



Heartbeat

Newsletter of the Cardiovascular Health Study (CHS)
for Participants, Family, and Friends **Winter 2016**

Scientific Findings from CHS: Blood Pressure Research

Michelle Odden, PhD, Oregon State University

You may have heard or read about blood pressure in the news recently. It can be hard to keep track of what is important, so this article will provide an update, and summarize some important CHS findings.

First, let's start with the basics. Blood pressure is recorded in two numbers; systolic blood pressure is the top number, and diastolic blood pressure is the bottom number. For example, if blood pressure is reported as 120/80 mmHg, that means that 120 is the systolic pressure and 80 is the diastolic. As people age, systolic blood pressure tends to increase, whereas diastolic blood pressure usually remains steady or may even decrease.

High systolic blood pressure is associated with the risk of many health outcomes including heart disease, heart failure, stroke, peripheral arterial disease and kidney disease. However, recently in the CHS, we found that higher blood pressure may not be as risky for the very old¹. The most recent guidelines for treating high blood pressure reflected this by setting a higher treatment target of 150 mmHg for systolic blood pressure in people over 60 years of age. This compares to a treatment target of 140 mmHg for younger adults².

New CHS research also found diastolic blood pressure that is *too low* may be risky in people who have difficulty with activities of daily living such as bathing and dressing, or who walk more slowly than others their age³. Low diastolic blood pressure can cause people to feel dizzy or lightheaded, which could result in

a fall, so it is important to let your doctor know if you have these symptoms.

On the other end of the spectrum, a new clinical trial called SPRINT just found that older adults without a history of diabetes, stroke, or heart failure may benefit from much lower systolic blood pressure – even down to 120 mmHg⁴. This “intensive blood pressure control” reduced the risk of heart disease, but also increased the risk of some side effects.

So you may be wondering – which is it, 150, 140 or 120 mmHg? CHS researchers have determined that the best blood pressure for you depends on more than just your age. If you are at risk for heart disease, then a lower goal may be better. But if you don't tolerate blood pressure medications well, or have a history of falls or have difficulty walking or performing the basic daily living activities we ask you about on every call, then you may do better with a higher blood pressure. Talk to your health care provider and she or he can help you decide which goal is best for you. ❤️

1. Odden MC, Shlipak MG, Whitson HE, et al. Risk factors for cardiovascular disease across the spectrum of older age: the Cardiovascular Health Study. *Atherosclerosis* 2014;237(1):336-42.
2. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311(5):507-20.
3. Peralta CA, Katz R, Newman AB, Psaty BM, Odden MC. Systolic and diastolic blood pressure, incident cardiovascular events, and death in elderly persons: the role of functional limitation in the cardiovascular health study. *Hypertension* 2014;64(3):472-80.
4. Group SR. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med* 2015.





Parkinson's Disease and Epilepsy

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The Cardiovascular Health Study was designed to focus on problems with blood vessels (vascular disease) that may lead to heart attacks or strokes. During the course of CHS, many participants have developed other diseases, with the result that CHS is able to contribute to medical knowledge in multiple areas. The CHS Neurology Working Group of scientists is interested in those other diseases that affect the brain. Probably the most important are problems with memory and thinking, namely cognitive impairment, which at an extreme can lead to dementia. That key topic is addressed in a separate article authored by Dr. Kuller. This article addresses two other brain diseases: Parkinson's disease and epilepsy.

Parkinson's disease can slow a person's movements and is often associated with tremors (or shaking) and falls. Epilepsy causes seizures that temporarily alter the way the brain works, leading to sudden collapse with stiffening and shaking, namely a convulsion. Both have treatments that can help to control symptoms but do not cure the disease.

One of the challenges in studying these two conditions is figuring out which CHS participants have them as we do not routinely ask participants about these conditions. This is the first step of our research in this area. Although both diseases

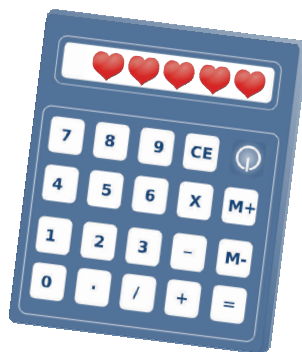
are more common with aging, most people will never experience them. Identifying participants with Parkinson's or epilepsy is possible because information collected in CHS has been combined with information collected by the Centers for Medicare & Medicaid Services (CMS). CMS is a Federal government agency that provides health insurance coverage for hospital admissions, outpatient visits, and other medical needs through its Medicare program for eligible persons ages 65 and older. In this way, we have identified which CHS participants have developed Parkinson's disease or epilepsy. Now we can proceed to address important questions about the causes, treatments, and most importantly the prevention of these conditions using data that we have collected over time from CHS participants.

