Kaiser Permanente Research Brief

Cardiovascular Disease

This brief summarizes the contributions of Kaiser Permanente Research since 2007 on the topic of cardiovascular disease. Although CVD encompasses a wide array of health conditions, this brief will focus primarily on research related to stroke, coronary heart disease, and heart failure.

According to the Centers for Disease Control and Prevention, cardiovascular disease is responsible for more than 600,000 deaths in the United States each year.[1] Though mostly preventable, it is the leading cause of death in both men and women, and across nearly all racial and ethnic groups.[1] Coronary heart disease, or the accumulation of atherosclerotic plaque within the arterial vessels of the heart, is the most common form of heart disease, and is associated with 370,000 deaths each year.[1] An estimated 6.2 million Americans also suffer from heart failure, or the heart's inability to pump sufficient blood and oxygen to the body's organ systems.[2] Heart failure is considered a contributing cause in approximately 1 in 9 deaths, and up to half of patients with heart failure may die within 5 years of diagnosis.[2] Stroke, or a disruption in the blood supply to the brain caused by a burst or blocked blood vessel, occurs in nearly 800,000 Americans each year.[3] Stroke kills approximately 140,000 Americans annually,[4] and is a leading cause of significant long-term disability, with consequences that often require long-term skilled nursing care.[3]

Kaiser Permanente Publications Related to CVD since 2007

Source: Kaiser Permanente Publications Library and PlumX metrics, as of December 30, 2020.

a Number of citing journal articles, according to Scopus.

b Number of references in PubMed guidelines.

c Citations in DynaMed Plus, a point-of-care clinical reference tool.

Cardiovascular disease is an active area of study for Kaiser Permanente Research. Scientists across the organization have used our rich, comprehensive, longitudinal data to advance knowledge in the areas of understanding risk, improving patient outcomes, and translating research findings into policy and practice. We have published nearly 1,700 articles related to CVD since 2007. Together, these articles have been cited nearly 89,000 times. These articles are the product of observational studies, randomized controlled trials,

This brief summarizes a selection of the publications contained within the Kaiser Permanente Publications Library, which indexes journal articles and other publications authored by individuals affiliated with Kaiser Permanente. The work described in this brief originated from across Kaiser Permanente's 8 regions and was supported by a wide range of funding sources including internal research support as well as both governmental and nongovernmental extramural funding.

meta-analyses, and other studies led by Kaiser Permanente scientists. Our unique environment – a fully integrated care and coverage model in which our research scientists, clinicians, medical groups, and health plan leaders collaborate – enables us to contribute important knowledge about CVD, and many other topics of research.

Understanding Risk

Who is at risk for developing cardiovascular disease?

Kaiser Permanente scientists have assessed a variety of cardiovascular disease risk factors in adults,[5,6] including diabetes,[7-11] atrial fibrillation,[12,13] high blood pressure,[7,10,14-18] high cholesterol,[9,10,17,19-21] smoking,[10,14] obesity,[9,22,23] insulin resistance,[23] kidney disease,[24-29] diet,[30] physical activity,[31-33] biomarkers,[34-37] and genetics.[38-45]

Physical Fitness Insights

Kaiser Permanente researchers have published important insights about physical fitness using data from CARDIA, a 30-year study of CVD risks and causes in 5, 115 young adults in 4 U.S. cities.

Greater fitness in young adulthood is associated with superior heart function in middle age.[115]

Short bursts of exercise (<10 minutes) can reduce the risk of high blood pressure.[116]

Active commuting to work is associated with lower BMI, blood pressure, and cholesterol.[118]

Walking or cycling to neighborhood amenities is associated with lower BMI and lower lifetime CVD risk.[117]

Our researchers have also studied CVD risk factors within pediatric populations,[46] including challenges in the family environment,[47] congenital heart defects,[48] high blood pressure,[49-51] and obesity.[52-54]

In large part because of Kaiser Permanente's emphasis on prevention,[55,56] high cholesterol[57] and uncontrolled blood pressure[58-60] are much less common among our members than in the broader U.S. population. In addition, the racial, ethnic, and socioeconomic disparities in these risk factors seen nationally are smaller among our members.[61-65]

What other health risks do people with cardiovascular disease face?

