depression had a 20%-30% increased risk of having a first heart attack.<sup>259</sup>

Of course, beyond the physiologic changes they may cause, chronic depression and anxiety may also increase the risk of CVD by leading to participation in unhealthy behaviors and by reducing heart rate variability.<sup>260,261</sup> Countering the gloom and doom around mood disorders and CVD risk are data showing that a Mediterranean-style dietary pattern can mitigate the increased risk in CVD otherwise associated with depression and anxiety,<sup>262</sup> likely by reducing inappropriate inflammation. Listening to music is also known to reduce anxiety and other stress-related measures in people with heart disease.<sup>81</sup>

#### PTSD

PTSD is independently associated with an increased risk for incident CVD, even after adjusting for depression and other covariates.<sup>263</sup> In fact, one study showed a 62% increased risk of heart disease in men and 68% increase in women with PTSD.<sup>264</sup> In a long-term study of middle-aged Vietnam-era Veteran twins, those with PTSD were found to be almost twice as likely (22.2% vs. 12.8%) to develop CVD as those without PTSD over a 13-year period.<sup>265</sup> Those with PTSD also had significant impairments in objective measures of myocardial perfusion (cardiac PET scanning).<sup>265</sup> Obesity, dyslipidemia, hypertension, diabetes, and sleep disturbances are prevalent among those with PTSD and contribute to risk.<sup>263,266</sup> Heart rate variability, a recognized indicator of increased CVD risk, is also reduced with PTSD.<sup>267</sup>

Additional information on the Integrative Whole Health approach to PTSD can be found in the "<u>PTSD</u>" Integrative Whole Health overview.

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

#### **Mind-Body Approaches**

Research indicates that behavioral interventions may help to reduce the impact of affective disorders and stress on CVD risk,<sup>268</sup> and there is still much to be learned. The 2015 Rotterdam study noted that individuals who routinely do mind-body practices have favorable cardiometabolic risk profiles compared with others, but more research is needed to explore why this is the case.<sup>269</sup> Psychological interventions are less studied than pharmacological and other interventions, but many show some promise.<sup>270,271</sup> A 2018 review noted that a variety of mind-body therapies, including relaxation, meditation, and biofeedback led to small-to moderate improvements in a number of measures, including quality of life, heart rate, and anxiety.<sup>272</sup>

**Meditation and heart disease.** Meditation has long been promoted as a safe and potentially effective means for reducing high blood pressure. A report commissioned by the Agency for Healthcare Research and Quality (AHRQ) concluded that Transcendental Meditation (TM), qi gong, and Zen Buddhist meditation could each reduce high blood pressure<sup>273</sup>, though the effects noted were small and the general quality of studies was felt to be suboptimal. A 2019 meta-analysis focused on TM for heart disease found inter-group improvements in blood pressure but otherwise concluded that more studies are needed.<sup>274</sup> Mindful awareness approaches have a favorable effect on blood pressure, cortisol, and inflammatory markers.<sup>275</sup> Some positive trials have been published where the effects could be considered of therapeutic import, but still modest.<sup>276-279</sup>

In 2017, the American Heart Association released a scientific statement noting that meditation can serve as a beneficial adjunct to other care:

Neurophysiological and neuroanatomical studies demonstrate that meditation can have long-standing effects on the brain, which provide some biological plausibility for beneficial consequences on the physiological basal state and on cardiovascular risk. Studies of the effects of meditation on cardiovascular risk have included those investigating physiological response to stress, smoking cessation, blood pressure reduction, insulin resistance and metabolic syndrome, endothelial function, inducible myocardial ischemia, and primary and secondary prevention of cardiovascular disease. Overall, studies of meditation suggest a possible benefit on cardiovascular risk, although the overall quality and, in some cases, quantity of study data are modest. Given the low costs and low risks of this intervention, meditation may be considered as an adjunct to guideline-directed cardiovascular risk reduction by those interested in this lifestyle modification, with the understanding that the benefits of such intervention remain to be better established.

**Biofeedback and heart disease.** Biofeedback involves the use of various methods for measuring body functions; measurement data helps people to consciously learn to control those functions more effectively. Increased levels of heart rate variability (HRV), the beat-to-beat difference in heart rate, correlate with vagal activation, increased parasympathetic tone, and overall better heart health. HRV is typically modified through breathing rate.<sup>280</sup> Learning to modify HRV can reduce hostility, an important psychosocial risk factor for coronary artery

disease.<sup>281</sup> Biofeedback has been found to lower high blood pressure in people with hypertension or pre-hypertension.<sup>282,283</sup> A 2018 trial found that people with CAD trained in HRV biofeedback had significantly fewer all-cause admissions and emergency visits as well as decreased depression and hostility. Baroreflex sensitivity also increased.<sup>284</sup> A general introduction to biofeedback can be found in "Mind and Emotions: Relaxing & Healing," Chapter 12 of the *Passport to Whole Health*. You can also go to the "<u>Heart Rate Variability and</u> <u>Arrhythmias</u>" Whole Health tool for more information.

A simple but powerful technique that can lower blood pressure while also reducing anxiety and the perception of stress is a slow abdominal breathing exercise. The breathing rate is slowed to 6 breaths per minute while the mind focuses on a peaceful image. The "<u>Breathing</u>" Integrative Whole Health tool contains more detailed information.

Clinical Hypnosis and Guided Imagery. Clinical hypnosis and Guided Imagery, while they have many potential benefits, have not been studied in depth for cardiac concerns. One review found that, while studies are limited, Guided Imagery may have potential benefit for symptom management in heart failure.<sup>285</sup> There have been a few promising studies indicating that in post-stroke recovery, it can be helpful for people to visualize performing a task in order to build their skills with actively doing it. This helps people more effectively relearn daily living tasks,<sup>286</sup> and it seems to help posture and gait function too.<sup>287</sup> Charles has PTSD and anxiety. He also has many potential stressors, and his support, at least at home, seems limited. Engaging Charles when it comes to improving his emotional well-being will be critical to optimizing his overall health. He might be interested in taking a meditation class, if he knows other Veterans will be present. Biofeedback may be a good fit too, particularly if he is someone who likes technological approaches or tracking data. Counseling, perhaps in the form of Cognitive Behavioral Therapy (CBT), also could be of great benefit. "Power of the Mind: Relaxing & Healing," Chapter 12 of the Passport to Whole Health, as well as the "Mind and Emotions" Whole Health overview and tools offer additional guidance on options that Charles and his care team could consider incorporating into his PHP.

# **Professional Care**

#### **Prevention and treatment**

Professional care can include preventive options, conventional therapies and procedures, and CIH.

**Tobacco cessation**. One preventive measure that has not yet been fully discussed is tobacco cessation. Charles needs to stop smoking—if not for himself, then for those around him. Tobacco use remains the leading cause of preventable death worldwide,<sup>288</sup> and CVD causes 29% of all tobacco-attributable deaths.<sup>289</sup> A smoker's risk of heart failure is twice that of non-smokers, and smoking can induce and worsen serious cardiac dysrythmias.<sup>290,291</sup> The risks of secondhand exposure, however, still are not fully recognized. Non-smokers who are regularly exposed to secondhand smoke have a 27% increased risk of CVD mortality<sup>292</sup> and a 23% higher risk of stroke. The good news is that the increased risk of CVD rapidly declines once a

person stops smoking,<sup>293</sup> with nearly half the excess risk of CVD being eliminated within 2 years of quitting.<sup>294,295</sup> The "<u>Nicotine Use Disorders</u>" Integrative Whole Health tool has additional information.

**Vaccines.** Receiving an annual flu vaccine might be protective against CVD to some degree; recent data suggest that getting vaccinated could help reduce risk of heart attack or stroke by about 50%.<sup>296,297</sup> Vaccination against Varicella zoster may also be helpful; shingles may be associated with an increased risk of CVD, especially stroke.<sup>298</sup>

**Dental hygiene**. Encouraging regular dental care is worthwhile, not only to maintain proper oral hygiene but also to improve cardiovascular health, as studies have linked periodontal disease to atherosclerosis and CVD.<sup>299,300</sup>

# **Complementary and Integrative Health Approaches**

A number of complementary and integrative health (CIH) approaches have now received research attention. Many of them show some promise, particularly as adjuncts to conventional care. Yoga and tai chi/qi gong are discussed in the Physical Activity section. Meditation, biofeedback, Guided Imagery and clinical hypnosis are discussed in the section on Mind and Emotions.

**Acupuncture for heart disease.** Several recent reviews have explored the value of using acupuncture for specific heart conditions. A 2018 review of 30 trials concluded that more studies are needed to determine if acupuncture is beneficial in the treatment of hypertension.<sup>301</sup> Another review published in 2019 concluded that acupuncture could be of benefit when used in addition to medications.<sup>302</sup> Two 2019 meta-analyses focused on people with stable angina found that acupuncture has a positive treatment effect,<sup>303,304</sup> including on ECG findings, suggesting that it could potentially serve as an adjunctive treatment. One 2018 review of acupuncture for CHF suggested that it may assist in symptom relief and help preserve cardiac function<sup>305</sup>; another 2018 review was inconclusive.<sup>306</sup> A 2018 study did not find conclusive evidence that acupuncture improved lifestyle risk factors (obesity, hypertension, tobacco use, or alcohol abuse).<sup>307</sup> Finally, a 2018 systematic review found one good-quality study that indicated that acupuncture may augment the effect of medications for premature ventribular beats, as well as decrease time to normal sinus rhythm in atrial fibrillation.<sup>308</sup>

In addition to the List One approaches, there are a variety of other CIH approaches that people with heart conditions or risks may be exploring. More information related specifically to diabetes (including for supplements) is featured in the "<u>Type 2 Diabetes Mellitus</u>" IntegrativeWhole Health tool.

# **Personal Health Plan**

Personal Health Plans (PHPs) are not necessarily created in just one visit, or by just one team member. That is certainly going to hold true when it comes to Charles and his CV risk. The key, of course, is to keep checking in with Charles about his priorities—his MAP—and then

proceed from there. In doing so, a few areas for initial focus have arisen: his relationship with his wife, his lack of exercise, and his emotional state. Working with him to create shared goals, his PACT members agree that couples counseling, a fitness prescription, and exploring mindbody options have potential benefit. Charles is comfortable setting SMART goals around each of these over time, and various team members will follow up with him over the next few weeks to check in and provide reinforcement and support. A health coach can prove quite helpful, if they are available at his site.

You acknowledge that your other goals for Charles include smoking cessation, improving his sleep, and working on his nutrition, all of which can help with risk factor reduction. The key is to have Charles engaged in his care and to acknowledge that if he has some initial successes with a few goals and is not overwhelmed, additional successes in other parts of the Circle of Health are increasingly likely.

Charles agrees that an additional team member who would be useful for him is a counselor who can help him address both personal and marital issues. You advise that regular exercise will also help him in many ways, and he expresses interest in trying tai chi. Charles also agrees he will walk briskly with his wife for at least 15 minutes for six days a week. He agrees to give meditation a try as well.

