The Brain-Heart Connection:

GCBH Recommendations to Manage Cardiovascular Risks to Brain Health

Global Council on Brain Health℠
A COLLABORATIVE FROM AARP

Background: About GCBH and Its Work

The Global Council on Brain Health (GCBH) is an independent collaborative of scientists, health professionals, scholars, and policy experts from around the world who are working in areas of brain health related to human cognition. The GCBH focuses on brain health relating to people's ability to think and reason as they age, including aspects of memory, perception and judgment. The GCBH is convened by AARP with support from Age UK to offer the best possible advice about what older adults can do to maintain and improve their brain health. GCBH members gather to discuss specific lifestyle issue areas that may impact people's brain health as they age, with the goal of providing evidence-based recommendations for people to consider incorporating into their lives.

We know many people across the globe are interested in learning that it is possible to influence their own brain health and in finding out what can be done to maintain their brain health as they age. We aim to be a trustworthy source of information, basing recommendations on current evidence supplemented by a consensus of experts from a broad array of disciplines and perspectives.

Brain Health and Cardiovascular Risks

In March 2019, members of the GCBH met in Washington, DC to examine the impact of cardiovascular risk factors on brain health in adults age 50 and older. Cardiovascular risk factors are those that affect the heart and the body's network of blood vessels including those in the brain. Throughout the discussion, experts examined the evidence of how risks to your heart and vascular system can influence your brain health. The staff drafted a report to capture their recommendations and conclusions, and the GCBH experts reviewed, edited and discussed subsequent drafts by email and conference calls throughout the Fall of 2019.

The final draft was reviewed by GCBH liasions in the Winter of 2019, enabling staff to incorporate many helpful comments from numerous experts at Age UK, the Administration for Community Living/Administration on Aging, the Alzheimer's Association, the American Heart Association, the Centers for Disease Control, the Healthy Ageing Program at the University of Melbourne, the Health Resources and Services Administration, the National Institute on Aging, and US Against Alzheimer's.

This paper summarizes the consensus reached by the experts and describes the major points of discussion that led to their recommendations on managing the impact of vascular risk factors for men and women age 50 and older. It also identifies gaps in our knowledge about cardiovascular risk factors and brain health. This paper is not intended to be a systematic, exhaustive review of all pertinent scientific literature on the topic. Rather, the selected references provided at the end of the document give helpful background material and present a sizeable sample of the current evidence underpinning the GCBH consensus in this area.

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Introduction

GCBH experts agree that the best evidence to date indicates that "what's good for the heart is good for the brain." Recent studies evaluating the incidence of dementia among large groups of people over several decades have found decreases in the age-adjusted incidence of dementia occurring simultaneously with improvement in overall cardiovascular health. This is very encouraging and empowering because it suggests that adults may be able to modify their behaviors to lower their risk of cognitive decline and dementia.

Despite the promising decrease in the rate and/or delay of onset of dementia shown in these studies, the worldwide burden of dementia is still expected to grow as average life expectancy increases and the population expands. Certain groups of people are at higher risk than others. For example, risks of dementia are generally higher for older adults, the economically vulnerable, and for people living in low-to-middle income countries, as well as in countries where prevalence of cardiovascular risk factors continues to rise.

These recommendations are based on the experts' evaluation of the best available evidence to date. The evidence comes from observational studies and randomized controlled trials published in peer-reviewed journals that examine the impact of cardiovascular risk factors in relation to brain health. Wherever possible the GCBH focused particularly on cognitive outcomes in older adults. The process used to develop this report and the complete list of participants are described in Appendix 1. Recommendations, practical tips, and definitions of the terms used in the consensus are provided in the discussion sections and the attached glossary (Appendix 3).

The following recommendations are meant for healthy adults, particularly for men and women age 50 and older who have not been diagnosed with a neurodegenerative disease such as Alzheimer's disease. The intent is to make broad recommendations relevant to adults interested in maintaining their brain health as they age. The GCBH encourages everyone to modify their lifestyles in ways that can help control for known risks to brain health. Managing your cardiovascular risk factors is amongst the most effective ways known to also help protect your brain. Adults who adopt healthy life-style habits and treat any cardiovascular risk factors as early as possible will help reduce their risks for cognitive decline later in life.

CONSENSUS STATEMENTS

1. What is good for the heart is good for the brain. Keeping your heart and blood vessels healthy likely reduces your risk for cognitive decline and dementia.

2. Cardiovascular risk factors (e.g., high blood pressure, high cholesterol, diabetes, smoking, sedentary lifestyle, and obesity) are bad for brain health.

    a. The more of these cardiovascular risks you have, the greater your risks of cognitive decline.

    b. However, there is something you can do about it. There is strong evidence that reducing or treating your cardiovascular risk factors can help to reduce your risk of cognitive decline and dementia.

3. Damage to your brain from cardiovascular risks can accumulate over your lifetime, but it's never too late to improve your risk of cognitive impairment.

4. Better control of high blood pressure has been proven to reduce risk for cognitive impairment.

5. Stroke is one of the strongest known risk factors for dementia.

    a. Steps to reduce the risk of stroke include reducing vascular risk factors (particularly high blood pressure) and treating additional conditions such as an atrial fibrillation (AFib), a dangerous irregular heartbeat.

    b. Treating high cholesterol by using a statin medication will reduce your risk of strokes.

6. Irregular heart beat (AFib) increases risk of cognitive decline and dementia.

7. Diabetes increases your risk of stroke, cognitive decline, and dementia.

8. Smoking damages your brain, not just your lungs and heart. It's never too late to stop smoking and improve your health.

9. Excessive alcohol is bad for your brain health and your heart.

10. Excessive dietary salt is bad for your brain health based upon risks to your heart health.

11. Poor sleep quality, quantity, and sleep disorders, including sleep apnea can increase risks for heart attacks and stroke as well as cause problems with memory and thinking skills.

EXPERT RECOMMENDATIONS

RECOMMENDATIONS FOR INDIVIDUALS:

1. Lead a physically active life.
2. Maintain a healthy weight through a balance of good nutrition and exercise.
3. Don't start smoking, and if you do smoke, quit. It's never too late to experience the positive health benefits from not smoking.
4. Check your blood pressure regularly. If it's too high, work with a health professional to lower it safely.
5. Have your cholesterol and lipid profile checked regularly. If your health care provider says it's too high, take steps to reduce it.
6. Keep blood sugar within a healthy range, as defined by your health care provider.
7. If you have diabetes or pre-diabetes, consult with a health care provider and nutritionist in order to help you manage these conditions.
8. Even after starting medication or lifestyle change, continue to regularly monitor your blood pressure, cholesterol, blood sugar, and weight.
9. People with symptoms of sleep apnea should be tested and treated if diagnosed.
10. Take the time and steps to manage your stress effectively.

Earlier reports by the GCBH have made numerous recommendations on how to maintain brain health by managing specific lifestyle factors including exercise, sleep, nutrition, social connections and mental well-being (providing tips on how to effectively cope with stress and anxiety). Many of those recommendations were made on the basis of evidence of their impact on the cardiovascular risk factors described above. Adopting the recommendations from these earlier reports will help you choose a host of healthy behaviors that can contribute to better brain health. Links to each report are available in Appendix 8.

RECOMMENDATIONS FOR HEALTHCARE PROVIDERS:

1. Emphasize the connection between brain health and vascular disease to your patients, encouraging adoption of healthy lifestyle habits and early treatment for cardiovascular risk factors to also reduce risks for cognitive impairment.
2. Be extra vigilant to look for vascular risk factors in women and underserved populations which may be at greater risk than the general population, e.g. African Americans, Native Americans.
3. Discuss blood pressure management regularly with your patients. Ensure you are getting an accurate and valid measure of blood pressure.
4. Treat blood pressure according to practice guidelines (e.g. American Heart Association/American College of Cardiology blood pressure guidelines, National Institute for Healthcare and Excellence guidelines, European Hypertension Society guidelines).
5. Recommend that your patients monitor their blood pressure at home.