The focus on the brain in CHS allows us to understand how the brain and its blood vessels can become diseased during aging. With this understanding, in the future, researchers can explore ways to keep the brain healthy as a person ages, an essential part of one's overall wellbeing. Such work is only possible because of the generosity of the CHS participants in sharing information about their health over many years. Thanks to you, we hope that our work as researchers will improve the brain aging process for generations to come. ❤️

Healthy Life Calculator

Alice Arnold, PhD, University of Washington

The CHS has developed a healthy life calculator based on responses that you have provided to questions about your health and functioning over the past decades.



For each participant, we calculated the total number of years in self-reported excellent, very good or good health and called that Years of Healthy Life. We also calculated the total number of years with no difficulty in any of the activities of daily living, such as walking, dressing, bathing or eating and called that Years of Able Life.

Dr. Paula Diehr used the data to develop a healthy life calculator that can help predict the number of Healthy and Able years a person has remaining if they are at least 65 years old (the minimum age at entry of CHS participants). She began by screening a lot of the questionnaire data we have collected to

see which items were the best predictors of Years of Healthy or Able Life. Although results of blood tests or other procedures might also be good predictors, Dr. Diehr wanted to include only items that could be responded to in a questionnaire in order to make it available to the most people.

The motivation behind the calculator was to help older adults who are facing important decisions about their future, including, for example, whether or not to remain in their primary residence. One might make a different decision if the likelihood of remaining healthy and able is high than if it is low. Of course, the calculator is based on the average experience over all CHS participants, and there is a lot of individual variation, as explained in the documentation with the on-line calculator. ❤️

Want to try it?

It can be found at:

<http://healthylifecalculator.org>



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Scientific Findings from CHS: Inflammation

Russell Tracy, PhD, University of Vermont

“Inflammation” is a term that is heard a lot in health circles these days. Often the context is something like: “heart disease is an inflammatory disorder” or “dementia has an inflammation component”. CHS was one of the first studies almost twenty years ago to demonstrate that inflammation was an important part of heart disease, using a new blood test called C-reactive protein or CRP¹.

As time has progressed, we have learned a lot of the details. CRP can be used clinically to determine a patient’s risk for future heart attack². Research in CHS helped us to understand that important chemical signals that circulate in blood, called cytokines, regulate inflammation and can also be used as biomarkers of this complex process³. And, it is now known that inflammation has three main components: blood clotting, innate immunity (the body’s immediate response to damage or infection) and adaptive immunity (a more complicated long term immune response). Blood clotting stops bleeding after injury, while innate immunity has several purposes: to clear dead and damaged tissue, to kill invading germs, and to rebuild damaged tissue. While absolutely critical to our health, when these actions get out of control they can make us sick due to formation of clots in blood vessels blocking blood flow or accumulation of unwanted scar tissue. CHS research over the years has helped clearly establish blood clotting⁴ and innate immunity⁵ as key pathways contributing to chronic diseases such as deep vein thrombosis, heart disease and stroke. The role of adaptive immunity is not yet clear, but CHS investigators were recently awarded a 4-year grant from the

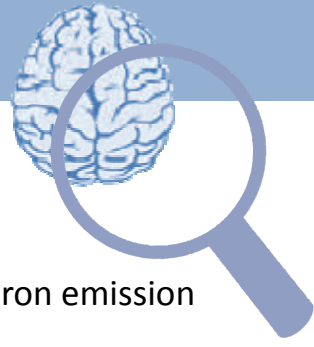
National Institutes of Health to study the adaptive immune system. They are using CHS blood samples in storage that were collected in 1998-1999. Early results suggest that adaptive immunity may be just as important to the development of chronic diseases such as heart disease as the other two components of inflammation, blood clotting and innate immunity⁶.