You ask that Charles come back to see you in 2-3 weeks, as you are eager to learn how he will be doing on following through with his PHP. You remind him that he is the captain of his care team when it comes to his own journey toward health, but he has dedicated teammates who have his best interests in mind. You are confident that he is on track to start improving and protecting his heart health.

# **Integrative Whole Health Tools**

- Heart Health
- Hypertension
- Lipids
- Heart Failure
- Heart Rate Variability and Arrhythmias
- The DASH Diet

#### Author(s)

"Heart Health" was adapted for the University of Wisconsin Integrative Health Program from the original written by <u>Russell H. Greenfield</u>, MD and updated by <u>J. Adam Rindfleisch</u>, MPhil, MD (2014, updated 2020).

This Whole Health overview was made possible through a collaborative effort between the University of Wisconsin Integrative Health Program, VA Office of Patient Centered Care and Cultural Transformation, and Pacific Institute for Research and Evaluation.

#### References

- 1. Mehta D. Integrative medicine and cardiovascular disorders. *Prim care*. Jun 2017;44(2):351-367. doi:10.1016/j.pop.2017.02.005
- 2. Devries S. Coronary Artery Disease. In: Rakel D, ed. *Intergrative Medicine* 4th ed. WH Saunders; 2017.
- 3. WHO. Global status report on noncommunicable diseases 2013. 2014.
- Arps K, Pallazola VA, Cardoso R, et al. Clinician's guide to the updated ABCs of cardiovascular disease prevention: a review part 2. *Am J Med*. Jul 2019;132(7):e599-e609. doi:10.1016/j.amjmed.2019.01.031
- 5. Centers for Disease Control and Prevention. Heart disease facts: Heart disease in the United States. Accessed September 9, 2020. <u>https://www.cdc.gov/heartdisease/facts.htm</u>
- 6. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. Dec 15 2012;380(9859):2095-128. doi:10.1016/s0140-6736(12)61728-0
- 7. Geovanini GR, Libby P. Atherosclerosis and inflammation: overview and updates. *Clin Sci (Lond)*. Jun 29 2018;132(12):1243-1252. doi:10.1042/cs20180306
- 8. Maguire EM, Pearce SWA, Xiao Q. Foam cell formation: A new target for fighting atherosclerosis and cardiovascular disease. *Vascul Pharmacol*. Jan 2019;112:54-71. doi:10.1016/j.vph.2018.08.002
- 9. Wojciechowska A, Braniewska A, Kozar-Kamińska K. MicroRNA in cardiovascular biology and disease. *Advances in clinical and experimental medicine : official organ Wroclaw Medical University*. Aug 2017;26(5):865-874. doi:10.17219/acem/62915
- 10. Kura B, Parikh M, Slezak J, Pierce GN. The influence of diet on microRNAs that impact cardiovascular disease. *Molecules*. Apr 17 2019;24(8)doi:10.3390/molecules24081509
- 11. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. *Circulation*. Jan 3 2012;125(1):e2-e220. doi:10.1161/CIR.0b013e31823ac046
- 12. Centers for Disease Control Prevention. Vital signs: prevalence, treatment, and control of hypertension--United States, 1999-2002 and 2005-2008. *MMWR*. 2011;60(4):103.
- Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. May 21 2003;289(19):2560-72. doi:10.1001/jama.289.19.2560
- 14. Barbaresko J, Rienks J, Nöthlings U. Lifestyle indices and cardiovascular disease risk: a metaanalysis. *Am J Prev Med*. Oct 2018;55(4):555-564. doi:10.1016/j.amepre.2018.04.046
- 15. Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC. Primary prevention of coronary heart disease in women through diet and lifestyle. *N Engl J Med*. Jul 6 2000;343(1):16-22. doi:10.1056/nejm200007063430103
- 16. Ijzelenberg W, Hellemans IM, van Tulder MW, et al. The effect of a comprehensive lifestyle intervention on cardiovascular risk factors in pharmacologically treated patients with stable cardiovascular disease compared to usual care: a randomised controlled trial. *BMC Cardiovasc Disord*. Sep 10 2012;12:71. doi:10.1186/1471-2261-12-71
- 17. Gupta R, Wood DA. Primary prevention of ischaemic heart disease: populations, individuals, and health professionals. *Lancet*. Aug 24 2019;394(10199):685-696. doi:10.1016/s0140-6736(19)31893-8
- 18. Lavie CJ, Ozemek C, Carbone S, Katzmarzyk PT, Blair SN. Sedentary behavior, exercise, and cardiovascular health. *Circ Res.* Mar 2019;124(5):799-815. doi:10.1161/circresaha.118.312669
- 19. Ekelund U, Tarp J, Steene-Johannessen J, et al. Dose-response associations between accelerometry measured physical activity and sedentary time and all cause mortality: systematic review and harmonised meta-analysis. *BMJ*. Aug 21 2019;366:I4570. doi:10.1136/bmj.I4570

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

- 20. Ozemek C, Laddu DR, Lavie CJ, et al. An update on the role of cardiorespiratory fitness, structured exercise and lifestyle physical activity in preventing cardiovascular disease and health risk. *Prog Cardiovasc Dis*. Nov-Dec 2018;61(5-6):484-490. doi:10.1016/j.pcad.2018.11.005
- 21. Tian D, Meng J. Exercise for prevention and relief of cardiovascular disease: Prognoses, mechanisms, and approaches. *Oxid Med Cell Longev*. 2019;2019:3756750. doi:10.1155/2019/3756750
- 22. Kraus WE, Powell KE, Haskell WL, et al. Physical activity, all-cause and cardiovascular mortality, and cardiovascular disease. *Med Sci Sports Exerc*. Jun 2019;51(6):1270-1281. doi:10.1249/mss.00000000001939
- 23. Lavie CJ, Kachur S, Sui X. Impact of fitness and changes in fitness on lipids and survival. *Prog Cardiovasc Dis*. Sep-Oct 2019;62(5):431-435. doi:10.1016/j.pcad.2019.11.007
- 24. Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet.* Sep 24 2016;388(10051):1302-10. doi:10.1016/s0140-6736(16)30370-1
- 25. Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Church TS. The role of exercise and physical activity in weight loss and maintenance. *Prog Cardiovasc Dis*. Jan-Feb 2014;56(4):441-7. doi:10.1016/j.pcad.2013.09.012
- 26. Barry VW, Caputo JL, Kang M. The joint association of fitness and fatness on cardiovascular disease mortality: a meta-analysis. *Prog Cardiovasc Dis*. Jul-Aug 2018;61(2):136-141. doi:10.1016/j.pcad.2018.07.004
- 27. Wei M, Kampert JB, Barlow CE, et al. Relationship between low cardiorespiratory fitness and mortality in normal-weight, overweight, and obese men. *JAMA*. 1999;282(16):1547-1553.
- 28. Swift DL, Lavie CJ, Johannsen NM, et al. Physical activity, cardiorespiratory fitness, and exercise training in primary and secondary coronary prevention. *Circ J*. 2013;77(2):281-92.
- McAuley PA, Kokkinos PF, Oliveira RB, Emerson BT, Myers JN. Obesity paradox and cardiorespiratory fitness in 12,417 male veterans aged 40 to 70 years. *Mayo Clin Proc*. Feb 2010;85(2):115-21. doi:10.4065/mcp.2009.0562
- 30. Hakim AA, Petrovitch H, Burchfiel CM, et al. Effects of walking on mortality among nonsmoking retired men. *N Engl J Med.* Jan 8 1998;338(2):94-9. doi:10.1056/nejm199801083380204
- 31. Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet*. Sep 11-17 2004;364(9438):937-52. doi:10.1016/s0140-6736(04)17018-9
- 32. Manson JE, Hu FB, Rich-Edwards JW, et al. A prospective study of walking as compared with vigorous exercise in the prevention of coronary heart disease in women. *N Engl J Med*. Aug 26 1999;341(9):650-8. doi:10.1056/nejm199908263410904
- 33. Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passe? *JAMA*. Mar 21 2001;285(11):1447-54.
- 34. Jeong SW, Kim SH, Kang SH, et al. Mortality reduction with physical activity in patients with and without cardiovascular disease. *Eur Heart J*. Nov 14 2019;40(43):3547-3555. doi:10.1093/eurheartj/ehz564
- 35. Jetté M, Sidney K, Blümchen G. Metabolic equivalents (METS) in exercise testing, exercise prescription, and evaluation of functional capacity. *Clin Cardiol*. Aug 1990;13(8):555-65. doi:10.1002/clc.4960130809
- 36. Wen CP, Wai JP, Tsai MK, et al. Minimum amount of physical activity for reduced mortality and extended life expectancy: a prospective cohort study. *Lancet*. Oct 1 2011;378(9798):1244-53. doi:10.1016/s0140-6736(11)60749-6
- 37. Kachur S, Lavie CJ, Morera R, Ozemek C, Milani RV. Exercise training and cardiac rehabilitation in cardiovascular disease. *Expert Rev Cardiovasc Ther*. Aug 2019;17(8):585-596. doi:10.1080/14779072.2019.1651198