PRACTICAL TIPS

1. Get moving. Strive for at least 150 minutes of weekly, moderate-intensity aerobic activity and two or more days a week of moderate-intensity, muscle-strengthening activities. Exercise is one of the most important things you can do to protect your heart **and** brain. See The Brain-Body Connection: GCBH Recommendations on Physical Activity and Brain Health.
2. In addition to purposeful exercise, lead a physically active lifestyle throughout the day. Any physical activity is better than none, and know that whatever your age or current health status, there are options to be physically active.
3. Consider buying a home blood pressure monitor and make sure you know how to use it accurately. Bring the monitor to your health care provider's office when you visit to check its accuracy.
4. If your blood pressure is higher than 130/80, talk to your health care providers about changes in diet and/or weight loss to lower it. Blood pressure medications may also be necessary, depending on your general health. It is important to take blood pressure medications as directed and work with your health care team to monitor their effect over time.
5. Have your cholesterol regularly tested. You should have a total cholesterol of 200 mg/dL (5 mmol/l) or lower. If your bad cholesterol (LDL) or triglyceride is high, or your good cholesterol (HDL) is low talk to your health care provider about making lifestyle changes and/or starting a cholesterol lowering medication (e.g., statin).
6. If you take cholesterol-lowering medications, take them as directed and have your cholesterol levels monitored regularly.
7. If you feel symptoms of a stroke or see signs of a stroke, call for emergency help. Remember the most common symptoms of stroke with the acronym F.A.S.T.: **F**ace drooping, **A**rm weakness, **S**peech difficulty means **T**ime to call for emergency help. There is no easy way to tell whether symptoms are from a transient ischemic attack (TIA), or a major stroke that could leave you with permanent damage. Getting emergency care quickly gives health care providers the greatest chance of reversing effects of stroke and any potentially permanent disability. Immediately call your local number for emergency attention. (9-1-1 in the United States or 9-9-9 in the United Kingdom).

Remember the most common symptoms of stroke with the acronym FAST: **F**ace drooping, **A**rm weakness, **S**peech difficulty means **T**ime to call for emergency help.

Transient ischemic attack (TIA)
Also called: mini-stroke

A transient ischemic attack (TIA) can be a precursor to a stroke. It happens when the blood supply to part of the brain is briefly blocked. Symptoms of a TIA are identical to other stroke symptoms, but do not last as long. They happen suddenly, and include:

- Confusion or trouble speaking or understanding speech
- Trouble seeing in one or both eyes
- Difficulty walking
- Dizziness
- Loss of balance or coordination
- Numbness or weakness, especially on one side of the body

While TIA symptoms disappear within 24 hours, there is no way to know right away if the symptoms will lead to resolution (TIA) or permanent disability (stroke). If you believe you are experiencing or have just experienced these symptoms, you should go to the hospital right away because risks for subsequent full-blown strokes are high even if the symptoms initially resolve.

Information adapted from: Medline Plus, National Institute of Neurological Disorders and Stroke

PRACTICAL TIPS *CONTINUED*

8. If you suspect that you or someone else has had a TIA (e.g., sudden onset face drooping, arm weakness, or speech difficulty that gets better within 10-30 minutes), still call for emergency help because people are at increased risk of a stroke over the next week. The risk is highest in the first few days following the TIA.
9. If you or your loved one had a TIA, after receiving emergency assistance, follow up with your regular health care provider to create an on-going plan to reduce your future stroke risks.
10. Not all strokes have symptoms listed in F.A.S.T. For example, a bleeding-type of stroke may suddenly appear as the most severe headache of your life or as sudden blindness in one or both eyes.
11. Contact your health care provider if you have any concerns about an unsual or irregular heart beat. If you notice you have an irregular heart rate — which may or may not be accompanied by other symptoms like lightheadedness— talk to your health care provider about being evaluated for atrial fibrillation (AFib). People with AFib – a dangerously irregular heart rhythm – are five times more likely to have a stroke than those who don't have the condition. While common heart rate monitors on a smartphone, smartwatch, or fitness tracker device are not as reliable as medical-grade heart monitoring, if you use one, contact your doctor if you have an indication of an irregular heartbeat or any concerns about your heart rate or rhythms.
12. Check labels on prepared and packaged foods and limit salt intake. Many people eat more salt than they realize, so try not to add it to cooking or at the table. There is already usually a great deal of sodium in most foods, especially pre-prepared bought foods. See, Brain Food: GCBH Recommendations on Nourishing Your Brain Health for more information about limiting sugar, saturated fat, and recommendations for overall dietary patterns that can promote brain health including suggestions for flavoring food while moderating consumption of salt.
13. If you do not drink alcohol, don't start. If you do drink, limit alcohol to no more than one drink a day for women and two drinks a day for men. See, Brain Food: GCBH Recommendations on Nourishing Your Brain Health for more information on wine and other alcohol.
14. If you smoke, quit. If you don't smoke, don't start. Smoking of any form is terrible for your heart and your brain.
15. Aim for 7 to 8 hours a sleep in a 24 hour period. If you or your partner thinks you may have sleep apnea, or another sleep disorder, talk to your doctor about a sleep study. Symptoms of sleep apnea are very common in adults 50+ and include frequent loud snoring, gasping for air during sleep, and excessive sleepiness during the day. You may need to sleep with a breathing device or receive another treatment. Treatment of sleep problems improves memory and thinking skills. See, The Brain Sleep Connection: GCBH Recommendations on Sleep and Brain Health.
16. Talk to your doctor about ways to support and optimize your brain health at all life stages and consider a cognitive assessment to establish a baseline.

DISCUSSION

What's good for the heart is good for the brain

Many studies over the years suggest that heart health and brain health are inexorably linked. Although the brain makes up only 2 percent of body weight, it uses 20 percent of the oxygen we breathe. This oxygen is carried by blood between the heart and the brain, and both healthy blood vessel walls and strong blood flow are crucial for a healthy brain. When there is an abrupt change in blood flow from the heart to the brain, people may quickly experience lightheadedness, impaired speech, weakness on one side of the body and/or loss of consciousness. Depending on the extent to which blood flow is obstructed and subsequently restored, some people can recover with no change in their health or significant disabilities.

If the change in the blood flow is more gradual—because of narrowing blood vessels from hardening of the arteries or weak blood flow from heart disease—people may experience more subtle but progressive symptoms. Factors that cause damage to blood vessel walls over time (such as high blood pressure, high cholesterol, diabetes and smoking) likely increase the risk of dementia, including Alzheimer's disease. These conditions and behaviors can directly damage the brain through tiny strokes, and their effects will add up over time. It remains unclear how these tiny strokes contribute to the development of Alzheimer's disease and other dementias. It could be that stiff or clogged arteries leading to or in the brain's blood vessels may slow down the elimination of toxic proteins related to Alzheimer's disease, or reduce the amount of healthy brain tissue to combat the effects of other types of dementia, such as Lewy body. One study published in March 2019 in the *European Heart Journal* found that high blood pressure, diabetes, obesity and smoking are all linked to abnormal brain changes seen in dementia.

Regardless of the exact mechanism, scientists and doctors agree that keeping the blood vessels and blood flow healthy is key to maintaining your brain function as you age. A heart-healthy lifestyle that includes plenty of exercise and a healthy diet reduces the risk of cognitive decline. See the GCBH reports on diet, exercise, sleep and mental well-being. The GCBH recommendations on modifiable lifestyle factors to promote brain health are strikingly similar to the list of tips from the American Heart Association (AHA) called "Life's Simple 7." The AHA recommends nonsmoking, a healthy diet, physical activity and a good body mass index (BMI)—as well as management of blood pressure, reducing blood sugar and controlling cholesterol levels—because, in part, all these factors are associated with lower incidence of cognitive impairment.

Just as dementia risk increases as we get older, a risk of heart disease increases with age as well. People over age 50 are much more likely to have problems with their hearts. But this doesn't have to happen. Older people who exercise, have a healthy diet, keep their weight at a healthy level, and keep blood pressure and cholesterol in check can have hearts that are similar to those of much younger people. While people with great heart health can still develop Alzheimer's disease or other dementias, there is overwhelming evidence that taking care of your heart is one of the most important things you can do to lower your risk of dementia and keep your brain healthy as you age.

Vascular contributions to cognitive impairment and dementia

Up until the last decade, scientists have largely studied vascular dementia and Alzheimer's disease as distinct diseases. According to the National Heart, Lung, and Blood Institute, vascular dementia is the second most common type of dementia in the United States, after Alzheimer's disease. It may even be as common as Alzheimer's disease in some East Asian countries. You may have heard that vascular dementia is a disease of the white matter in the brain and Alzheimer's is a disease of the brain's grey matter. White matter is sometimes called the highway system of the brain, because white matter connects the different parts of the brain. When there are white matter lesions, these are like potholes in the brain's highways. The more potholes there are, the more the workings of the brain are disrupted.