People with CVD face several associated health risks. While death is a well-known consequence of many cardiovascular diseases,[66-70] superior risk-factor control within Kaiser Permanente has reduced fatal and nonfatal CVD rates among our members.[71-78] Nevertheless, CVD carries other significant risks, including long-term disability[79,80] and the need for long-term post-acute care following stroke,[61,81,82] repeated hospitalization among patients with heart failure,[83-89] and dementia[90-93] and diabetes[94,95] among heart failure and coronary heart disease patients. Our scientists have highlighted the unique challenges the COVID-19 pandemic has posed for optimal management of cardiovascular illness.[96-98]

Moreover, the medications used to treat various cardiovascular diseases carry significant risks and side effects.[99,100] Patients receiving anticoagulants for prevention of stroke may be at increased risk of severe bleeding events,[101-106] myocardial infarction,[107] and death.[108] In addition, common treatments for heart failure and high blood pressure frequently have serious side effects, including high blood potassium,[109] serious injuries from falls,[110] and risk of birth defects.[111]

Improving Patient Outcomes

What strategies are effective in preventing cardiovascular disease?

Prevention strategies in CVD focus primarily on measuring and treating risk factors. Kaiser Per-

Kaiser Permanente employs effective strategies to help patients with CVD

 Email	 Telestroke	 Refills by Mail	 Interactive Voice Response
Email communication between physicians and patients with high blood pressure and/or diabetes was associated with improved performance scores.[152]	Rates of tissue plaminogen activator administration for acute stroke increased in emergency departments with an on-call neurologist available by phone.[220,221]	Patients enrolled in a mail-order pharmacy program were more likely to adhere to recommended hypertension treatment.[123]	In a randomized trial, statin adherence and cholesterol control were enhanced by IVR reminders.[186,190-192,194]

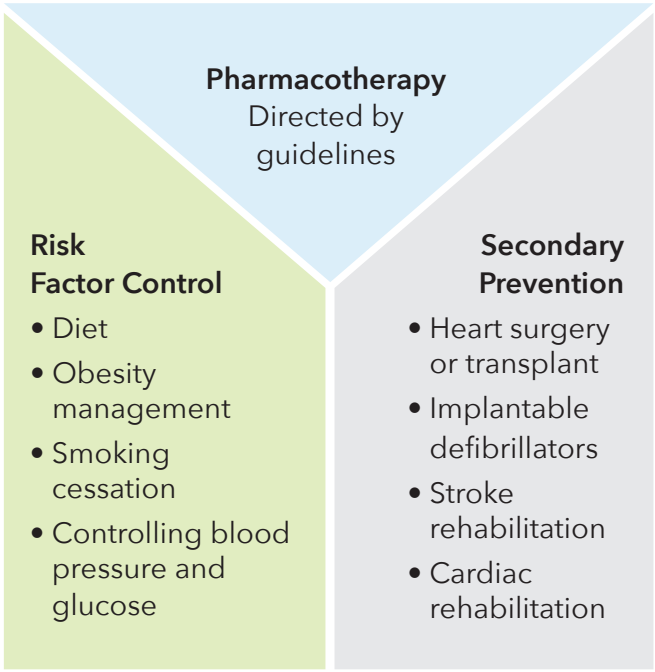
manente tracks nearly all of the American Heart Association's "Life's Simple 7" cardiovascular health metrics, including physical activity,[112-118] obesity,[9,119] blood pressure,[58-60,120-124] blood glucose,[9,122,125,126] cholesterol,[9,19,121,122,127] and smoking,[112] and uses them to measure treatment response and perform ongoing surveillance.[128] This work is conducted by teams led by primary care physicians.[120,129-131] Screening also plays a significant role in CVD prevention. For example, early identification of elevated blood pressure has been shown to improve outcomes in adult patients.[132,133] Our researchers have also studied prehospital screening strategies for patients with suspected strokes,[134] risk scoring and care pathway systems for evaluating patients entering the emergency department with chest pain,[135,136] as well as targeted cholesterol screening in pediatric patients.[137,138]

What are the key factors in effective treatment of people with cardiovascular disease?