- 38. Zheng X, Zheng Y, Ma J, et al. Effect of exercise-based cardiac rehabilitation on anxiety and depression in patients with myocardial infarction: A systematic review and meta-analysis. *Heart Lung*. Jan 2019;48(1):1-7. doi:10.1016/j.hrtlng.2018.09.011
- 39. Zhang H, Chang R. Effects of exercise after percutaneous coronary intervention on cardiac function and cardiovascular adverse events in patients with coronary heart disease: Systematic review and meta-analysis. *J Sports Sci Med.* Jun 2019;18(2):213-222.
- 40. Solloway MR, Taylor SL, Shekelle PG, et al. An evidence map of the effect of Tai Chi on health outcomes. *Systematic reviews*. Jul 27 2016;5(1):126. doi:10.1186/s13643-016-0300-y
- 41. Hartley L, Lee MS, Kwong JS, et al. Qigong for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev.* Jun 11 2015;2015(6):Cd010390. doi:10.1002/14651858.CD010390.pub2
- 42. Hartley L, Flowers N, Lee MS, Ernst E, Rees K. Tai chi for primary prevention of cardiovascular disease. *Cochrane Database Syst Rev.* Apr 9 2014;(4):Cd010366. doi:10.1002/14651858.CD010366.pub2
- 43. Sun L, Zhuang LP, Li XZ, Zheng J, Wu WF. Tai Chi can prevent cardiovascular disease and improve cardiopulmonary function of adults with obesity aged 50 years and older: A long-term follow-up study. *Medicine (Baltimore)*. Oct 2019;98(42):e17509. doi:10.1097/md.00000000017509
- 44. Lauche R, Peng W, Ferguson C, et al. Efficacy of tai chi and qigong for the prevention of stroke and stroke risk factors: A systematic review with meta-analysis. *Medicine (Baltimore)*. Nov 2017;96(45):e8517. doi:10.1097/md.00000000008517
- 45. Liu T, Chan AW, Liu YH, Taylor-Piliae RE. Effects of Tai Chi-based cardiac rehabilitation on aerobic endurance, psychosocial well-being, and cardiovascular risk reduction among patients with coronary heart disease: A systematic review and meta-analysis. *Eur J Cardiovasc Nurs*. Apr 2018;17(4):368-383. doi:10.1177/1474515117749592
- 46. Chang MY. Qigong effects on heart rate variability and peripheral vasomotor responses. *West J Nurs Res.* Nov 2015;37(11):1383-403. doi:10.1177/0193945914535669
- 47. Lu X, Hui-Chan CW, Tsang WW. Tai Chi, arterial compliance, and muscle strength in older adults. *Eur J Prev Cardiol*. Aug 2013;20(4):613-9. doi:10.1177/2047487312443483
- 48. Field T. Tai Chi research review. *Complement Ther Clin Pract.* Aug 2011;17(3):141-6. doi:10.1016/j.ctcp.2010.10.002
- 49. Tao J, Rao T, Lin L, et al. Evaluation of Tai Chi Yunshou exercises on community-based stroke patients with balance dysfunction: a study protocol of a cluster randomized controlled trial. *BMC Complement Altern Med*. Feb 25 2015;15:31. doi:10.1186/s12906-015-0555-1
- 50. Desveaux L, Lee A, Goldstein R, Brooks D. Yoga in the management of chronic disease: A systematic review and meta-analysis. *Med Care*. Jul 2015;53(7):653-61. doi:10.1097/mlr.0000000000372
- 51. Kizhakkeveettil A, Whedon J, Schmalzl L, Hurwitz EL. Yoga for quality of life in individuals with chronic disease: A systematic review. *Altern Ther Health Med.* Jan 2019;25(1):36-43.
- 52. Cramer H, Lauche R, Haller H, Dobos G, Michalsen A. A systematic review of yoga for heart disease. *Eur J Prev Cardiol*. Mar 2015;22(3):284-95. doi:10.1177/2047487314523132
- 53. Chu P, Pandya A, Salomon JA, Goldie SJ, Hunink MG. Comparative effectiveness of personalized lifestyle management strategies for cardiovascular disease risk reduction. *J Am Heart Assoc*. Mar 29 2016;5(3):e002737. doi:10.1161/jaha.115.002737
- 54. Cramer H, Langhorst J, Dobos G, Lauche R. Yoga for metabolic syndrome: A systematic review and meta-analysis. *Eur J Prev Cardiol*. Dec 2016;23(18):1982-1993. doi:10.1177/2047487316665729
- 55. Hartley L, Dyakova M, Holmes J, et al. Yoga for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev.* May 13 2014;(5):Cd010072. doi:10.1002/14651858.CD010072.pub2

- 56. Christa E, Srivastava P, Chandran DS, et al. Effect of yoga-based cardiac rehabilitation on heart rate variability: Randomized controlled trial in patients post-MI. *Int J Yoga Therap*. Nov 2019;29(1):43-50. doi:10.17761/2019-00019
- 57. Djalilova DM, Schulz PS, Berger AM, Case AJ, Kupzyk KA, Ross AC. Impact of yoga on inflammatory biomarkers: a systematic review. *Biol Res Nurs*. Mar 2019;21(2):198-209. doi:10.1177/1099800418820162
- 58. Brandani JZ, Mizuno J, Ciolac EG, Monteiro HL. The hypotensive effect of Yoga's breathing exercises: A systematic review. *Complement Ther Clin Pract*. Aug 2017;28:38-46. doi:10.1016/j.ctcp.2017.05.002
- 59. Bhatnagar Á. Environmental determinants of cardiovascular disease. *Circ Res.* Jul 7 2017;121(2):162-180. doi:10.1161/circresaha.117.306458
- 60. Cohen MC, Rohtla KM, Lavery CE, Muller JE, Mittleman MA. Meta-analysis of the morning excess of acute myocardial infarction and sudden cardiac death. *Am J Cardiol*. Jun 1 1997;79(11):1512-6. doi:10.1016/s0002-9149(97)00181-1
- 61. Marti-Soler H, Gubelmann Ć, Aeschbacher S, et al. Seasonality of cardiovascular risk factors: an analysis including over 230 000 participants in 15 countries. *Heart*. Oct 2014;100(19):1517-23. doi:10.1136/heartjnl-2014-305623
- 62. Ostro B, Rauch S, Green R, Malig B, Basu R. The effects of temperature and use of air conditioning on hospitalizations. *Am J Epidemiol*. Nov 1 2010;172(9):1053-61. doi:10.1093/aje/kwq231
- 63. Fujimoto N, Matsubayashi K, Miyahara T, et al. The risk factors for ischemic heart disease in Tibetan highlanders. *Jpn Heart J*. Jan 1989;30(1):27-34. doi:10.1536/ihj.30.27
- 64. de Mendoza S, Nucete H, Ineichen E, Salazar E, Zerpa A, Glueck CJ. Lipids and lipoproteins in subjects at 1,000 and 3,500 meter altitudes. *Arch Environ Health*. Sep-Oct 1979;34(5):308-11. doi:10.1080/00039896.1979.10667422
- 65. Dadvand P, Bartoll X, Basagaña X, et al. Green spaces and general health: Roles of mental health status, social support, and physical activity. *Environ Int*. May 2016;91:161-7. doi:10.1016/j.envint.2016.02.029
- 66. James P, Banay RF, Hart JE, Laden F. A review of the health benefits of greenness. *Current epidemiology reports*. Jun 2015;2(2):131-142. doi:10.1007/s40471-015-0043-7
- 67. Twohig-Bennett C, Jones A. The health benefits of the great outdoors: A systematic review and meta-analysis of greenspace exposure and health outcomes. *Environ Res.* Oct 2018;166:628-637. doi:10.1016/j.envres.2018.06.030
- 68. Maas J, Verheij RA, Groenewegen PP, de Vries S, Spreeuwenberg P. Green space, urbanity, and health: how strong is the relation? *J Epidemiol Community Health*. Jul 2006;60(7):587-92. doi:10.1136/jech.2005.043125
- 69. Donneyong MM, Taylor KC, Kerber RA, Hornung CA, Scragg R. Is outdoor recreational activity an independent predictor of cardiovascular disease mortality NHANES III? *Nutr Metab Cardiovasc Dis*. Aug 2016;26(8):735-42. doi:10.1016/j.numecd.2016.02.008
- 70. James P, Hart JE, Banay RF, Laden F. Exposure to greenness and mortality in a nationwide prospective cohort study of women. *Environ Health Perspect*. Sep 2016;124(9):1344-1352. doi:10.1289/ehp.1510363
- 71. Donovan GH, Butry DT, Michael YL, et al. The relationship between trees and human health: evidence from the spread of the emerald ash borer. *Am J Prev Med*. Feb 2013;44(2):139-45. doi:10.1016/j.amepre.2012.09.066
- 72. Rostand SG. Ultraviolet light may contribute to geographic and racial blood pressure differences. *Hypertension*. Aug 1997;30(2 Pt 1):150-6. doi:10.1161/01.hyp.30.2.150
- 73. Opländer C, Volkmar CM, Paunel-Görgülü A, et al. Whole body UVA irradiation lowers systemic blood pressure by release of nitric oxide from intracutaneous photolabile nitric oxide derivates. *Circ Res.* Nov 6 2009;105(10):1031-40. doi:10.1161/circresaha.109.207019
- 74. Diez Roux AV, Merkin SS, Arnett D, et al. Neighborhood of residence and incidence of coronary heart disease. *N Engl J Med*. Jul 12 2001;345(2):99-106. doi:10.1056/nejm200107123450205

- 75. Pope CA, 3rd, Bhatnagar A, McCracken JP, Abplanalp W, Conklin DJ, O'Toole T. Exposure to fine particulate air pollution is associated with endothelial injury and systemic inflammation. *Circ Res.* Nov 11 2016;119(11):1204-1214. doi:10.1161/circresaha.116.309279
- 76. Bauer M, Moebus S, Möhlenkamp S, et al. Urban particulate matter air pollution is associated with subclinical atherosclerosis: results from the HNR (Heinz Nixdorf Recall) study. *J Am Coll Cardiol*. Nov 23 2010;56(22):1803-8. doi:10.1016/j.jacc.2010.04.065
- 77. Swinburn TK, Hammer MS, Neitzel RL. Valuing quiet: An economic assessment of U.S. environmental noise as a cardiovascular health hazard. *Am J Prev Med*. Sep 2015;49(3):345-53. doi:10.1016/j.amepre.2015.02.016
- 78. Said MA, El-Gohary OA. Effect of noise stress on cardiovascular system in adult male albino rat: implication of stress hormones, endothelial dysfunction and oxidative stress. *Gen Physiol Biophys.* Jul 2016;35(3):371-7. doi:10.4149/gpb\_2016003
- 79. Münzel T, Schmidt FP, Steven S, Herzog J, Daiber A, Sørensen M. Environmental noise and the cardiovascular system. *J Am Coll Cardiol*. Feb 13 2018;71(6):688-697. doi:10.1016/j.jacc.2017.12.015
- 80. Münzel T, Gori T, Babisch W, Basner M. Cardiovascular effects of environmental noise exposure. *Eur Heart J.* Apr 2014;35(13):829-36. doi:10.1093/eurheartj/ehu030
- 81. Bradt J, Dileo C, Potvin N. Music for stress and anxiety reduction in coronary heart disease patients. *Cochrane Database Syst Rev*. Dec 28 2013;(12):Cd006577. doi:10.1002/14651858.CD006577.pub3
- 82. Lloyd-Jones D, Adams RJ, Brown TM, et al. Heart disease and stroke statistics--2010 update: a report from the American Heart Association. *Circulation*. Feb 23 2010;121(7):e46-e215. doi:10.1161/circulationaha.109.192667
- 83. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. *J Am Coll Cardiol*. May 19 2004;43(10):1731-7. doi:10.1016/j.jacc.2003.12.047
- 84. Heianza Y, Zheng Y, Ma W, et al. Duration and life-stage of antibiotic use and risk of cardiovascular events in women. *Eur Heart J*. Dec 14 2019;40(47):3838-3845. doi:10.1093/eurheartj/ehz231
- 85. Kivimäki M, Jokela M, Nyberg ST, et al. Long working hours and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603,838 individuals. *Lancet*. Oct 31 2015;386(10005):1739-46. doi:10.1016/s0140-6736(15)60295-1
- 86. Virtanen M, Nyberg ST, Batty GD, et al. Perceived job insecurity as a risk factor for incident coronary heart disease: systematic review and meta-analysis. *BMJ*. 2013;347
- 87. Kivimaki M, Nyberg ST, Fransson EI, et al. Associations of job strain and lifestyle risk factors with risk of coronary artery disease: a meta-analysis of individual participant data. *CMAJ*. Jun 11 2013;185(9):763-9. doi:10.1503/cmaj.121735
- 88. Belkic K, Schnall P, Landsbergis P, Baker D. The workplace and cardiovascular health: conclusions and thoughts for a future agenda. *Occup Med*. Jan-Mar 2000;15(1):307-21, v-vi.
- 89. Eller NH, Netterstrom B, Gyntelberg F, et al. Work-related psychosocial factors and the development of ischemic heart disease: a systematic review. *Cardiology in review*. Mar-Apr 2009;17(2):83-97. doi:10.1097/CRD.0b013e318198c8e9
- 90. Kivimaki M, Nyberg ST, Batty GD, et al. Job strain as a risk factor for coronary heart disease: a collaborative meta-analysis of individual participant data. *Lancet*. Oct 27 2012;380(9852):1491-7. doi:10.1016/s0140-6736(12)60994-5
- 91. Kivimaki M, Virtanen M, Elovainio M, Kouvonen A, Vaananen A, Vahtera J. Work stress in the etiology of coronary heart disease--a meta-analysis. *Scand J Work Environ Health*. Dec 2006;32(6):431-42.
- 92. Yusuf S, Hawken S, Ounpuu S, et al. Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet*. Nov 5 2005;366(9497):1640-9. doi:10.1016/s0140-6736(05)67663-5