As with much of brain science, however, the more researchers learn about these diseases, the more complicated the picture becomes. Many studies have shown that in early Alzheimer's disease, blood vessels in the brain are not functioning properly, and this can be due to Alzheimer's disease or vascular disease. When people's brains are

examined after death, those diagnosed with Alzheimer's disease during life are often found to have signs of Alzheimer's disease but also changes related to vascular problems and other diseases. So people diagnosed with Alzheimer's dementia may have developed Alzheimer's disease first, followed by vascular changes, or developed two or more of these diseases simultaneously.

Doctors used to consider Alzheimer's disease and vascular dementia as diseases with different symptoms—that those with vascular dementia were more likely to have problems with motor problems (such as balance, speech and walking difficulties). But experts now think that vascular dementia often does not result in motor changes, and memory/thinking difficulties can be quite similar between the two diseases. Because brain changes of Alzheimer's and vascular diseases together become increasingly common with older age, some scientists have argued that most people given a dementia diagnosis likely have mixed Alzheimer's and vascular dementia (as well as other dementias), with very few people having pure forms of either.

Since the risk factors for vascular disease (high blood pressure, high cholesterol and diabetes) are increasingly common, people with cognitive impairment will frequently have some amount of vascular damage in their brains. Due to the common co-occurrence of Alzheimer's and vascular diseases in aging and the subtle differences in memory and thinking between the two diseases, the GCBH does not advise treating vascular dementia as a condition entirely unrelated to Alzheimer's disease and other dementias. Rather than discussing vascular dementia as a separate disease, researchers in the field prefer to describe the damages to the brain caused by cardiovascular problems as vascular contributions to cognitive impairment and dementia.

Vascular contributions to cognitive impairment are caused by conditions that damage blood vessels or white matter in the brain and ultimately deprive the brain of oxygen and other nutrients. High blood pressure, high cholesterol, diabetes and smoking all increase the risk of vascular contributions to cognitive impairment and its more severe form, dementia. Vascular contributions to dementia can occur when someone has a series of small strokes over a long period, even if the person never felt any signs typically associated with strokes, such as speech change or paralysis.

If someone with memory decline has a history of stroke or TIA, doctors may suspect vascular contributions to dementia. While it is possible for there to be vascular forms of dementia without memory loss, memory problems can also be a main or even the first symptom of vascular disease in the brain (sometimes called cerebrovascular disease). It is also common for people with vascular disease not to have a history of stroke or TIA. In this case, they often have signs of health problems in other organs—for example, blood vessel damage in the kidneys or heart disease—and they invariably have cardiac risk factors like high blood pressure. Although the reasons for this are not yet understood, this underscores some of the important similarities between so-called vascular and so-called Alzheimer's dementia, meaning that efforts to maintain healthy blood vessels in the brain are likely beneficial to both conditions.

In addition to strokes and blood vessel damage, cardiovascular diseases can cause changes to brain cells and in hormones that can contribute to cognitive impairment. Rare genetic conditions can also cause vascular contributions to dementia, especially in younger people. Young-onset dementia cases in particular need to be evaluated for this.

We know that controlling blood pressure will slow or even stop cardiovascular damage to the brain. Recent studies have found that lowering high blood pressure can slow the worsening of white matter lesions in people's brains. Some evidence suggests that improving diet and increasing exercise likely benefit brain health by reducing new white matter lesions. While there is no cure for the diseases that cause cognitive impairment—whether it's from vascular contributions or other types of dementia—the best approach is to focus on diagnosing cognitive impairment or dementia, identify cardiovascular risk factors such as high blood pressure, and manage and treat them effectively. Then, if warranted, doctors can also prescribe specific treatments for Alzheimer's disease or other related dementias.

Heart disease

Heart disease is the world's leading cause of death, according to the World Health Organization. Coronary artery disease, the most common type of heart disease, is a disease in which plaque builds up inside the arteries that supply oxygen-rich blood to your heart muscle. When plaque builds up in your arteries, the condition is called atherosclerosis. This can progress over many years, making the arteries narrow and stiff. Over time, the plaque can harden or break open. If the plaque hardens, the arteries narrow and the flow of blood to the heart is reduced. This is sometimes called hardening of the arteries. If the plaque breaks open, a blood clot forms and blocks the blood

flowing to the heart. If the flow of blood to your heart muscle is blocked, this causes a heart attack. Any condition that blocks the flow of blood in the body has the potential to damage both the heart and the brain.

High blood pressure (also known as hypertension)

High blood pressure is known as a silent killer because it usually has no warning signs or symptoms, and many people don't know they have it. It can lead to heart attacks, strokes, kidney disease and other ailments. It also damages the brain directly. Researchers aren't exactly sure why high blood pressure can damage the brain, but it may be that high blood pressure causes stress on arteries that changes the walls of blood vessels.

An estimated 1 billion people have high blood pressure worldwide, including an estimated 100 million Americans. That's nearly half of all adults in the United States. In most western populations, hypertension is more common than normal blood pressure in people over the age of 60. In China, more than half of older people are estimated to have high blood pressure.

Blood pressure is measured using two numbers. The top number, systolic blood pressure, measures the pressure in blood vessels when the heart beats. The bottom number, called diastolic blood pressure, measures the pressure in blood vessels when the heart rests between beats. The systolic pressure has the strongest relationship to heart and brain health. Blood pressure numbers of less than 120/80 mm Hg are considered ideal. A blood pressure of 130/90 mm Hg or more is too high. People with levels in between 120/80 and 130/90 have prehypertension, which means they are at risk for high blood pressure. (See the chart below for more information.)

High blood pressure is a major risk factor for stroke, but scientists say that it likely damages the brain in other ways as well. High blood pressure increases the risk of memory and thinking problems, as well as dementia. While we don't yet know whether controlling blood pressure will prevent dementia—the most advanced form of memory loss—one important new study published in the *Journal of the American Medical Association* in January 2019 showed that intensive blood pressure control reduces the risk for mild cognitive impairment (MCI), a serious loss of memory and thinking skills.

For some people, MCI is the earliest phase of Alzheimer's disease and other forms of dementia. The research study, called SPRINT MIND, was a randomized clinical trial, which is considered the gold standard of medical research. Researchers in SPRINT MIND wanted to see if lowering systolic blood pressure to below 120 would be better than providing standard treatment to keep it below 140. They studied over 9,000 ethnically and racially diverse people over age 50 with high blood pressure. Those who received intensive treatment for blood pressure (goal blood pressure of 120/80) were less likely than those who received standard treatment (below 140/90) to develop MCI. In fact this treatment was so successful, the researchers ended the trial early to make sure all participants got the optimal treatment. This is the strongest evidence so far that lowering high blood pressure reduces the risk of MCI and is good for not only the heart but also the brain.

Eating a healthy diet—including limiting salt—exercising regularly, maintaining a healthy weight and limiting alcohol consumption, along with getting enough quality sleep, can all help to manage blood pressure. If healthy lifestyle habits are not sufficient by themselves to lower blood pressure, medication can be very effective. While most research supports controlling blood pressure to maintain health, there are some individuals with advanced frailty and multiple medical conditions who may not benefit from intensive blood pressure control. The final decision for anyone's blood pressure goal should depend on a discussion with the individual's health care provider.

Importantly, blood pressure that is too low can also be unhealthy. Blood pressure can be too low if someone is dehydrated, is taking too many medications or has a disorder that causes low blood pressure. A systolic blood pressure (the top number) of less than 90 mm Hg is considered low blood pressure. When someone is healthy and well-hydrated, the brain can generally ensure adequate blood flow to the brain even when the systolic blood pressure drops slightly below 90 mm Hg. Because older adults are more prone to dehydration and diseases that affect this regulation, they can be at greater risk for low blood pressure. Low blood pressure problems can be revealed, for example, when a person attempting to stand up from a seated position becomes dizzy.

Normal Blood Pressure	Less than 120/80 mm Hg
At Risk for High Blood Pressure (Prehypertension)	Between 120/80 mm Hg and 129/89 mm Hg
High Blood Pressure (Hypertension)	More than 130/90 mm Hg

Blood pressure treatment should be based on functional status rather than chronological age. Although there has been some debate in the past about whether it's worthwhile to treat heart disease in people who are age 80 and older, research suggests that octogenarians benefit from preventive therapy just as much as younger people do. For example, when people 75 years of age or older take statins to lower cholesterol, they have similar reduction in stroke risks as younger people. Other studies have found that lowering blood pressure in people over 80 with high blood pressure helps protect both their hearts and their brains. At the same time, doctors should be careful prescribing medications to lower blood pressure in some older people, especially the frail. Treatment of heart disease may need to be proportionate in older patients who tend to have multiple illnesses, which can make the heart disease more difficult to treat.