Risk-factor management: In addition to direct treatment of CVD, ongoing risk-factor management is a critical component of the care of these patients. Studies conducted in Kaiser Permanente have found improved outcomes from smoking cessation interventions,[139,140] dietary advice,[140-148] and physical activity[113,140,141,149-152] interventions in patients with CVD. Increased use of secure email between patients and clinicians has been associated with improved outcomes in patients with high blood pressure and diabetes,[153] as has self-monitoring in conjunction with counseling, education, and assistance with medication management,[154-157] and the provision of additional support to primary care physicians.[158]

Pharmacotherapy: Medications are an established component of evidence-based care for both CVD management and control of risk factors. While a discussion of specific medications is beyond the scope of this brief, our researchers have led or collaborated on key studies exploring the efficacy and safety of numerous medications in CVD populations. These have included key studies of glucose-lowering medications for control of type 2 diabetes and prevention of cardiovascular complications of diabetes,[125,126,159-163] drugs to lower blood pressure,[58,164-175] and cholesterol-lowering medications,[168,169,176-180] as well as recent studies of anticoagulant treatments for stroke prevention among patients with atrial fibrillation[107,181-184] and medications for acute heart failure.[185-189]

CVD Management



Given its importance in the care of patients with CVD, medication adherence has also been a significant focus of research in Kaiser Permanente. Large cohort studies conducted by our scientists have found that nonadherence to medications such as ACE inhibitors, statins, and beta-blockers is associated with increased risks for all-cause and cardiovascular mortality, revascularization (an invasive medical procedure that restores blood flow to blocked or narrowed coronary arteries), and cardiovascular hospitalization.[190,191] A large study of at-risk members starting statins found that 84% were still receiving them 1 year later, but only 42% had experienced no treatment gaps during that time.[192] The trend of suboptimal preventive use of statins has proven difficult to reverse, as shown by a national-level study conducted by Kaiser Permanente scientists.[193] Furthermore, patients at lower CVD risk are less likely to comply with prescribed statin therapy.[194] We have evaluated several medication-adherence interventions for patients with CVD involving clinical pharmacist[120,177,195,196] or community health worker[197] outreach, interactive voice response calls and reporting,[195,198-201] mail-order pharmacy programs,[123] or web-based medication self-management.[202] A study, conducted in our members with diabetes, found that addressing undertreatment in addition to nonadherence could significantly improve outcomes for people with uncontrolled blood glucose, cholesterol, or blood pressure.[125]

Other secondary prevention: In addition to medication and lifestyle modifications, surgical procedures (including heart transplantation) and device implantation are also components of CVD management in targeted patients. Coronary revascularization has been studied extensively within Kaiser Permanente. Our researchers have explored the adoption[203] of this family of technologies and geographic variations in their use.[204] Studies have found that improved patient outcomes are associated with the appropriate use of specific invasive procedures,[205-211] particular clinical characteristics,[212,213] surgeons who perform more procedures,[214] and improved practices for managing blood clots.[215]

For patients with certain severe heart conditions, heart transplantation is an important treatment strategy. Our researchers have found that receiving a heart from a donor with diabetes mellitus,[216] a history of transplant rejection,[217]

In several studies, Kaiser Permanente researchers found that the absence of appropriate treatment intensification was more common than medication non-adherence in CVD patients with uncontrolled risk factors [95,98,132,134,141,157]

Uncontrolled Risk Factor	Non-Adherence	Treatment Not Escalated
Blood Pressure	19-42%	26-78%
Blood Sugar	18-42%	26-47%
Cholesterol	19-49%	25-55%

and longer wait times before transplantation[218] are associated with poorer heart transplant outcomes. Another study described a DNA-based method for noninvasive diagnosis of heart transplant rejection,[219] increasing the ease of post-transplant monitoring. Our research on implantable cardiac defibrillator, or ICD, usage has explored how often these devices are used in off-label[220,221] or non-guideline-directed fashion.[222] Other studies have found that mortality outcomes in patients with ICDs are associated with heart function, the heart's structure,[85] and higher BMI (body mass index),[223] and have evaluated algorithms for the prediction of survival and sudden death in these patients.[224,225]

Translating Research Findings Into Policy and Practice

How has Kaiser Permanente research on cardiovascular disease contributed to changes in policy and practice?