Heart Health Overview University of Wisconsin Integrative Health www.fammed.wisc.edu/integrative

- Siegrist J, Peter R, Junge A, Cremer P, Seidel D. Low status control, high effort at work and ischemic heart disease: prospective evidence from blue-collar men. *Soc Sci Med*. 1990;31(10):1127-34.
- 94. De Witte H. Job insecurity: Review of the international literature on definitions, prevalence, antecedents and consequences. *SAJIP*. 2005;31(4):p. 1-6.
- 95. Ferrie JE, Shipley MJ, Newman K, Stansfeld SA, Marmot M. Self-reported job insecurity and health in the Whitehall II study: potential explanations of the relationship. *Soc Sci Med*. Apr 2005;60(7):1593-602. doi:10.1016/j.socscimed.2004.08.006
- 96. Georgiades A, Janszky I, Blom M, Laszlo KD, Ahnve S. Financial strain predicts recurrent events among women with coronary artery disease. *Int J Cardiol*. Jun 26 2009;135(2):175-83. doi:10.1016/j.ijcard.2008.03.093
- 97. Lee G, Carrington M. Tackling heart disease and poverty. *Nurs Health Sci*. Dec 2007;9(4):290-4. doi:10.1111/j.1442-2018.2007.00363.x
- 98. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation*. Oct 1993;88(4 Pt 1):1973-98. doi:10.1161/01.cir.88.4.1973
- 99. Marmot MG, Shipley MJ, Rose G. Inequalities in death--specific explanations of a general pattern? *Lancet.* May 5 1984;1(8384):1003-6. doi:10.1016/s0140-6736(84)92337-7
- 100. Lemstra M, Rogers M, Moraros J. Income and heart disease: Neglected risk factor. *Can Fam Physician*. Aug 2015;61(8):698-704.
- Gupta R, Yusuf S. Challenges in management and prevention of ischemic heart disease in low socioeconomic status people in LLMICs. *BMC Med.* Nov 26 2019;17(1):209. doi:10.1186/s12916-019-1454-y
- 102. Sin NL. The protective role of positive well-being in cardiovascular disease: Review of current evidence, mechanisms, and clinical implications. *Curr Cardiol Rep.* Nov 2016;18(11):106. doi:10.1007/s11886-016-0792-z
- 103. DuBois CM, Lopez OV, Beale EE, Healy BC, Boehm JK, Huffman JC. Relationships between positive psychological constructs and health outcomes in patients with cardiovascular disease: A systematic review. *Int J Cardiol*. Sep 15 2015;195:265-80. doi:10.1016/j.ijcard.2015.05.121
- 104. Giltay EJ, Kamphuis MH, Kalmijn S, Zitman FG, Kromhout D. Dispositional optimism and the risk of cardiovascular death: the Zutphen Elderly Study. *Arch Intern Med*. Feb 27 2006;166(4):431-6. doi:10.1001/archinte.166.4.431
- 105. Kim ES, Hagan KA, Grodstein F, DeMeo DL, De Vivo I, Kubzansky LD. Optimism and causespecific mortality: A prospective cohort study. *Am J Epidemiol*. Jan 1 2017;185(1):21-29. doi:10.1093/aje/kww182
- 106. Denollet J, Schiffer AA, Spek V. A general propensity to psychological distress affects cardiovascular outcomes: evidence from research on the type D (distressed) personality profile. *Circ Cardiovasc Qual Outcomes*. Sep 2010;3(5):546-57. doi:10.1161/circoutcomes.109.934406
- Cao X, Wong EM, Chow Choi K, Cheng L, Ying Chair S. Interventions for cardiovascular patients with type D personality: A systematic review. *Worldviews Evid Based Nurs*. Aug 2016;13(4):314-23. doi:10.1111/wvn.12153
- 108. Yeung JWK, Zhang Z, Kim TY. Volunteering and health benefits in general adults: cumulative effects and forms. *BMC Public Health*. 2017/07/11 2017;18(1):8. doi:10.1186/s12889-017-4561-8
- 109. Morrow-Howell N, Hinterlong J, Rozario PA, Tang F. Effects of volunteering on the well-being of older adults. *J Gerontol B Psychol Sci Soc Sci*. 2003;58(3):S137-S145.
- 110. Tang F. Late-life volunteering and trajectories of physical health. *J Appl Gerontol.* 2009;28(4):524-533.
- 111. Harris AH, Thoresen CE. Volunteering is associated with delayed mortality in older people: analysis of the longitudinal study of aging. *J Health Psychol*. Nov 2005;10(6):739-52. doi:10.1177/1359105305057310
- 112. Luoh MC, Herzog AR. Individual consequences of volunteer and paid work in old age: health and mortality. *J Health Soc Behav*. Dec 2002;43(4):490-509.

- 113. Sneed RS, Cohen S. A prospective study of volunteerism and hypertension risk in older adults. *Psychol Aging*. Jun 2013;28(2):578-86. doi:10.1037/a0032718
- 114. Warren TY, Barry V, Hooker SP, Sui X, Church TS, Blair SN. Sedentary behaviors increase risk of cardiovascular disease mortality in men. *Med Sci Sports Exerc*. May 2010;42(5):879-85. doi:10.1249/MSS.0b013e3181c3aa7e
- 115. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. *JAMA*. Apr 5 2006;295(13):1549-55. doi:10.1001/jama.295.13.1549
- 116. Klein S, Burke LE, Bray GA, et al. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation*. Nov 2 2004;110(18):2952-67. doi:10.1161/01.cir.0000145546.97738.1e
- 117. Dieter BP, Tuttle KR. Dietary strategies for cardiovascular health. *Trends Cardiovasc Med*. Jul 2017;27(5):295-313. doi:10.1016/j.tcm.2016.12.007
- 118. Martinez-Gonzalez MA, Bes-Rastrollo M. Dietary patterns, Mediterranean diet, and cardiovascular disease. *Curr Opin Lipidol*. Feb 2014;25(1):20-6. doi:10.1097/mol.0000000000044
- 119. Chiavaroli L, Nishi SK, Khan TA, et al. Portfolio dietary pattern and cardiovascular disease: a systematic review and meta-analysis of controlled trials. *Prog Cardiovasc Dis*. May-Jun 2018;61(1):43-53. doi:10.1016/j.pcad.2018.05.004
- 120. de Cabo R, Mattson MP. Effects of intermittent fasting on health, aging, and disease. *N Engl J Med*. Dec 26 2019;381(26):2541-2551. doi:10.1056/NEJMra1905136
- 121. Freeman AM, Morris PB, Barnard N, et al. Trending cardiovascular nutrition controversies. *J Am Coll Cardiol.* Mar 7 2017;69(9):1172-1187. doi:10.1016/j.jacc.2016.10.086
- 122. Barnard ND, Levin SM, Yokoyama Y. A systematic review and meta-analysis of changes in body weight in clinical trials of vegetarian diets. *J Acad Nutr Diet*. Jun 2015;115(6):954-69. doi:10.1016/j.jand.2014.11.016
- 123. Yokoyama Y, Nishimura K, Barnard ND, et al. Vegetarian diets and blood pressure: a metaanalysis. *JAMA Intern Med*. Apr 2014;174(4):577-87. doi:10.1001/jamainternmed.2013.14547
- 124. Crowe FL, Appleby PN, Travis RC, Key TJ. Risk of hospitalization or death from ischemic heart disease among British vegetarians and nonvegetarians: results from the EPIC-Oxford cohort study. *Am J Clin Nutr.* Mar 2013;97(3):597-603. doi:10.3945/ajcn.112.044073
- 125. Gould KL, Ornish D, Scherwitz L, et al. Changes in myocardial perfusion abnormalities by positron emission tomography after long-term, intense risk factor modification. *JAMA*. Sep 20 1995;274(11):894-901. doi:10.1001/jama.1995.03530110056036
- 126. Qi L, van Dam RM, Liu S, Franz M, Mantzoros C, Hu FB. Whole-grain, bran, and cereal fiber intakes and markers of systemic inflammation in diabetic women. *Diabetes Care*. Feb 2006;29(2):207-11.
- 127. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab*. Jun 2004;89(6):2548-56. doi:10.1210/jc.2004-0395
- 128. Ma XY, Liu JP, Song ZY. Glycemic load, glycemic index and risk of cardiovascular diseases: metaanalyses of prospective studies. *Atherosclerosis*. Aug 2012;223(2):491-6. doi:10.1016/j.atherosclerosis.2012.05.028
- 129. Jakobsen MU, Dethlefsen C, Joensen AM, et al. Intake of carbohydrates compared with intake of saturated fatty acids and risk of myocardial infarction: importance of the glycemic index. *Am J Clin Nutr*. Jun 2010;91(6):1764-8. doi:10.3945/ajcn.2009.29099
- 130. Rossi M, Turati F, Lágiou P, et al. Mediterranean diet and glycaemic load in relation to incidence of type 2 diabetes: results from the Greek cohort of the population-based European Prospective Investigation into Cancer and Nutrition (EPIC). *Diabetologia*. Nov 2013;56(11):2405-13. doi:10.1007/s00125-013-3013-y
- 131. Olendzki B, Speed C, Domino FJ. Nutritional assessment and counseling for prevention and treatment of cardiovascular disease. *Am Fam Physician*. Jan 15 2006;73(2):257-64.