There is no one-size-fits-all recommendation for blood pressure treatment among older adults. Whether people 80 years of age or older should start or continue the same medications for reducing the risk of stroke has to be judged against their fitness level and how well they are functioning. The GCBH recommends that high blood pressure be evaluated by health care professionals and managed in all people of all ages.

High cholesterol

Nearly a third of American adults have high cholesterol, and globally an estimated 40 percent of adults have raised cholesterol (higher than 190), according to the World Health Organization. Like high blood pressure, high cholesterol alone usually has no symptoms, but it can increase the risks of heart disease and strokes. However, not all cholesterols are the same. For example, although low-density lipoproteins (LDL), the "bad" cholesterol, increase the chances of having a stroke or heart attack, high-density lipoproteins (HDL), the "good" cholesterol, are protective against heart disease and strokes. In fact, cholesterol is essential to the function of many organs, including the brain. Because having strokes increases the chance of dementia, we might expect reducing LDL and increasing HDL to improve brain health.

When scientists have followed large groups of people over time, they have observed that people with high cholesterol between the ages of 40 to 64 have greater dementia risks at age 65 and older. Therefore, it makes sense that using a cholesterol-lowering medication for high cholesterol would improve brain health. However, studies of adults 65 and over do not show a strong link between high cholesterol and worse brain health, and not all studies of people taking cholesterol-lowering medicines have shown a reduction in dementia risks. There may be several explanations for this.

First, cholesterol in the brain is constantly being made and broken down, and not much of the cholesterol in the blood—associated with plaques in the arteries—actually gets into the brain. Second, drugs used to lower blood cholesterol may have other effects that even out their protective properties. Finally, some studies suggest that the same genes that make people susceptible to high cholesterol may increase dementia risks, so lowering cholesterol alone may not be enough to lower that risk. Because people 75 and older were often not included in studies of cholesterol-lowering drugs to prevent heart disease and strokes, more studies are needed to address whether using these medications can improve these older adults' brain health. The National Institute on Aging in the United States (NIA) is now funding the PREVENTABLE study, looking at statin use in individuals age 75-plus.

Following are general guidelines for healthy levels of cholesterol.

Adult men

Type of Cholesterol	Healthy Level
Total Cholesterol	125 to 200mg/dL (3.2 to 5.1 mmol/L)
Non-HDL	Less than 130mg/dL (3.4 mmol/L)
LDL	Less than 100mg/dL (2.6 mmol/L)
HDL	40mg/dL or higher (1.0 mmol/L)

Adult women

Type of Cholesterol	Healthy Level
Total Cholesterol	125 to 200mg/dL (3.2 to 5.1 mmol/L)
Non-HDL	Less than 130mg/dL (3.4 mmol/L)
LDL	Less than 100mg/dL (2.6 mmol/L)
HDL	50mg/dL or higher (1.3 mmol/L)

Other fats in the blood, such as triglycerides and lipids, are being studied for their relationship to brain health. Currently we don't have good evidence of the impact these fats have on brain health—or evidence on their relationship to cognitive

decline or dementia—to make any recommendations regarding them.

Different professional organizations have offered guidelines on when someone should make lifestyle changes (such as diet, exercise and weight loss) to reduce total cholesterol and when someone should start a cholesterol-lowering medicine such as statins. Everyone agrees that lifestyle changes are the first line of defense. Lifestyle changes to lower LDL include eating a heart-healthy diet that limits saturated and trans fats, losing weight and increasing daily exercise to at least 30 minutes.

The primary goals of these recommendations to manage cholesterol are to reduce future risks of heart disease and strokes, both of which are bad for brain health. Most guidelines depend on your overall heart health risks and assume that you do not currently have symptoms from these diseases (such as exercise-induced chest pain), so it is important for you to discuss with your physician whether medication is right for you—in addition to lifestyle changes. Below we provide a sampling of guidelines from around the world about when statin use is appropriate.

Stroke

A stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked or ruptured. When that happens, parts of the brain cannot get enough blood and oxygen, and these parts can become permanently damaged if the blood flow is not quickly restored. Stroke causes 6 million deaths annually, making it the second leading cause of death worldwide for individuals over the age of 60, according to the World Stroke Organization. It is the fifth leading cause of death in the United States. Stroke is also the third leading cause of disability worldwide. There are three main types of stroke.

- **Ischemic stroke** occurs when clots or other particles block the flow of blood through a blood vessel to the brain, or when blood vessels narrow.
- **Hemorrhagic stroke** occurs when a blood vessel tears within the brain, or when a weakened or damaged blood vessel (aneurysm) bursts around the brain. Blood can then build up and cause severe damage to the surrounding brain tissue or even death.
- **TIA (transient ischemic attack**) has the same causes and symptoms as regular ischemic strokes, but the blood flow is restored when the clot is dissolved or there is enough blood flow from elsewhere. Even though a TIA (sometimes called a ministroke) doesn't cause permanent damage, it is a serious warning sign that you're at a high risk for a stroke—which causes permanent damages.

The most common symptoms of stroke are sudden:

- Numbness or weakness in the face or an arm or leg
- Confusion or trouble speaking
- Trouble seeing in one or both eyes
- Dizziness, trouble walking or loss of balance
- Severe headache with no known cause

In addition to potentially causing long-term damage to the brain and even death, having a stroke is one of the strongest

Organization	Age	Statins should be offered to:
UK National Institute for Health and Care Excellence	40+	Asymptomatic individuals with 10-year artherosclerotic cardiovascular disease (ASCVD) risk > 10%, or any individual with chronic kidney disease
US Preventive Services Task Force	40-75	Asymptomatic individuals with 1 or more ASCVD risks AND a 10-year risk of any ASCVD ≥ 10%
Canadian Cardiovascular Society	40-75 (consider earlier for South Asian or First Nation individuals)	Asymptomatic individuals with a 10-year risk of any ASCVD ≥ 20%, or 10-year risk of any ASCVD 10-20% and LDL ≥ 193 mg/dL Any individual with diabetes (≥30 if more than 15 years in duration) Individuals with kidney disease (50 or older)
European Society of Cardiology/ European Atherosclerosis Society	40-65 40+	Asymptomatic individuals with 10-year risk of fatal ASCVD ≥ 10% and LDL ≥ 97 mg/dL, or fatal ASCVD 5-10% and LDL ≥ 155 mg/dL Asymptomatic individual with familial hypercholesterolemia, non-dialysis dependent chronic kidney disease, or diabetes
American College of Cardiology/ American Heart Association	40-75	Asymptomatic individuals with LDL ≥ 190 mg/dL, or diabetes, or 10-year risk of any ASCVD ≥ 7.5%

risk factors for dementia. Multiple strokes increase the risk even more. The best way to prevent dementia in someone who has had a stroke is to prevent a second stroke, and yet there is evidence that only 1 percent of stroke survivors take the necessary steps to improve their heart health. African American and Hispanic men and women have a higher risk of stroke in the United States.

The good news is that up to 80 percent of strokes can be prevented. Having high cholesterol, high blood pressure and diabetes all increase the risk of stroke, and treating those conditions can significantly reduce the risk of stroke. Smoking and drinking too much alcohol also increase the risk of stroke.

Atrial fibrillation

Atrial fibrillation (A-fib) is an irregular heartbeat (arrhythmia) that can lead to blood clots and strokes. The American Heart Association defines A-fib as a "quivering heartbeat or irregular heartbeat that can lead to stroke and other heart-related complications."

It is caused when the atrium and ventricle in the heart do not beat in sync and the chambers of the heart don't beat effectively. Symptoms include:

- Fatigue
- Rapid and irregular heartbeat
- Shortness of breath
- Dizziness or fainting
- Low blood pressure
- Sweating
- Chest pain or pressure

The risk of A-fib increases with age, especially after age 65. According to the National Heart Lung and Blood Institute, some studies have found that problems with thinking skills and memory, Alzheimer's disease and vascular dementia happen more in those with atrial fibrillation. Atrial fibrillation increases the risk of stroke, heart attack and heart failure. Again, when oxygen-rich blood is not being regularly pumped to the brain, damage occurs.