As part of a learning health care organization that uses research to inform and improve practice, Kaiser Permanente's research, clinical, and operational partners have tested a range of interventions to reduce the risk of cardiovascular disease and improve outcomes for patients with CVD. For example, research supporting the efficacy of combining ACE inhibitors and thiazide diuretics in a single pill for blood pressure management[169] led to broad adoption of this practice in Kaiser Permanente's blood pressure management program.[59] The spread of single-pill blood-pressure-lowering therapy increased the ease of removing beta-blockers as a first-line treatment, a transition prompted by our research data questioning the benefits of these medications.[171] Our research in acute stroke management[226] has led to implementation of effective telestroke programs with an on-call neurologist available via telemedicine technology to emergency department physicians in our Northern California[227] and Southern California regions.[228]

Collectively, research from Kaiser Permanente authors has been cited nearly 900 times within recent consensus statements and clinical practice guidelines published by a wide range of entities, including the American Stroke Association and American Heart Association.[229] In addition, our researchers and clinician scientists have directly contributed as authors of 3 hypertension guidelines,[230-232] the atrial fibrillation guidelines of the American College of Chest Physicians,[233] the obesity guidelines of the American College of Cardiology, the American Heart Association, and The Obesity Society,[234] a guideline published by the American College of Cardiology and other societies pertaining to treatment of aortic stenosis,[235] policy statements regarding physical activity and management of myocardial infarction from the American Heart Association,[236-239] the Western Vascular Society's guidelines for managing patients with ruptured abdominal aortic aneurysm,[240] a position statement on blood pressure measurement from the Lancet Commission on Hypertension,[241] and various statements by the U.S. Preventive Services Task Force.[242-244] Kaiser Permanente researchers have also taken part in the Implementation Science Work Group convened by the National Heart, Lung, and Blood Institute, in which the implementation of CVD guidelines was studied.[245] Our scientists have also participated in regional health collaboratives in the city of San Diego and Sonoma County aimed at reducing the burden of cardiovascular disease.[246,247] Finally, the hypertension management efforts implemented in our California regions[58,59] have received widespread recognition,[248] particularly with respect to reducing racial disparities in blood pressure control.[249]

Heart attacks and high blood pressure rates

Thanks to interventions validated by our researchers, rates of heart attacks and high blood pressure dropped sharply in Kaiser Permanente Northern California between 1999 and 2014.

	1999	2014
% with high blood pressure[173]	54%	10%
Heart attacks per 100,000 members[73,74]	274	185

Kaiser Permanente has shown considerable leadership in the field of cardiovascular disease research. We have endorsed and actively supported the Department of Health and Human Services' Million Hearts Initiative,[250] and our Colorado,[251] Northern California,[252] and Georgia[253] regions have been recognized as Million Hearts Hypertension Control Champions. Kaiser Permanente has supported care improvement efforts in safety net health care providers that operate in the same communities.[254,255] Our researchers have led or collaborated on many notable studies related to epidemiology, prevention, risk factors, and treatment of CVD, including the Coronary Artery Risk Development in Young Adults (CARDIA) study, the Cardiovascular Research Network (CVRN), and the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study, all of which have been sponsored by the NIH's National Heart, Lung, and Blood Institute.

Kaiser Permanente's nearly 170 research scientists and more than 1,600 support staff are based at 8 regional research centers and 1 national center. There are currently more than 2,400 studies underway, including clinical trials. Since 2007 our research scientists have published more than 12,000 articles in peer-reviewed journals. Kaiser Permanente currently serves more than 12.4 million members in 8 states and the District of Columbia.

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