- 132. Erkkila AT, Lichtenstein AH. Fiber and cardiovascular disease risk: how strong is the evidence? *J Cardiovasc Nurs*. Jan-Feb 2006;21(1):3-8.
- 133. Rimm EB, Ascherio A, Giovannucci E, Spiegelman D, Stampfer MJ, Willett WC. Vegetable, fruit, and cereal fiber intake and risk of coronary heart disease among men. *JAMA*. Feb 14 1996;275(6):447-51.
- 134. Giacco R, Costabile G, Della Pepa G, et al. A whole-grain cereal-based diet lowers postprandial plasma insulin and triglyceride levels in individuals with metabolic syndrome. *Nutr Metab Cardiovasc Dis*. 2014;
- 135. Harris KA, Kris-Etherton PM. Effects of whole grains on coronary heart disease risk. *Curr Atheroscler Rep.* Nov 2010;12(6):368-76. doi:10.1007/s11883-010-0136-1
- 136. Cohn JS, Kamili A, Wat E, Chung RW, Tandy S. Reduction in intestinal cholesterol absorption by various food components: mechanisms and implications. *Atheroscler Suppl.* Jun 2010;11(1):45-8. doi:10.1016/j.atherosclerosissup.2010.04.004
- 137. Reynolds A, Mann J, Cummings J, Winter N, Mete E, Te Morenga L. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. *Lancet*. Feb 2 2019;393(10170):434-445. doi:10.1016/s0140-6736(18)31809-9
- 138. Matvienko OA, Lewis DS, Swanson M, et al. A single daily dose of soybean phytosterols in ground beef decreases serum total cholesterol and LDL cholesterol in young, mildly hypercholesterolemic men. *Am J Clin Nutr.* Jul 2002;76(1):57-64.
- 139. Neil HA, Meijer GW, Roe LS. Randomised controlled trial of use by hypercholesterolaemic patients of a vegetable oil sterol-enriched fat spread. *Atherosclerosis*. Jun 2001;156(2):329-37.
- 140. Nestel PJ. Dietary fat and blood pressure. *Curr Hypertens Rep*. Feb 12 2019;21(2):17. doi:10.1007/s11906-019-0918-y
- 141. Dragsted LO, Pedersen A, Hermetter A, et al. The 6-a-day study: effects of fruit and vegetables on markers of oxidative stress and antioxidative defense in healthy nonsmokers. *Am J Clin Nutr*. Jun 2004;79(6):1060-72.
- 142. Tresserra-Rimbau A, Rimm E, Medina-Remón A, et al. Inverse association between habitual polyphenol intake and incidence of cardiovascular events in the PREDIMED study. *Nutr Metab Cardiovasc Dis*. 2014;24(6):639-647.
- 143. Lilamand M, Kelaiditi E, Guyonnet S, et al. Flavonoids and arterial stiffness: Promising perspectives. *Nutr Metab Cardiovasc Dis.* 2014;
- 144. Beauchamp GK, Keast RS, Morel D, et al. Phytochemistry: ibuprofen-like activity in extra-virgin olive oil. *Nature*. Sep 1 2005;437(7055):45-6. doi:10.1038/437045a
- 145. Kromhout D, de Goede J. Update on cardiometabolic health effects of omega-3 fatty acids. *Curr Opin Lipidol*. Feb 2014;25(1):85-90. doi:10.1097/mol.00000000000041
- 146. Xin W, Wei W, Li XY. Short-term effects of fish-oil supplementation on heart rate variability in humans: a meta-analysis of randomized controlled trials. *Am J Clin Nutr*. May 2013;97(5):926-35. doi:10.3945/ajcn.112.049833
- 147. Freeman AM, Morris PB, Aspry K, et al. A clinician's guide for trending cardiovascular nutrition controversies: Part II. *J Am Coll Cardiol*. Jul 31 2018;72(5):553-568. doi:10.1016/j.jacc.2018.05.030
- 148. Rix TA, Christensen JH, Schmidt EB. Omega-3 fatty acids and cardiac arrhythmias. *Curr Opin Clin Nutr Metab Care*. Mar 2013;16(2):168-73. doi:10.1097/MCO.0b013e32835bf39b
- 149. Macchia A, Grancelli H, Varini S, et al. Omega-3 fatty acids for the prevention of recurrent symptomatic atrial fibrillation: results of the FORWARD (Randomized Trial to Assess Efficacy of PUFA for the Maintenance of Sinus Rhythm in Persistent Atrial Fibrillation) trial. *J Am Coll Cardiol*. Jan 29 2013;61(4):463-8. doi:10.1016/j.jacc.2012.11.021
- 150. Djousse L, Akinkuolie AO, Wu JH, Ding EL, Gaziano JM. Fish consumption, omega-3 fatty acids and risk of heart failure: a meta-analysis. *Clin Nutr*. Dec 2012;31(6):846-53. doi:10.1016/j.clnu.2012.05.010
- 151. Li YH, Zhou CH, Pei HJ, et al. Fish consumption and incidence of heart failure: a meta-analysis of prospective cohort studies. *Chin Med J (Engl)*. Mar 2013;126(5):942-8.

- 152. Chowdhury R, Warnakula S, Kunutsor S, et al. Association of dietary, circulating, and supplement fatty acids with coronary risk: a systematic review and meta-analysis. *Ann Intern Med*. Mar 18 2014;160(6):398-406. doi:10.7326/m13-1788
- 153. He K, Song Y, Daviglus ML, et al. Accumulated evidence on fish consumption and coronary heart disease mortality: a meta-analysis of cohort studies. *Circulation*. Jun 8 2004;109(22):2705-11. doi:10.1161/01.Cir.0000132503.19410.6b
- 154. Aung T, Halsey J, Kromhout D, et al. Associations of omega-3 fatty acid supplement use with cardiovascular disease risks: meta-analysis of 10 trials involving 77 917 individuals. *JAMA cardiology*. Mar 1 2018;3(3):225-234. doi:10.1001/jamacardio.2017.5205
- 155. Lloyd-Williams F, O'Flaherty M, Mwatsama M, Birt C, Ireland R, Capewell S. Estimating the cardiovascular mortality burden attributable to the European Common Agricultural Policy on dietary saturated fats. *Bulletin of the World Health Organization*. Jul 2008;86(7):535-541a.
- 156. Mozaffarian D, Micha R, Wallace S. Effects on coronary heart disease of increasing polyunsaturated fat in place of saturated fat: a systematic review and meta-analysis of randomized controlled trials. *PLoS Med*. 2010;7(3):e1000252.
- 157. Astrup A, Dyerberg J, Elwood P, et al. The role of reducing intakes of saturated fat in the prevention of cardiovascular disease: where does the evidence stand in 2010? *Am J Clin Nutr*. Apr 2011;93(4):684-8. doi:10.3945/ajcn.110.004622
- 158. Grundy SM, Balady GJ, Criqui MH, et al. Primary prevention of coronary heart disease: guidance from Framingham: a statement for healthcare professionals from the AHA Task Force on Risk Reduction. American Heart Association. *Circulation*. May 12 1998;97(18):1876-87.
- 159. Siri-Tarino PW, Sun Q, Hu FB, Krauss RM. Meta-analysis of prospective cohort studies evaluating the association of saturated fat with cardiovascular disease. *Am J Clin Nutr.* Mar 2010;91(3):535-46. doi:10.3945/ajcn.2009.27725
- 160. Lawrence GD. Dietary fats and health: dietary recommendations in the context of scientific evidence. *Adv Nutr.* May 2013;4(3):294-302. doi:10.3945/an.113.003657
- 161. Malhotra A. Saturated fat is not the major issue. BMJ. 2013;347
- 162. Lopez-Garcia E, Schulze MB, Meigs JB, et al. Consumption of trans fatty acids is related to plasma biomarkers of inflammation and endothelial dysfunction. *J Nutr*. Mar 2005;135(3):562-6.
- Mozaffarian D, Katan MB, Ascherio A, Stampfer MJ, Willett WC. Trans fatty acids and cardiovascular disease. N Engl J Med. Apr 13 2006;354(15):1601-13. doi:10.1056/NEJMra054035
- 164. Micha R, Shulkin ML, Peñalvo JL, et al. Etiologic effects and optimal intakes of foods and nutrients for risk of cardiovascular diseases and diabetes: Systematic reviews and meta-analyses from the Nutrition and Chronic Diseases Expert Group (NutriCoDE). *PLoS One*. 2017;12(4):e0175149. doi:10.1371/journal.pone.0175149
- 165. Li Y, Hruby A, Bernstein AM, et al. Saturated fats compared with unsaturated fats and sources of carbohydrates in relation to risk of coronary heart disease: A prospective cohort study. J Am Coll Cardiol. Oct 6 2015;66(14):1538-1548. doi:10.1016/j.jacc.2015.07.055
- 166. Malik VS, Hu FB. Sugar-sweetened beverages and cardiometabolic health: An update of the evidence. *Nutrients*. Aug 8 2019;11(8)doi:10.3390/nu11081840
- 167. Micha R, Peñalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States. *JAMA*. Mar 7 2017;317(9):912-924. doi:10.1001/jama.2017.0947
- 168. Wedick NM, Pan A, Cassidy A, et al. Dietary flavonoid intakes and risk of type 2 diabetes in US men and women. *Am J Clin Nutr*. Apr 2012;95(4):925-33. doi:10.3945/ajcn.111.028894
- 169. Cassidy A, Mukamal KJ, Liu L, Franz M, Eliassen AH, Rimm EB. High anthocyanin intake is associated with a reduced risk of myocardial infarction in young and middle-aged women. *Circulation*. Jan 15 2013;127(2):188-96. doi:10.1161/circulationaha.112.122408
- 170. Greenberg JA, Dunbar CC, Schnoll R, Kokolis R, Kokolis S, Kassotis J. Caffeinated beverage intake and the risk of heart disease mortality in the elderly: a prospective analysis. *Am J Clin Nutr*. Feb 2007;85(2):392-8. doi:10.1093/ajcn/85.2.392