Treatment for A-fib includes lifestyle changes, including being physically active, managing stress, quitting smoking and healthy eating. Maintenance of normal weight is very important. A number of medications can also help slow the heart or make the heart rhythm more regular. A majority of people with A-fib need to take blood thinning medications to prevent stroke. One Swedish study published in 2018 in the journal *Neurology* found that people with A-fib who took blood thinners were less likely to develop dementia than those who did not take blood thinners. Although there is no evidence of a direct effect of A-fib prevention on dementia, successful treatment of A-fib has been shown to reduce the risk of stroke.

Diabetes

Diabetes is a disease caused by high blood glucose, also sometimes called high blood sugar. The two most common types of diabetes are type 1 and type 2. In type 1 diabetes, the body doesn't make enough insulin. Type 1 diabetes is usually diagnosed in children and young adults. In those who have type 2 diabetes, the body does not make or use insulin well. Type 2 diabetes is diagnosed most often in middle age and older people and is often linked with obesity, high blood pressure and high cholesterol.

An estimated 425 million people have diabetes worldwide, according to the World Heart Foundation, with 90 percent of these cases being type 2 diabetes. Urbanization, unhealthy diets and an increasingly sedentary lifestyle have caused growing rates of obesity and diabetes worldwide. The World Heart Foundation predicts that there will be more than 600 million people with diabetes by 2050. Type 2 diabetes affects a quarter of people over age 65 in the United States, and 25 percent don't know they have the disease, according to the Centers for Disease Control and Prevention. In the United States, 40 percent of those with diabetes also have a least 3 other cardiovascular risk factors. Native Americans, African Americans and Hispanics are more likely to have diabetes than other groups.

Diabetes can lead to kidney disease, heart disease, stroke and nerve damage. Diabetes, especially type 2 diabetes, is a risk factor for memory problems as people age and also increases the risk for dementia. Some studies have also found connections between memory problems and higher-than-normal blood sugar—even among those who don't have diabetes. High blood sugar may damage the small blood vessels in the brain over time. However, no study has yet shown that improved glucose control can reduce the risk of memory decline.

The longer people have uncontrolled diabetes, the higher the risk of dementia. People with both types of diabetes are significantly more likely to develop memory problems and Alzheimer's disease. This may be at least in part because of the other conditions that are often linked to diabetes, such as

high blood pressure. Diabetes is also a risk factor for stroke, which damages the brain, and having a stroke is a risk factor for dementia. High blood sugar also causes inflammation, which may damage brain cells. Doctors can do several tests to check for diabetes. The chart below reflects commonly used tests to evaluate if someone has high blood glucose levels and the values that indicate whether someone is diabetic, prediabetic or normal.

Diabetes may be effectively controlled by weight reduction. The European Society of Cardiology (ESC) diabetes guidelines from 2019 recommend that overweight people lose more than 15 kilograms for very effective diabetes control. For patients with prediabetes, even losing 10 to 15 pounds can make a big difference. Brisk walking for 30 minutes a day, five days a week, can also help. For those with diabetes, doctors may also recommend medications that may help lose weight and lower the risk of cardiovascular problems, including stroke.

Healthy diet

In an earlier report, "Brain Food: GCBH Recommendations on Nourishing Your Brain Health," the GCBH concluded that diet affects brain health and also noted that a "heart-healthy diet is a brain-healthy diet." Diet affects all of the conditions discussed in this report: high blood pressure, high cholesterol and diabetes. The typical Western diet that is high in salt, sugar, excess calories and saturated fats is bad for both the heart and the brain. Brain- and heart-healthy diets include the Mediterranean diet, the DASH diet and the MIND diet.

For more information on brain- and heart-healthy nutrition—including information on recommended foods, food that you should limit, specifics on fish, limiting salt and fat intake, and alcohol use—see "Brain Food." The experts' discussions on diet during the preparation of this report focused primarily on limiting salt intake and alcohol consumption. Highlights of their discussion follow.

Salt/sodium

Lowering the amount of sodium in the foods you eat is an important step to benefit your heart and brain health. Excessive salt can contribute to high blood pressure, which is an important risk factor for stroke. There is a well-established link between consuming too much salt and having a stroke. Because we know strokes are detrimental to cognitive health, we therefore know excessive salt intake is harmful for your brain health. In addition to raising blood pressure, too much salt may also increase inflammation in the body, which can be bad for both the heart and the brain.

Most of the sodium in people's diets comes from packaged, processed foods, rather than the salt shaker. Many people have more salt in their diets than they realize. Processed foods, canned foods and baked goods such as bread are often high in salt. While canned soups and frozen foods are typically high in salt, if you purchase these foods, try to look for lower sodium options. Note also that frozen vegetables and fruit are typically low in salt and high in essential nutrients, while frozen, ready-to-eat meals are usually very high in salt.

In Japan, a public health education intervention in the 1960s showed the effectiveness of dietary interventions to reduce sodium intake. A 50 percent reduction of salt in the diet was associated with an 85 percent reduction in mortality caused by stroke.

Guidelines on salt intake vary slightly around the world, but the important thing to remember is that limiting salt intake will benefit both your heart and your brain. For example, the American Heart Association recommends an ideal limit of 1,500 milligrams a day—equivalent to a half teaspoon of salt—and yet the average American consumes more than twice that. For more details on salt and brain health, see "Brain Food: GCBH Recommendations on Nourishing Your Brain Health."

Result	A1C Test	Fasting Blood Sugar Test	Glucose Tolerance Test	Random Blood Sugar Test
Diabetes	6.5% or above	126 mg/dL (7 mmol/L) or above	200 mg/dL (11 mmol/L) or above	200 mg/dL (11 mmol/L) or above
Prediabetes	5.7 – 6.4%	100-125 mg/dL (5.6-7.0 mmol/L)	140-199 mg/dL (7.8-11.0 mmol/L)	N/A
Normal	Below 5.7%	99 mg/dL (5.4 mmol/L) or below	140 mg/dL (7.8 mmol/L) or below	N/A

Adapted from: Centers for Disease Control and Prevention

Alcohol

There is a great deal of interest about whether alcohol is good or bad for the heart and brain. This is a question that is heatedly debated by top scientists, but most agree that the relationship between alcohol and health is a complex one. Excessive alcohol can lead to high blood pressure, heart failure and irregular heart beat, according to the National Institute on Alcohol Abuse and Alcoholism. It can also lead to excess calories, which contribute to obesity. Even in moderate quantities, alcohol has been linked to adverse brain health outcomes.

While the risks of excessive alcohol consumption are clear, there is some evidence that moderate alcohol consumption may have protective heart benefits. The brain-healthy Mediterranean diet, which typically includes a moderate amount of wine with meals, has been linked to reduced risk of dementia and evidence of better brain health. Other studies have found that moderate drinking, particularly wine, may reduce dementia risk, and that those who abstain from alcohol may be at higher risk of heart disease and dementia. Research has also found that drinking alcohol in moderate amounts decreases the risk of heart disease. On the other hand, a large study published in 2018 in the journal *Lancet* analyzing data from 195 countries found that just one drink a day slightly *increases* the risk for health problems and death, especially from cancer.

It's important to note that there are limitations with studies that find the brain health of people who drink moderate amounts is better than the health of people who do not drink any alcohol. People might abstain from alcohol because they are already in poor health. Many studies don't distinguish between those who never drink and those who have quit drinking. It may be that those who aren't drinking alcohol are abstaining because they already have a health condition or disease that increases their risk of heart disease or dementia. Thus, the increased risk for abstinence found in the studies may not be due to not drinking, but rather due to the health problems that made people stop drinking in the first place. It could also be that those who drink moderately have other healthy habits that are helping their brain health, such as exercising or socializing with others.

Many people underestimate the size and the quantity of their drinks and are drinking more alcohol than they realize. As you age, your body processes alcohol differently, and experts often recommend older people consume even smaller quantities.

If you do not drink alcohol, you should not start doing so for your heart or your brain. For more information on alcohol and brain health, see "Brain Food: GCBH Recommendations on Nourishing Your Brain Health."