As you can see, the samples that you contributed years ago as a CHS participant are still playing an important role in furthering medical research. ❤️

1. Tracy R, Lemaitre R, Psaty B, et al Relationship of C-reactive protein to risk of cardiovascular disease in the elderly: results from the Cardiovascular Health Study and the Rural Health Promotion Project. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 1997;17:1121-1127.
2. Pearson TA, Mensah GA, Alexander RW, et al. Markers of inflammation and cardiovascular disease: application to clinical and public health practice: a statement for healthcare professionals from the centers for disease control and prevention and the american heart association. *Circulation*. 2003;107:499-511.
3. Walston JD, Matteini AM, Nievergelt C, et al. Inflammation and stress-related candidate genes, plasma interleukin-6 levels, and longevity in older adults. *Exp Gerontol*. 2009;44:350-5.
4. Cushman M, Folsom AR, Wang L, et al. Fibrin fragment D-dimer and the risk of future venous thrombosis. *Blood*. 2003;101:1243-1248.
5. Reiner AP, Lange EM, Jenny NS, et al. Soluble CD14: genomewide association analysis and relationship to cardiovascular risk and mortality in older adults. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2013;33:158-64.
6. Durda P, Sabourin J, Lange EM, et al. Plasma Levels of Soluble Interleukin-2 Receptor alpha: Associations With Clinical Cardiovascular Events and Genome-Wide Association Scan. *Arteriosclerosis, Thrombosis, and Vascular Biology*. 2015;35:2246-53.



A heartfelt thank you to CHS participants who have stayed with us through so many years!



Dementia Evaluation in the Cardiovascular Health Study

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There are currently about 5 million people in the U.S. living with dementia. The most common type is Alzheimer's disease, characterized by abnormal amyloid deposits in the brain. Other types of dementia include frontal temporal dementia, Lewy body dementia, dementia associated with Parkinson's disease, and vascular dementia. There are rare families with very high risk of dementia, primarily at younger ages. These are caused by genetic problems with amyloid, an abnormal protein deposited between cells. Apart from this, people with genetic differences in blood apolipoprotein E have an increased risk of dementia, which tends to start at younger ages. Interestingly, these people also have problems with amyloid in their brain.

Dementia is diagnosed by a change in cognitive performance. There is usually an effect on the ability to do normal daily functioning. The evaluation of cognition is based on the results of tests that measure memory, language, construction of objects, thinking speed and the ability to do complex tasks. Information about cognition and subsequent disability is often obtained from family members and close friends of the patient. A change in cognition that does not result in substantial disability is classified as "mild cognitive impairment" or MCI.

Fortunately, some individuals who report changes in memory have normal cognitive testing, so the testing is very important to diagnosis. In addition, brain imaging is done, usually with magnetic resonance imaging

(MRI) and, more recently, positron emission tomography (PET) imaging.

The CHS has measured cognition over time and imaged the brain using MRI. In 1998-99, detailed evaluations were done for some participants who had a brain MRI in 1992-94 and 480 dementia cases were identified. We found that the risk factors for dementia were older age, the presence of apolipoprotein E4 gene, poorer results on cognitive testing, and MRI measurements of brain size and brain vascular disease. Lower education levels, lack of exercise, and prior cardiovascular and kidney disease were also risk factors for dementia. There was little difference in the incidence of dementia between men and women and blacks and whites. Individuals who were classified as having MCI had a subsequent substantial increase in the risk of dementia at a later time.

A new method to measure the amount of amyloid in the brain called Pittsburgh compound B (PiB) PET imaging was applied to 180 older adults in Pittsburgh, including some who were in CHS. Initial follow-up over 3-4 years has shown that a combination of brain findings on MRI and PET were major predictors of the risk of dementia, the amount of amyloid and vascular disease in the brain and loss of brain structure.

At the present time, there are no proven methods to prevent dementia. Medication can sometimes slow the progression of cognitive problems in dementia patients.

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Focus on the brain

Dementia *(continued from page 5)*

Clinical trials are evaluating drugs that may remove or delay the progression of amyloid in the brain. Other clinical trials are evaluating drugs for the treatment of diabetes and hypertension as a way to prevent dementia. Based on rigorous review of the latest evidence, the Institute of Medicine recommended the following activities to promote cognitive health: 1) be physically active (walking); 2) reduce and manage cardiovascular disease risk factors, including hypertension, diabetes and smoking; 3) regularly review health conditions and medications with a health care professional;

and 4) be socially and intellectually engaged. Finally, it is very important to note that dementia, like heart disease, diabetes, and hypertension is a chronic disease which, for many older individuals, has a very slow progression to disability. It is likely that maximizing the prevention and treatment of other diseases among older individuals can slow the progression of the disability associated with dementia. Fortunately, there is considerable support for ongoing research to find the causes, prevention, and better treatment of dementia. ❤️

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