- 171. Ding M, Bhupathiraju SN, Satija A, van Dam RM, Hu FB. Long-term coffee consumption and risk of cardiovascular disease: a systematic review and a dose-response meta-analysis of prospective cohort studies. *Circulation*. Feb 11 2014;129(6):643-59. doi:10.1161/circulationaha.113.005925
- 172. Cheng M, Hu Z, Lu X, Huang J, Gu D. Caffeine Intake and Atrial Fibrillation Incidence: Dose Response Meta-analysis of Prospective Cohort Studies. *Can J Cardiol*. 2014;30(4):448-454.
- 173. Li X, Yu C, Guo Y, et al. Tea consumption and risk of ischaemic heart disease. *Heart*. May 2017;103(10):783-789. doi:10.1136/heartjnl-2016-310462
- 174. Kuriyama S, Shimazu T, Ohmori K, et al. Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: the Ohsaki study. *JAMA*. 2006;296(10):1255-1265.
- 175. Misaka S, Yatabe J, Müller F, et al. Green tea ingestion greatly reduces plasma concentrations of nadolol in healthy subjects. *Clin Pharmacol Ther*. 2014;
- 176. Drouin-Chartier JP, Côté JA, Labonté M, et al. Comprehensive review of the impact of dairy foods and dairy fat on cardiometabolic risk. *Adv Nutr.* Nov 2016;7(6):1041-1051. doi:10.3945/an.115.011619
- 177. Higgins JP, Tuttle TD, Higgins CL. Energy beverages: content and safety. *Mayo Clin Proc*. Nov 2010;85(11):1033-41. doi:10.4065/mcp.2010.0381
- 178. McGuire S. Scientific report of the 2015 dietary guidelines advisory committee. Washington, DC: US Departments of Agriculture and Health and Human Services, 2015. Adv Nutr. Jan 2016;7(1):202-4. doi:10.3945/an.115.011684
- 179. Berger S, Raman G, Vishwanathan R, Jacques PF, Johnson EJ. Dietary cholesterol and cardiovascular disease: a systematic review and meta-analysis. *Am J Clin Nutr.* Aug 2015;102(2):276-94. doi:10.3945/ajcn.114.100305
- 180. Weggemans RM, Zock PL, Katan MB. Dietary cholesterol from eggs increases the ratio of total cholesterol to high-density lipoprotein cholesterol in humans: a meta-analysis. *Am J Clin Nutr.* May 2001;73(5):885-91. doi:10.1093/ajcn/73.5.885
- 181. Bondonno CP, Liu AH, Croft KD, et al. Short-term effects of a high nitrate diet on nitrate metabolism in healthy individuals. *Nutrients*. Mar 12 2015;7(3):1906-15. doi:10.3390/nu7031906
- Li M, Fan Y, Zhang X, Hou W, Tang Z. Fruit and vegetable intake and risk of type 2 diabetes mellitus: meta-analysis of prospective cohort studies. *BMJ open*. Nov 5 2014;4(11):e005497. doi:10.1136/bmjopen-2014-005497
- 183. Joshipura KJ, Hung HC, Li TY, et al. Intakes of fruits, vegetables and carbohydrate and the risk of CVD. *Public Health Nutr.* Jan 2009;12(1):115-21. doi:10.1017/s1368980008002036
- 184. U.S. Department of Agriculture, Economic Research Service. Dried beans. 2013.
- 185. Poddar KH, Ames M, Hsin-Jen C, Feeney MJ, Wang Y, Cheskin LJ. Positive effect of mushrooms substituted for meat on body weight, body composition, and health parameters. A 1-year randomized clinical trial. *Appetite*. Dec 2013;71:379-87. doi:10.1016/j.appet.2013.09.008
- 186. Afshin A, Micha R, Khatibzadeh S, Mozaffarian D. Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis. *Am J Clin Nutr*. Jul 2014;100(1):278-88. doi:10.3945/ajcn.113.076901
- 187. Sabaté J, Oda K, Ros E. Nut consumption and blood lipid levels: a pooled analysis of 25 intervention trials. *Arch Intern Med*. May 10 2010;170(9):821-7. doi:10.1001/archinternmed.2010.79
- 188. Luo C, Zhang Y, Ding Y, et al. Nut consumption and risk of type 2 diabetes, cardiovascular disease, and all-cause mortality: a systematic review and meta-analysis. *Am J Clin Nutr.* Jul 2014;100(1):256-69. doi:10.3945/ajcn.113.076109
- 189. Flores-Mateo G, Rojas-Rueda D, Basora J, Ros E, Salas-Salvadó J. Nut intake and adiposity: meta-analysis of clinical trials. *Am J Clin Nutr*. Jun 2013;97(6):1346-55. doi:10.3945/ajcn.111.031484
- 190. Wolk A. Potential health hazards of eating red meat. *J Intern Med*. Feb 2017;281(2):106-122. doi:10.1111/joim.12543



- 191. Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. Intersalt Cooperative Research Group. *BMJ*. Jul 30 1988;297(6644):319-28. doi:10.1136/bmj.297.6644.319
- 192. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med*. Jan 4 2001;344(1):3-10. doi:10.1056/nejm200101043440101
- 193. Graudal N, Jürgens G, Baslund B, Alderman MH. Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a meta-analysis. *Am J Hypertens*. Sep 2014;27(9):1129-37. doi:10.1093/ajh/hpu028
- 194. Javaheri S, Redline S. Insomnia and risk of cardiovascular disease. *Chest*. Aug 2017;152(2):435-444. doi:10.1016/j.chest.2017.01.026
- 195. Liu H, Chen A. Roles of sleep deprivation in cardiovascular dysfunctions. *Life Sci*. Feb 15 2019;219:231-237. doi:10.1016/j.lfs.2019.01.006
- 196. Laugsand LE, Vatten LJ, Platou C, Janszky I. Insomnia and the risk of acute myocardial infarction: a population study. *Circulation*. Nov 8 2011;124(19):2073-81. doi:10.1161/circulationaha.111.025858
- 197. Fernandez-Mendoza J, Vgontzas AN, Liao D, et al. Insomnia with objective short sleep duration and incident hypertension: the Penn State Cohort. *Hypertension*. Oct 2012;60(4):929-35. doi:10.1161/hypertensionaha.112.193268
- 198. Swanson LM, Favorite TK, Horin E, Arnedt JT. A combined group treatment for nightmares and insomnia in combat veterans: a pilot study. *J Trauma Stress*. Dec 2009;22(6):639-42. doi:10.1002/jts.20468
- 199. Khan H, Kella D, Kunutsor SK, Savonen K, Laukkanen JA. Sleep duration and risk of fatal coronary heart disease, sudden cardiac death, cancer death, and all-cause mortality. *Am J Med*. Dec 2018;131(12):1499-1505.e2. doi:10.1016/j.amjmed.2018.07.010
- 200. Lao XQ, Liu X, Deng HB, et al. Sleep quality, sleep duration, and the risk of coronary heart disease: A prospective cohort study with 60,586 adults. *J Clin Sleep Med*. Jan 15 2018;14(1):109-117. doi:10.5664/jcsm.6894
- 201. Cheng Y, Du CL, Hwang JJ, Chen IS, Chen MF, Su TC. Working hours, sleep duration and the risk of acute coronary heart disease: a case-control study of middle-aged men in Taiwan. *Int J Cardiol*. Feb 15 2014;171(3):419-22. doi:10.1016/j.ijcard.2013.12.035
- Virtanen M, Heikkila K, Jokela M, et al. Long working hours and coronary heart disease: a systematic review and meta-analysis. *Am J Epidemiol*. Oct 1 2012;176(7):586-96. doi:10.1093/aje/kws139
- 203. Virtanen M, Ferrie JE, Gimeno D, et al. Long working hours and sleep disturbances: the Whitehall II prospective cohort study. *Sleep*. Jun 2009;32(6):737-45.
- 204. Coniglio AC, Mentz RJ. Sleep breathing disorders in heart failure. *Heart Fail Clin*. Jan 2020;16(1):45-51. doi:10.1016/j.hfc.2019.08.009
- 205. Tietjens JR, Claman D, Kezirian EJ, et al. Obstructive sleep apnea in cardiovascular disease: A review of the literature and proposed multidisciplinary clinical management strategy. *J Am Heart Assoc.* Jan 8 2019;8(1):e010440. doi:10.1161/jaha.118.010440
- 206. Walters AS, Rye DB. Review of the relationship of restless legs syndrome and periodic limb movements in sleep to hypertension, heart disease, and stroke. *Sleep*. May 2009;32(5):589-97.
- 207. Stopford E, Ravi K, Nayar V. The Association of Sleep Disordered Breathing with Heart Failure and Other Cardiovascular Conditions. *Cardiol Res Pract.* 2013;2013
- 208. Monahan K, Storfer-Isser A, Mehra R, et al. Triggering of nocturnal arrhythmias by sleep-disordered breathing events. *J Am Coll Cardiol*. Nov 3 2009;54(19):1797-804. doi:10.1016/j.jacc.2009.06.038
- 209. Krakow B, Melendrez D, Warner TD, Dorin R, Harper R, Hollifield M. To breathe, perchance to sleep: sleep-disordered breathing and chronic insomnia among trauma survivors. *Sleep Breath*. Dec 2002;6(4):189-202. doi:10.1007/s11325-002-0189-7

- 210. Azevedo Da Silva M, Singh-Manoux A, Shipley MJ, et al. Sleep duration and sleep disturbances partly explain the association between depressive symptoms and cardiovascular mortality: the Whitehall II cohort study. *J Sleep Res.* Feb 2014;23(1):94-7. doi:10.1111/jsr.12077
- Valtorta NK, Kanaan M, Gilbody S, Hanratty B. Loneliness, social isolation and risk of cardiovascular disease in the English Longitudinal Study of Ageing. *Eur J Prev Cardiol*. Sep 2018;25(13):1387-1396. doi:10.1177/2047487318792696
- 212. Christakis NA, Fowler JH. The spread of obesity in a large social network over 32 years. *N Engl J Med*. Jul 26 2007;357(4):370-9. doi:10.1056/NEJMsa066082
- 213. Barabási AL. Network medicine--from obesity to the "diseasome". *N Engl J Med*. Jul 26 2007;357(4):404-7. doi:10.1056/NEJMe078114
- 214. Xia N, Li H. Loneliness, social isolation, and cardiovascular health. *Antioxidants & redox signaling*. Mar 20 2018;28(9):837-851. doi:10.1089/ars.2017.7312
- 215. Kaplan JR, Chen H, Manuck SB. The relationship between social status and atherosclerosis in male and female monkeys as revealed by meta-analysis. *Am J Primatol*. Sep 2009;71(9):732-41. doi:10.1002/ajp.20707
- 216. Kaplan JR, Manuck SB, Clarkson TB, Lusso FM, Taub DM, Miller EW. Social stress and atherosclerosis in normocholesterolemic monkeys. *Science*. May 13 1983;220(4598):733-5.
- 217. Holt-Lunstad J, Smith TB, Layton JB. Social relationships and mortality risk: a meta-analytic review. *PLoS Med.* Jul 2010;7(7):e1000316. doi:10.1371/journal.pmed.1000316
- 218. Orth-Gomer K, Wamala SP, Horsten M, Schenck-Gustafsson K, Schneiderman N, Mittleman MA. Marital stress worsens prognosis in women with coronary heart disease: The Stockholm Female Coronary Risk Study. *JAMA*. 2000;284(23):3008-3014.
- 219. Mostofsky E, Maclure M, Sherwood JB, Tofler GH, Muller JE, Mittleman MA. Risk of acute myocardial infarction after the death of a significant person in one's life: the Determinants of Myocardial Infarction Onset Study. *Circulation*. Jan 24 2012;125(3):491-6. doi:10.1161/circulationaha.111.061770
- 220. Li J, Hansen D, Mortensen PB, Olsen J. Myocardial infarction in parents who lost a child: a nationwide prospective cohort study in Denmark. *Circulation*. Sep 24 2002;106(13):1634-9.
- 221. Lee S, Colditz GA, Berkman LF, Kawachi I. Caregiving and risk of coronary heart disease in U.S. women: a prospective study. *Am J Prev Med*. Feb 2003;24(2):113-9.
- 222. Fang J, Wang JW, Li J, Li H, Shao C. The correlates of social capital and adherence to healthy lifestyle in patients with coronary heart disease. *Patient Prefer Adherence*. 2017;11:1701-1707. doi:10.2147/ppa.S140787
- 223. Ein N, Li L, Vickers K. The effect of pet therapy on the physiological and subjective stress response: A meta-analysis. *Stress Health*. Oct 2018;34(4):477-489. doi:10.1002/smi.2812
- 224. Yeh TL, Lei WT, Liu SJ, Chien KL. A modest protective association between pet ownership and cardiovascular diseases: A systematic review and meta-analysis. *PLoS One*. 2019;14(5):e0216231. doi:10.1371/journal.pone.0216231
- 225. McPherson M, Smith-Lovin L, Brashears ME. Social isolation in America: changes in core discussion networks over two decades. *Am Sociol Rev.* 2006;71(3):353-375.
- 226. House JS. Social isolation kills, but how and why? Psychosom Med. Mar-Apr 2001;63(2):273-4.
- 227. Brummett BH, Barefoot JC, Siegler IC, et al. Characteristics of socially isolated patients with coronary artery disease who are at elevated risk for mortality. *Psychosom Med*. Mar-Apr 2001;63(2):267-72.
- 228. Hawkley LC, Thisted RA, Masi CM, Cacioppo JT. Loneliness predicts increased blood pressure: 5year cross-lagged analyses in middle-aged and older adults. *Psychol Aging*. Mar 2010;25(1):132-41. doi:10.1037/a0017805
- 229. Udell JA, Steg PG, Scirica BM, et al. Living alone and cardiovascular risk in outpatients at risk of or with atherothrombosis. *Arch Intern Med*. Jul 23 2012;172(14):1086-95. doi:10.1001/archinternmed.2012.2782