Smoking

The chemicals in tobacco smoke harm your blood cells and can also damage the function of your heart and blood vessels, according to the National Heart, Lung, and Blood Institute. This damage increases buildup of plaque in blood vessels, lowers "good" HDL cholesterol and makes blood more likely to clot, which can block blood flow to the heart and brain. Smoking increases the risk of heart attack, heart failure and problems with the heartbeat, called arrhythmia. Smoking thins the brain's cortex (where the nerve bodies are) and worsens silent strokes. Smoking is a major risk factor for stroke and causes one third of deaths from cardiovascular diseases, according to the Centers for Disease Control and Prevention. It's never too late to benefit from quitting smoking. Quitting smoking, even later in life, can lower your risk of heart disease, stroke and cancer. E-cigarettes or vaping is unsafe for people of all ages.

Stress

Chronic and excessive stress increases the risk for heart disease, especially high blood pressure, which in turn can cause problems with brain health. We want to be clear we are not discussing mild transient stress or the normal stress of daily life, but prolonged serious stress. Severe stress and stress disorders may be especially dangerous. A very large, long-running Swedish study published April 2019 in the *British Medical Journal (BMJ)* found that stress-related disorders such as post-traumatic stress disorder (PTSD), acute stress reaction and other stress reactions are strongly linked to heart disease, regardless of family background. Adverse socioeconomic status in adulthood increases stress and the risks of stroke, and a shock due to traumatic event can precipitate a stroke.

For recommendations on how to manage and relieve stress, see "Brain Health and Mental Well-Being: GCBH Recommendations on Feeling Good and Functioning Well."

Sleep

Getting good sleep is critical to good health. The GCBH report on sleep and brain health concluded that: "People with chronic inadequate sleep are at higher risk for and experience more severe conditions of dementia, depression, heart disease,

obesity, diabetes, fall-related injuries and cancer." Most adults should get 7 to 8 hours of sleep each night, yet a third of American adults say they don't. Because blood pressure tends to go down at night, those with inadequate sleep have higher blood pressure for a longer period of time. Some studies show that getting enough sleep may help improve blood sugar control and lower the risk of type 2 diabetes. Getting too little sleep is also linked to unhealthy weight gain, which in turn increases the risk of heart problems. Sleep is also thought to be important for clearing out the waste products of brain activity that have built up during daytime activities.

Additionally, sleep disorders such as sleep apnea and insomnia can contribute to an increased risk of high blood pressure and heart disease. Sleep apnea, which occurs when the airway is repeatedly blocked during sleep and people stop breathing for short amounts of time, has been found to increase the risk for high blood pressure, heart attack and stroke, and may increase risk for dementia. Sleep apnea also increases the risk of A-fib and uncontrolled hypertension. About 10 percent of adults have long-lasting insomnia, which means they have trouble falling asleep or staying asleep, or both. Insomnia is linked to high blood pressure and heart disease, which in turn are connected with brain health problems. For tips and suggestions on how to get better sleep, see "The Brain-Sleep Connection: GCBH Recommendations on Sleep and Brain Health."

Sex-based differences in heart health show up in brain health

Heart disease is the leading cause of death in women, causing more than two million premature deaths each year, according to the World Heart Foundation. Heart attack symptoms can be different in women than in men. Women are more likely to experience chest pain that is sharp and burning, as well as pain in the neck, jaw, throat, abdomen or back. More women than men have strokes, largely thought to be because age is a risk factor and women live longer. In the United States, 60 percent of those who die from stroke are women. Heart disease is often considered a "man's disease," and that mistaken perception can be deadly. Women often delay getting help when heart attack symptoms start, waiting on average 30 minutes longer than men to call for help. Women are also less likely than men to get clot-busting drugs that can save lives and help prevent long-term damage from strokes and heart attacks. Women are also more likely than men to experience more subtle signs of stroke including fatigue, nausea, dizziness and memory loss. In the SPRINT-MIND study mentioned previously, there was no evidence of differences between women and men in the effectiveness of lowering blood pressure to reduce the risk of mild cognitive impairment, meaning that both genders seem to benefit equally from keeping blood pressures at ideal rates.

After many years of exclusion in major cardiovascular research studies, in the mid 1990s the United States Food and Drug Administration mandated inclusion of female subjects in clinical trials. We now understand that heart disease presentation, symptoms, treatment, prognosis and long term management is often different in women than in men. Given that 2/3 of all dementia cases are in females and the known gender differences in vascular health, this is a crucial area to understand. Otherwise we risk making recommendations that are not optimal for either men or women.

Socioeconomic status

People who have a lower socioeconomic status are more likely to have heart disease than those who are wealthier. Being poor is linked to lower education, less access to healthy foods, higher blood pressure, having diabetes and less medical care. Economically disadvantaged people are also less likely to have dangerous conditions treated. A full 80 percent of adults who have suffered a stroke now live in low- and mid-income countries, where stroke incidence rates have more than doubled in the last decade.

Consideration of differences amongst diverse population groups

In the United States, Alzheimer's disease is not only more common in women but is also more prevalent in certain racial and ethnic groups, including Hispanics, African Americans and Native Americans. This could be due to a number of reasons. The prevalence of high blood pressure and stroke among African Americans is higher than for whites. The prevalence of diabetes is higher among Native Americans, African Americans and Hispanics than whites. These cardiovascular risk factors may help explain some of the differences observed in the incidence rates of dementia. At the same time, different genetic and environmental factors have also been linked to the difference. Regardless of whether cardiovascular health directly accounts for the greater dementia risks in these groups, better management of diabetes, high blood pressure and stroke risks remains a key

priority for all groups of people because of its direct impact on brain health.

Much more research regarding dementia rates in certain population groups needs to be done, and it is crucial that studies on both heart disease and Alzheimer's disease and other causes of dementia include diverse racial and ethnic groups in order to evaluate any differences in incidence rates and ways different racial/ethnic groups may react to treatment. For example, in the SPRINT-MIND study, scientists found no evidence of differences in the effectiveness of blood pressure lowering to reduce the risk of mild cognitive impairment between black, white or Hispanic people. Intensive blood pressure control was shown to benefit all groups studied. The researchers were only able to evaluate effectiveness across groups because the study population was ethnically and racially diverse.

According to the Alzheimer's Association, "African Americans are seriously underrepresented in current clinical trials of potential treatments for Alzheimer's disease, particularly in trials conducted by drug companies. This has occurred even though evidence of genetic differences and response to drugs varies significantly by race and ethnicity." Similar underrepresentation exists for Hispanics and Native Americans. A report from UsAgainstAlzheimer's and the University of Southern California Edward R. Roybal Institute on Aging found that although "Latinos make up 17 percent of the U.S. population, they make up less than 1 percent of participants in all National Institutes of Health clinical trials. Further, Latinos make up just 7.5 percent of research participants across the approximately 32 Alzheimer's Disease Research Centers" across the country.

There is evidence that some statins may work better than others to lower cholesterol in African Americans, but more of these types of studies need to be done before any conclusions can be drawn. The African American Rosuvastatin Investigation of Efficacy and Safety study (ARIES) was the first large-scale, prospective, randomized, controlled trial exclusively designed to provide a head-to-head comparison of the effects of two statins in African Americans, and the researchers found that rosuvastatin was more effective than atorvastatin in lowering cholesterol. But in another trial, Statins Use In Intracerebral Hemorrhage Patients, (SATURN), which was also designed to test the effectiveness of these same drugs, no differences in effectiveness were found among African Americans. Therefore, we do not currently have enough information to make a recommendation on use of particular statins based on racial differences. Nor do we have such evidence for optimal effectiveness of statin therapy for women.

KNOWLEDGE GAPS

In addition to cholesterol, other fats in the blood, such as triglycerides and lipids, are being studied for their relationship to brain health. But currently we don't have good evidence of the impact that these fats have on brain health—or on their relationship to cognitive decline or dementia—to make any recommendations regarding them. We want to know, for example, whether using medication to lower cholesterol benefits the brain.

While there have been many clinical trials on stroke prevention after someone has had a stroke, there aren't adequate studies to address the best approaches to alleviating vascular contributions to cognitive decline and dementia.

While there has been an increase in studies evaluating multi-domain interventions, we still don't know which combination of interventions are most effective for reducing vascular risk. We want to know, for example, which combinations of diet, exercise, blood pressure lowering or weight loss are most helpful for optimizing brain function as we age.

We need research into whether effective diabetes treatment can reduce the risk of cognitive decline and dementia.

We do not know whether reversing vascular damage to the brain can also reverse cognitive decline, or how much vascular damage can occur in the brain before it significantly begins to impact cognitive function.