- Pantell M, Rehkopf D, Jutte D, Syme SL, Balmes J, Adler N. Social isolation: a predictor of mortality comparable to traditional clinical risk factors. *Am J Public Health*. Nov 2013;103(11):2056-62. doi:10.2105/ajph.2013.301261
- 231. Masic I, Alajbegovic J. The significance of the psychosocial factors influence in pathogenesis of cardiovascular disease. *Int J Prev Med.* Nov 2013;4(11):1323-30.
- 232. Steptoe A, Shankar A, Demakakos P, Wardle J. Social isolation, loneliness, and all-cause mortality in older men and women. *Proc Natl Acad Sci U S A*. Apr 9 2013;110(15):5797-801. doi:10.1073/pnas.1219686110
- Brown EG, Gallagher S, Creaven AM. Loneliness and acute stress reactivity: A systematic review of psychophysiological studies. *Psychophysiology*. May 2018;55(5):e13031. doi:10.1111/psyp.13031
- 234. Koenig HG. Religion, spirituality, and health: a review and update. *Advances in mind-body medicine*. Summer 2015;29(3):19-26.
- 235. Lucchese FA, Koenig HG. Religion, spirituality and cardiovascular disease: research, clinical implications, and opportunities in Brazil. *Rev Bras Cir Cardiovasc*. Mar 2013;28(1):103-28. doi:10.5935/1678-9741.20130015
- 236. Nonnemaker J, McNeely CA, Blum RW. Public and private domains of religiosity and adolescent smoking transitions. *Soc Sci Med*. Jun 2006;62(12):3084-95. doi:10.1016/j.socscimed.2005.11.052
- 237. Whooley MA, Boyd AL, Gardin JM, Williams DR. Religious involvement and cigarette smoking in young adults: the CARDIA study (Coronary Artery Risk Development in Young Adults)study. *Arch Intern Med.* Jul 22 2002;162(14):1604-10.
- 238. Feinstein M, Liu K, Ning H, Fitchett G, Lloyd-Jones DM. Burden of cardiovascular risk factors, subclinical atherosclerosis, and incident cardiovascular events across dimensions of religiosity: The multi-ethnic study of atherosclerosis. *Circulation*. Feb 9 2010;121(5):659-66. doi:10.1161/circulationaha.109.879973
- 239. Roncella A. Psychosocial risk factors and ischemic heart disease: A new perspective. *Rev Recent Clin Trials*. 2019;14(2):80-85. doi:10.2174/1574887114666190301141628
- 240. Young DR, Reynolds K, Sidell M, et al. Effects of physical activity and sedentary time on the risk of heart failure. *Circ Heart Fail*. Jan 2014;7(1):21-7. doi:10.1161/circheartfailure.113.000529
- 241. 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
- 242. Sheps DS, Frasure-Smith N, Freedland KE, Carney RM. The INTERHEART study: intersection between behavioral and general medicine. *Psychosom Med.* Nov-Dec 2004;66(6):797-8. doi:10.1097/01.psy.0000147479.29050.0a
- 243. Truelsen T, Nielsen N, Boysen G, Gronbaek M. Self-reported stress and risk of stroke: the Copenhagen City Heart Study. *Stroke*. Apr 2003;34(4):856-62. doi:10.1161/01.str.0000062345.80774.40
- 244. Davidson KW, Alcántara C, Miller GE. Selected psychological comorbidities in coronary heart disease: Challenges and grand opportunities. *Am Psychol*. Nov 2018;73(8):1019-1030. doi:10.1037/amp0000239
- 245. Barbiero S, Aimo A, Castiglione V, et al. Healthy hearts at hectic pace: From daily life stress to abnormal cardiomyocyte function and arrhythmias. *Eur J Prev Cardiol*. Sep 2018;25(13):1419-1430. doi:10.1177/2047487318790614
- 246. Austin AW, Wissmann T, von Kanel R. Stress and hemostasis: an update. *Seminars in thrombosis and hemostasis*. Nov 2013;39(8):902-12. doi:10.1055/s-0033-1357487
- 247. Huffman JC, Celano CM, Beach SR, Motiwala SR, Januzzi JL. Depression and cardiac disease: epidemiology, mechanisms, and diagnosis. *Cardiovasc Psychiatry Neurol*. 2013;2013
- 248. Sara JD, Prasad M, Eleid MF, Zhang M, Widmer RJ, Lerman A. Association between work-related stress and coronary heart disease: A review of prospective studies through the job strain, effort-

reward balance, and organizational justice models. *J Am Heart Assoc*. Apr 27 2018;7(9)doi:10.1161/jaha.117.008073

- 249. Lyon AR, Rees PS, Prasad S, Poole-Wilson PA, Harding SE. Stress (Takotsubo) cardiomyopathy-a novel pathophysiological hypothesis to explain catecholamine-induced acute myocardial stunning. *Nat Clin Pract Cardiovasc Med.* Jan 2008;5(1):22-9. doi:10.1038/ncpcardio1066
- 250. Steptoe A, Kivimaki M. Stress and cardiovascular disease: an update on current knowledge. *Annu Rev Public Health*. 2013;34:337-54. doi:10.1146/annurev-publhealth-031912-114452
- 251. Babyak MA, Blumenthal JA, Hinderliter A, et al. Prognosis after change in left ventricular ejection fraction during mental stress testing in patients with stable coronary artery disease. *Am J Cardiol.* Jan 1 2010;105(1):25-8. doi:10.1016/j.amjcard.2009.08.647
- 252. Steinberg JS, Arshad A, Kowalski M, et al. Increased incidence of life-threatening ventricular arrhythmias in implantable defibrillator patients after the World Trade Center attack. *J Am Coll Cardiol*. Sep 15 2004;44(6):1261-4. doi:10.1016/j.jacc.2004.06.032
- 253. O'Keefe EL, O'Keefe JH, Lavie CJ. Exercise counteracts the cardiotoxicity of psychosocial stress. *Mayo Clin Proc.* Sep 2019;94(9):1852-1864. doi:10.1016/j.mayocp.2019.02.022
- 254. Silverman AL, Herzog AA, Silverman DI. Hearts and minds: stress, anxiety, and depression: Unsung risk factors for cardiovascular disease. *Cardiol Rev.* Jul/Aug 2019;27(4):202-207. doi:10.1097/crd.0000000000228
- 255. Wu Q, Kling JM. Depression and the risk of myocardial infarction and coronary death: A metaanalysis of prospective cohort studies. *Medicine (Baltimore)*. Feb 2016;95(6):e2815. doi:10.1097/md.00000000002815
- 256. Di Palo KE. Psychological disorders in heart failure. *Heart Fail Clin*. Jan 2020;16(1):131-138. doi:10.1016/j.hfc.2019.08.011
- 257. Feng L, Li L, Liu W, et al. Prevalence of depression in myocardial infarction: A PRISMA-compliant meta-analysis. *Medicine (Baltimore)*. Feb 2019;98(8):e14596. doi:10.1097/md.000000000014596
- 258. McGuigan K. Higher rates of depression among women living with Coronary Heart Disease are associated with poorer treatment outcomes and prognosis. *Evid Based Nurs*. Apr 2019;22(2):47. doi:10.1136/ebnurs-2018-103012
- 259. Gustad LT, Laugsand LE, Janszky I, Dalen H, Bjerkeset O. Symptoms of anxiety and depression and risk of acute myocardial infarction: the HUNT 2 study. *Eur Heart J*. 2014;35(21):1394-1403.
- 260. Jonas BS, Franks P, Ingram DD. Are symptoms of anxiety and depression risk factors for hypertension? Longitudinal evidence from the National Health and Nutrition Examination Survey I Epidemiologic Follow-up Study. *Arch Fam Med.* Jan-Feb 1997;6(1):43-9.
- Hamer M, Molloy GJ, Stamatakis E. Psychological distress as a risk factor for cardiovascular events: pathophysiological and behavioral mechanisms. *J Am Coll Cardiol*. Dec 16 2008;52(25):2156-62. doi:10.1016/j.jacc.2008.08.057
- 262. Antonogeorgos G, Panagiotakos DB, Pitsavos C, et al. Understanding the role of depression and anxiety on cardiovascular disease risk, using structural equation modeling; the mediating effect of the Mediterranean diet and physical activity: the ATTICA study. *Ann Epidemiol*. Sep 2012;22(9):630-7. doi:10.1016/j.annepidem.2012.06.103
- 263. Dyball D, Evans S, Boos CJ, Stevelink SAM, Fear NT. The association between PTSD and cardiovascular disease and its risk factors in male veterans of the Iraq/Afghanistan conflicts: a systematic review. Int Rev Psychiatry. Feb 2019;31(1):34-48. doi:10.1080/09540261.2019.1580686
- 264. Jordan HT, Miller-Archie SA, Cone JE, Morabia A, Stellman SD. Heart disease among adults exposed to the September 11, 2001 World Trade Center disaster: results from the World Trade Center Health Registry. *Prev Med*. Dec 2011;53(6):370-6. doi:10.1016/j.ypmed.2011.10.014
- 265. Vaccarino V, Goldberg J, Rooks C, et al. Post-traumatic stress disorder and incidence of coronary heart disease: a twin study. *J Am Coll Cardiol*. Sep 10 2013;62(11):970-8. doi:10.1016/j.jacc.2013.04.085
- 266. Rosenbaum S, Stubbs B, Ward PB, Steel Z, Lederman O, Vancampfort D. The prevalence and risk of metabolic syndrome and its components among people with posttraumatic stress disorder: a

systematic review and meta-analysis. *Metabolism*. Aug 2015;64(8):926-33. doi:10.1016/j.metabol.2015.04.009