As mentioned above, we need more evidence on treatment and outcome differences among different groups of people. For example, we don't know whether some statins work more

effectively in some racial and ethnic groups than others, or if some statins work better in women than others. We also must find out why women and underserved racial groups get less standard of care treatment for vascular disease and to understand how to prevent this. We need better evidence on whether the same treatment can result in different outcomes for different groups of people when it comes to treating high blood pressure or cholesterol.

Lessons from the SPRINT MIND study should inform the design of future trials. For example, we now know we need to increase the length of follow-up among trial participants and to increase sample sizes in studying the impact of vascular interventions on cognitive outcomes. This is partly because we have realized, only relatively recently, that dementia can take 30 years to develop. Future trials need to be designed taking the long preclinical stage into account, so that we can better understand when and at what ages it is best to begin treatments, and for how long a period.

Many of our earlier dementia trials recruited people over age 70. We are aware now that the disease process starts much earlier—even before people start showing symptoms of cognitive decline—and that there is evidence that people with stroke who had lower baseline cognitive status were at higher risk of dementia over time. It would be very helpful for establishing accurate baselines to require cognitive testing earlier on—even for people in their 40s.

We also need better evidence of the impact of mitigating cardiovascular risk factors in the oldest population. While there is some evidence to suggest people over age 90 might be better off with higher blood pressure, we do not know whether there is an age at which raised blood pressure is really better.

Similarly, we have clear evidence that high cholesterol and a higher body-mass index (BMI) in midlife create a higher risk for cognitive decline in later life. But in late life, higher cholesterol and BMI may be beneficial. We need further research to clarify these distinctions.

As the debate between GCBH experts for this report revealed, while there is consensus that excessive alcohol consumption is bad for heart and brain health, we still do not have a consensus on whether abstinence from all alcohol is better for cardiovascular and brain health than drinking one moderately sized glass of wine with meals.

We have made significant progress in understanding vascular contributions to cognitive health in recent years and therefore feel confident in making the recommendations above. Nevertheless, many important questions remain.

CONCLUSION

As one of the most modifiable aspects of brain health, managing cardiovascular risk factors presents an enormous opportunity to reduce the risk for cognitive decline as people age, and to help prevent and treat vascular contributions to dementia. Healthy lifestyle choices and taking medications—when necessary—to reduce high blood pressure, manage diabetes and control cholesterol have long been known to help your heart. We know it can help your brain as you age as well.

LIST OF APPENDICES

1. PARTICIPANTS, LIAISONS AND PROCESS USED TO PRODUCE THE REPORT

Members of the Global Council on Brain Health are independent health care professionals and experts coming from a variety of disciplines. The issue specialists and governance committee members formulated these recommendations. Liaisons reviewed the draft and provided suggestions, and the governance committee approved them on January 20, 2020.

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**Participation in this activity by these individuals does not necessarily represent the official viewpoint of the U.S. Department of Health and Human Services.*

Process used to produce the consensus and recommendations

Issue specialists from around the world, who are leaders in their fields, were selected to participate on the GCBH panel on brain health and vascular risk. These experts have conducted research that has significantly contributed to the body of evidence that links cardiovascular health with brain health in older adults. Their diverse areas of expertise represent perspectives from disciplines including cardiology, geriatric psychiatry, internal medicine, neurology, neuroscience, physiology and public health.

Eleven issue specialists from four continents were asked to critically examine the state of the science as of March 2019. They discussed findings from observational studies as well as randomized controlled trials. The experts considered the cumulative body of evidence to determine whether it is sufficient to issue recommendations for individuals to maintain and improve brain health. The issue specialists considered 11 different questions as a framework to guide their deliberations.

After an in-depth moderated discussion, several follow-up conference calls, and an exchange and refinement of drafts, the issue specialists arrived at 11 consensus statements to summarize the impact of vascular risk factors on brain health. Based on their consensus, they made 10 recommendations for individuals and five for health care providers related to cardiovascular health in the context

of brain health and cognitive decline. Further, they agreed on 16 practical tips aimed at helping people around the world adopt behaviors to improve their brain health.

Liaisons from civic and nonprofit organizations with relevant expertise in brain and cardiovascular health were invited to provide input and technical feedback during the refinement of the draft recommendations.

Seven governance committee members attended the meeting in Washington, D.C. The entire governance committee reviewed and finalized the document during subsequent conference calls and emails from October 2019 to January 2020. The governance committee members issuing the recommendations are independent health professionals representing diverse expertise in epidemiology, psychology, public health, neurology, psychiatry, geriatrics, cognitive neuroscience, neuropsychology, pharmacology, medical ethics, health policy and neurodegeneration.

The governance committee applied their expertise to determine whether they concurred with the statements and to evaluate the objectivity and feasibility of the proposed recommendations. The GCBH governance committee reviewed this summary document to decide whether it accurately reflected the expert opinions expressed and the current state of science in the field. The governance committee approved the document in January 2020.

2. PARTICIPANTS AND LIAISONS' LIST OF ADDITIONAL RESOURCES

American Diabetes Association

- Resources available at: diabetes.org/resources

The American Heart Association

- Life's Simple 7: heart.org/en/healthy-living/healthy-lifestyle/my-life-check--lifes-simple-7
- Find more here on brain health, sodium (salt) and atrial fibrillation: heart.org/brainhealth; heart.org/en/healthy-living/healthy-eating/eat-smart/sodium/salty-six-infographic; heart.org/en/health-topics/atrial-fibrillation/what-are-the-symptoms-of-atrial-fibrillation-afib-or-af

American Stroke Association

- Steps to Better Brain Health: brainhealth.strokeassociation.org
- Stroke Risk Factors: strokeassociation.org/en/about-stroke/stroke-risk-factors/understanding-risky-conditions/atherosclerosis-and-stroke

Asia-Pacific Heart Network

- aphn.info/prevention/advocacy/

The Brain Health Resource from the Administration on Community Living (ACL)

- Find more here: acl.gov/node/293

British Heart Association

- Understanding vascular dementia: bhf.org.uk/informationsupport/conditions/vascular-dementia

Centers for Disease Control and Prevention (CDC)

- Find more here on brain health, cholesterol, stroke and added sodium (salt):
- cdc.gov/cholesterol/communications-kit.htm; cdc.gov/stroke/about.htm; cdc.gov/salt/pdfs/sodium_role_processed.pdf
- Is your heart older than you? cdc.gov/vitalsigns/heartage/index.html

European Society of Cardiology

- Cardiovascular disease prevention guidelines: escardio.org/Guidelines/Clinical-Practice-Guidelines/CVD-Prevention-in-clinical-practice-European-Guidelines-on

United Kingdom National Institute for Health and Care Excellence (NICE) impact cardiovascular disease prevention

- Find more here: nice.org.uk/Media/Default/About/what-we-do/Into-practice/measuring-uptake/nice-impact-cardiovascular-disease-prevention.pdf

United States National Institutes of Health (NIH)

- National Institute on Aging: nia.nih.gov/
- National Institute on Aging (NIA) Healthy Eating Resource: https://www.nia.nih.gov//health/healthy-eating and https://go4life.nia.nih.gov/
- National Heart, Lung, and Blood Institute: nhlbi.nih.gov
- National Institute of Diabetes and Digestive and Kidney Diseases: niddk.nih.gov
- National Institute of Neurological Disorders and Stroke: ninds.nih.gov

World Heart Federation

- See: world-heart-federation.org/resources

3. GLOSSARY

The glossary highlights how the GCBH used these terms within the context of their discussions and in this document.

Arrhythmia. An irregular heartbeat or abnormal heart rhythm, causing the heart to beat too fast, too slowly or erratically.

Atrial fibrillation (A-fib). An irregular heartbeat that occurs when the heart's chambers do not beat in sync, often causing the heart to beat much faster than normal.

Blood pressure. The force of blood pushing against the walls of arteries. A blood pressure number of 120/80 mm Hg is generally considered ideal.

Brain health. A state of having good underlying neural mechanisms to support high functioning mental processes of cognition that support well-being.

Cholesterol. A waxy, fat-like substance in the blood that is produced by the body and found in food. The body needs some cholesterol, but high levels of cholesterol raises the risk of heart disease.

Cognitive decline. The Institutes of Medicine (IOM) in 2015 defined a similar term, cognitive aging, as the lifelong process of gradual and ongoing, yet highly variable, change in cognitive functions that occur as people get older. Cognitive decline is a term used by the experts to describe losing cognitive abilities over time as people age absent a specific disease or condition.