- 267. Minassian A, Baker DG, Risbrough VB. Heart rate variability and posttraumatic stress disorder. *JAMA psychiatry*. Feb 2016;73(2):178-9. doi:10.1001/jamapsychiatry.2015.2663
- 268. Graves KD, Miller PM. Behavioral medicine in the prevention and treatment of cardiovascular disease. *Behavior modification*. Jan 2003;27(1):3-25. doi:10.1177/0145445502238690
- 269. Younge JO, Leening MJ, Tiemeier H, et al. Association between mind-body practice and cardiometabolic risk factors: The rotterdam study. *Psychosom Med*. Sep 2015;77(7):775-83. doi:10.1097/psy.00000000000213
- 270. Tan MP, Morgan K. Psychological interventions in cardiovascular disease: an update. *Curr Opin Psychiatry*. Sep 2015;28(5):371-7. doi:10.1097/yco.0000000000181
- 271. Younge JO, Gotink RA, Baena CP, Roos-Hesselink JW, Hunink MG. Mind-body practices for patients with cardiac disease: a systematic review and meta-analysis. *Eur J Prev Cardiol*. Nov 2015;22(11):1385-98. doi:10.1177/2047487314549927
- 272. Gok Metin Ż, Ejem D, Dionne-Odom JN, et al. Mind-body interventions for individuals with heart failure: A systematic review of randomized trials. *J Card Fail*. Mar 2018;24(3):186-201. doi:10.1016/j.cardfail.2017.09.008
- 273. Ospina MB, Bond K, Karkhaneh M, et al. Meditation practices for health: state of the research. *Evid Rep Technol Assess (Full Rep)*. Jun 2007;(155):1-263.
- 274. Gathright EC, Salmoirago-Blotcher E, DeCosta J, et al. The impact of transcendental meditation on depressive symptoms and blood pressure in adults with cardiovascular disease: A systematic review and meta-analysis. *Complement Ther Med*. Oct 2019;46:172-179. doi:10.1016/j.ctim.2019.08.009
- 275. Pascoe MC, Thompson DR, Jenkins ZM, Ski CF. Mindfulness mediates the physiological markers of stress: Systematic review and meta-analysis. *J Psychiatr Res*. Dec 2017;95:156-178. doi:10.1016/j.jpsychires.2017.08.004
- 276. Rainforth MV, Schneider RH, Nidich SI, Gaylord-King C, Salerno JW, Anderson JW. Stress reduction programs in patients with elevated blood pressure: a systematic review and metaanalysis. *Curr Hypertens Rep.* Dec 2007;9(6):520-8.
- 277. Brook RD, Appel LJ, Rubenfire M, et al. Beyond medications and diet: alternative approaches to lowering blood pressure: a scientific statement from the american heart association. *Hypertension*. Jun 2013;61(6):1360-83. doi:10.1161/HYP.0b013e318293645f
- 278. Anderson JW, Liu C, Kryscio RJ. Blood pressure response to transcendental meditation: a metaanalysis. *Am J Hypertens*. Mar 2008;21(3):310-6. doi:10.1038/ajh.2007.65
- 279. 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
- Bornemann B, Kovacs P, Singer T. Voluntary upregulation of heart rate variability through biofeedback is improved by mental contemplative training. *Sci Rep.* May 27 2019;9(1):7860. doi:10.1038/s41598-019-44201-7
- 281. Lin IM, Fan SY, Lu HC, et al. Randomized controlled trial of heart rate variability biofeedback in cardiac autonomic and hostility among patients with coronary artery disease. *Behav Res Ther*. Jul 2015;70:38-46. doi:10.1016/j.brat.2015.05.001
- 282. 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
- 283. Chen S, Sun P, Wang S, Lin G, Wang T. Effects of heart rate variability biofeedback on cardiovascular responses and autonomic sympathovagal modulation following stressor tasks in prehypertensives. *J Hum Hypertens*. Feb 2016;30(2):105-11. doi:10.1038/jhh.2015.27

- 284. Yu LC, Lin IM, Fan SY, Chien CL, Lin TH. One-year cardiovascular prognosis of the randomized, controlled, short-term heart rate variability biofeedback among patients with coronary artery disease. *Int J Behav Med*. Jun 2018;25(3):271-282. doi:10.1007/s12529-017-9707-7
- 285. Kwekkeboom KL, Bratzke LC. A systematic review of relaxation, meditation, and guided imagery strategies for symptom management in heart failure. *J Cardiovasc Nurs*. Sep-Oct 2016;31(5):457-68. doi:10.1097/jcn.0000000000274
- Liu KP, Chan CC, Lee TM, Hui-Chan CW. Mental imagery for promoting relearning for people after stroke: a randomized controlled trial. *Arch Phys Med Rehabil*. Sep 2004;85(9):1403-8. doi:10.1016/j.apmr.2003.12.035
- 287. Hosseini SA, Fallahpour M, Sayadi M, Gharib M, Haghgoo H. The impact of mental practice on stroke patients' postural balance. *J Neurol Sci*. Nov 15 2012;322(1-2):263-7. doi:10.1016/j.jns.2012.07.030
- 288. WHO Global Report: mortality attributable to tobacco. World Health Organization. http://whqlibdoc.who.int/publications/2012/9789241564434 eng.pdf
- 289. Parikh A, Lipsitz SR, Natarajan S. Association between a DASH-like diet and mortality in adults with hypertension: findings from a population-based follow-up study. *Am J Hypertens*. Apr 2009;22(4):409-16. doi:10.1038/ajh.2009.10
- 290. Shah AM, Pfeffer MA, Hartley LH, et al. Risk of all-cause mortality, recurrent myocardial infarction, and heart failure hospitalization associated with smoking status following myocardial infarction with left ventricular dysfunction. *Am J Cardiol*. Oct 1 2010;106(7):911-6. doi:10.1016/j.amjcard.2010.05.021
- 291. D'Alessandro A, Boeckelmann I, Hammwhoner M, Goette A. Nicotine, cigarette smoking and cardiac arrhythmia: an overview. *Eur J Prev Cardiol*. Jun 2012;19(3):297-305.
- 292. Diver WR, Jacobs EJ, Gapstur SM. Secondhand smoke exposure in childhood and adulthood in relation to adult mortality among never smokers. *Am J Prev Med*. Sep 2018;55(3):345-352. doi:10.1016/j.amepre.2018.05.005
- 293. Control CfD, Prevention. *How tobacco smoke causes disease: The biology and behavioral basis for smoking-attributable disease: A report of the surgeon general.* Centers for Disease Control and Prevention (US); 2010.
- 294. Kawachi I, Colditz GA, Stampfer MJ, et al. Smoking cessation and time course of decreased risks of coronary heart disease in middle-aged women. *Arch Intern Med.* Jan 24 1994;154(2):169-75.
- 295. Shinton R, Beevers G. Meta-analysis of relation between cigarette smoking and stroke. *BMJ*. Mar 25 1989;298(6676):789-94.
- 296. Macintyre CR, Heywood AE, Kovoor P, et al. Ischaemic heart disease, influenza and influenza vaccination: a prospective case control study. *Heart*. Dec 2013;99(24):1843-8. doi:10.1136/heartjnl-2013-304320
- 297. Udell JA, Zawi R, Bhatt DL, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: a meta-analysis. *JAMA*. Oct 23 2013;310(16):1711-20. doi:10.1001/jama.2013.279206
- 298. Breuer J, Pacou M, Gauthier A, Brown MM. Herpes zoster as a risk factor for stroke and TIA: a retrospective cohort study in the UK. *Neurology*. Jan 21 2014;82(3):206-12. doi:10.1212/wnl.00000000000038
- 299. Jimenez M, Krall EA, Garcia RI, Vokonas PS, Dietrich T. Periodontitis and incidence of cerebrovascular disease in men. *Ann Neurol*. Oct 2009;66(4):505-12. doi:10.1002/ana.21742
- 300. Desvarieux M, Demmer RT, Jacobs DR, Papapanou PN, Sacco RL, Rundek T. Changes in clinical and microbiological periodontal profiles relate to progression of carotid intima-media thickness: the oral infections and vascular disease epidemiology study. *J Am Heart Assoc*. 2013;2(6):e000254.
- 301. 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

- 302. Niu JF, Zhao XF, Hu HT, Wang JJ, Liu YL, Lu DH. Should acupuncture, biofeedback, massage, Qi gong, relaxation therapy, device-guided breathing, yoga and tai chi be used to reduce blood pressure?: Recommendations based on high-quality systematic reviews. *Complement Ther Med.* Feb 2019;42:322-331. doi:10.1016/j.ctim.2018.10.017
- 303. Huang X, Guo S, Li F, et al. Acupuncture as an adjunctive treatment for Angina due to Coronary Artery Disease: A meta-analysis. *Med Sci Monit*. Feb 16 2019;25:1263-1274. doi:10.12659/msm.913379
- 304. Liu Y, Meng HY, Khurwolah MR, et al. Acupuncture therapy for the treatment of stable angina pectoris: An updated meta-analysis of randomized controlled trials. *Complement Ther Clin Pract.* Feb 2019;34:247-253. doi:10.1016/j.ctcp.2018.12.012
- 305. Ni YM, Frishman WH. Acupuncture and cardiovascular disease: focus on heart failure. *Cardiol Rev.* Mar/Apr 2018;26(2):93-98. doi:10.1097/crd.000000000000179
- 306. Lee H, Kim TH, Leem J. Acupuncture for heart failure: a systematic review of clinical studies. *Int J Cardiol*. Nov 1 2016;222:321-331. doi:10.1016/j.ijcard.2016.07.195
- 307. Sibbritt D, Peng W, Lauche R, Ferguson C, Frawley J, Adams J. Efficacy of acupuncture for lifestyle risk factors for stroke: A systematic review. *PLoS One*. 2018;13(10):e0206288. doi:10.1371/journal.pone.0206288
- Liu J, Li SN, Liu L, et al. Conventional acupuncture for cardiac arrhythmia: A systematic review of randomized controlled trials. *Chin J Integr Med*. Mar 2018;24(3):218-226. doi:10.1007/s11655-017-2753-9