Dementia. Dementia isn't a specific disease. Instead, dementia describes a group of symptoms related to memory, thinking and social abilities and affecting them severely enough to interfere with independent daily functioning. Though dementia generally involves memory loss, memory loss has many different causes. Alzheimer's disease is the most common cause of a dementia in older adults, but there are a number of types of dementia. Depending on the cause and type of dementia, some dementia symptoms can be reversed.

Diabetes. A disease caused by high blood glucose, also called blood sugar. Type 2 diabetes, the most common type of diabetes, affects primarily middle-aged and older people and is often linked with obesity, high blood pressure and high cholesterol.

Diet. A specific, habitual pattern of food, drink and nutrient choices. Some diets are tied to health goals, such as cognitive health, weight loss or heart health, but diets can also reflect a regional culture.

Epidemiological studies. In these studies, which are observational in nature, scientists try to establish a link between lifestyle activities over time (such as education) and long-term outcomes (brain health with aging). They can be cross-sectional or longitudinal.

Heart attack. A heart attack occurs when an artery supplying the heart with blood and oxygen becomes blocked.

Heart disease. A term covering a variety of conditions that affect the heart's structure and function. Coronary artery disease, the most common type of heart disease, is caused by a buildup of fatty deposits called plaque in the walls of the arteries that supply blood to the heart.

Heart rate. Also known as pulse, heart rate is the number of times a person's heart beats per minute. A normal resting heart rate for adults is generally between 60 to 100 beats per minute.

Hypertension. Also known as high blood pressure, hypertension occurs when the force of blood against artery walls is persistently elevated.

Intervention. Any measure whose purpose is to improve health or alter the course of disease.

Lewy body dementia. Lewy body dementia (LBD) is a disease associated with abnormal deposits of a protein called alpha-synuclein in the brain. These deposits, called Lewy bodies, affect chemicals in the brain whose changes, in turn, can lead to problems with thinking, movement, behavior and mood. Lewy body dementia is one of the most common causes of dementia. (National Institute on Aging).

Longitudinal studies. In longitudinal research, scientists observe changes over an extended period of time to establish the time-sequence in which things occur or the effect of a factor over time.

Nutrients. A food or biochemical substance used by the body that must be supplied in adequate amounts from foods consumed. There are six classes of nutrients: water, proteins, carbohydrates, fats, minerals and vitamins.

Processed foods. Food processing is any deliberate change in a food that occurs before it's available for us to eat. The International Agency for Research on Cancer (IARC) classified processed meat as "meat that has been transformed through salting, curing, fermentation, smoking or other processes to enhance flavor or improve preservation."

Randomized controlled trial (RCT). In a typical randomized controlled trial, people are randomly selected to receive either the intervention or a control condition. In a double-blind trial, both the participants and the researchers are unaware of (or "blinded" to) which person received the intervention until after the results are analyzed.

Risk. Risk is the chance or probability of a particular event happening in a group of people with similar characteristics or traits, compared with those not having that characteristic or trait. Making up an individual's overall risk of having a condition is the cumulative effects of factors that increase the chance of developing the condition (risk factors) as well as factors that decrease the chance of developing the same condition (protective factors).

Saturated fats. A group of fats that have no double bonds between carbon molecules because they are "saturated" with hydrogen molecules; often found in animal products such as red meat, tropical oils such as coconut and palm oil, and whole dairy products.

Risk reduction. Reducing risks for cognitive decline or impairment in the abilities to think, reason and remember means lowering your chances of experiencing loss in those abilities. A person's overall risk may also be reduced by increasing factors that protect against cognitive decline or dementia. Dementia (due to Alzheimer's disease or another related disorder) is one condition, and cognitive decline (the slowing of thinking and memory in the absence of a major brain disease) is another condition. When scientists study risk reduction strategies for cognitive decline, they are looking for factors that can reduce the risk of impairment to cognitive functions in the population in general. Therefore, some activity or intervention that reduces risk for a particular condition or disease means that a smaller proportion of people who engage in that activity are likely to have the condition or disease. However, risk reduction strategies are not the same as preventing any one individual from getting the condition or suffering from disease. For example, research has long shown that wearing a seatbelt reduces—but does not eliminate—the chance of injuries among people who are involved in automobile accidents, and we nevertheless now recommend people wear seatbelts while they are driving.

Statins. A class of drugs prescribed by doctors to help lower cholesterol levels in the blood.

Sleep apnea. A sleep disorder in which breathing is briefly and repeatedly interrupted during sleep. The "apnea" in sleep apnea refers to a breathing pause that lasts at least 10 seconds.

Stroke. A stroke occurs when a blood vessel that carries oxygen and nutrients to the brain is either blocked or ruptured. There are three main types of stroke:

1. **Ischemic stroke** occurs when clots or other particles block the flow of blood through a blood vessel to the brain, or when blood vessels narrow.
2. **Hemorrhagic stroke** occurs when a blood vessel tears within the brain, or when a weakened or damaged blood vessel (aneurysm) bursts around the brain.
3. **Transient ischemic attack (TIA)** occurs when the blood supply to part of the brain is briefly blocked. It is sometimes called a ministroke.

Vascular dementia. A type of dementia that may result from a series of small strokes over a long period, or from brain damage caused by numerous strokes or minor blood clots in heart or neck arteries that block a branch of a blood vessel in the brain.

Vascular system. The body's network of blood vessels—arteries, capillaries and veins—that, together with the heart, delivers oxygen and nutrients to tissues and removes waste.

4. DISCUSSION QUESTIONS FRAMING THE DELIBERATIONS

1. How do major cardiovascular risk factors impact brain health?
   a. High blood pressure (what about low blood pressure?)
   b. High cholesterol
   c. Diabetes (insulin resistance)
   d. Smoking
   e. Obesity

2. What can you say is known about the relationship between vascular health and cognitive function/brain health?

3. What are the key ways in which cardiovascular risk factors differ:
   a. between men and women?
   b. according to lifestage, specifically differences in midlife and in older age?
   c. by race/ethnicity/socioeconomic factors?

4. How do changes in the heart and blood vessels impact men and women as they age? Do those changes in blood vessels occur all over the body, including the brain?

5. What do we know about the link between brain health and stroke prevention?

6. What are the major issues surrounding cardiovascular health and its relationship to brain health in underserved populations?

7. What is vascular dementia, and what can be done about it?

8. Can lowering cardiovascular risk by making lifestyle changes help you maintain or improve your brain health? If so, what are your recommendations?

9. Is there a link between taking statins and cognitive function?
   a. Are there protective effects?
   b. Are there adverse side effects?

10. What is inflammation and how does the body cope with/handle inflammation over a lifetime?
    a. How does inflammation affect cardiovascular health?
    b. How does inflammation affect brain health?

11. Do irregular heart rhythms (A-fib) increase in prevalence with age, and do they have a relationship to brain health?

5. DISCLOSURE STATEMENT OF POTENTIAL FINANCIAL CONFLICTS OF INTEREST

All of the 24 GCBH experts participating in the formulation of this paper were asked to disclose potential conflicts of interest. Nineteen of the experts who participated in the meeting and contributed to the formulation of the recommendations attested they had no conflicts of interest. Five of the experts disclosed ongoing relationships that have the potential to raise perceived financial conflicts of interest involving consulting, serving on data and safety monitoring boards, or receiving speaking fees from for-profit pharmaceutical companies. These disclosures are available upon request by contacting staff of the Global Council on Brain Health. The authors are unaware of any affiliation that affected the objectivity of this paper and its recommendations.

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8. LIST AND LINKS TO OTHER REPORTS

All reports are available for download at GlobalCouncilonBrainHealth.org.

- "The Brain-Body Connection: GCBH Recommendations on Physical Activity and Brain Health"
- "The Brain Sleep Connection: GCBH Recommendations on Sleep and Brain Health"
- "The Brain and Social Connectedness: Recommendations on Social Engagement and Brain Health"
- "Engage Your Brain: GCBH Recommendations on Cognitively Stimulating Activities"
- "Brain Food: GCBH Recommendations on Nourishing Your Brain Health"
- "Brain Health and Mental Well-Being: GCBH Recommendations on Feeling Good and Functioning Well"
- "The Real Deal on Brain Health Supplements: GCBH Recommendations on Vitamins, Minerals, and Other Dietary Supplements"

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