

Department of Veterans Affairs: Risk Factors for Cardiovascular Diseases

A sedentary lifestyle, high calorie-fat diets and genetic susceptibility increase obesity, diabetes and cardiovascular disease risk with aging. These can be modified by disease-specific exercise and dietary interventions to improve health and function in the elderly.

Lead Agency:

Department of Veterans Affairs

Agency Mission:

"To care for him who shall have borne the battle and for his widow and his orphan."

Principal Investigator:

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Partner Agency:

University of Maryland
Veterans Health Administration
Baltimore Geriatric Research
Education and Clinical Center

General Description:

Aging research at the Baltimore VA GRECC examines the hypothesis that physiological declines in cardiovascular and metabolic function that accelerate cardiovascular disease (CVD) risk are predominately related to the influence of genetic susceptibility, a sedentary lifestyle and obesity—and that these can be effectively modified by exercise and dietary interventions. Research designed to modify CVD risk investigates 1) the effects of exercise and weight loss on CVD risk, 2) genetic predictors of disease, and 3) functional and health outcomes of structured exercise in chronic stroke. A multidisciplinary team leverages resources from six National Institutes of Health (NIH) and VA centers of excellence to conduct patient-oriented translational research and clinical trials in genetics, exercise and low-calorie feeding that translates basic science research into clinical practice to improve the health, function and quality of life in older Americans.

Our research demonstrates that structured exercise and diet interventions modify fundamental biological processes that underlie diabetes and obesity in advancing age. GRECC researchers examine the molecular, cellular and genetic mechanisms by which fat produces inflammatory proteins and muscle accumulates fat in type 2 diabetes and obesity, and how these disease processes are reduced by exercise and weight loss. The clinical translation exercise and weight loss program in the VA - *Managing Obesity for*

Veterans Everywhere (MOVE!) improves exercise capacity, functional performance and body composition to reduce diabetes and CVD risk. Research studies examining the molecular, genetic and physiologic basis of these improvements allow translation of basic mechanisms and novel rehabilitation techniques into effective treatment, prevention and rehabilitation modalities.

Researchers examine the genetic and environmental causes of adult onset diabetes in the genetically homogeneous “Founder Old Order” Amish population, ideal for studies of CVD-related diseases. The Amish are as obese as the U.S. population, but have half the prevalence of type 2 diabetes due to high levels of physical activity. Amish subjects who are genetically susceptible to weight gain reduce risk of obesity through physical activity, suggesting genetic risk of obesity is modifiable through healthy lifestyle choices. We have been able to identify several common gene variations that are associated with diabetes and metabolic syndrome. Extensions of these genetic studies have identified new genes for hypertension, hyperlipidemia, uric acid, and glucose levels that are under exploration in other US populations at high risk for CVD.

Stroke results in chronic impairments in walking and balance that limit functional independence and physical activity, even years after conventional rehabilitation care. This increases risk for diabetes and recurrent stroke. We developed a model of “task-oriented” treadmill training that facilitates recovery of walking by activating subcortical brain networks, while providing aerobic exercise to improve cardiovascular health and fitness in chronic stroke. This program improves glucose metabolism to reduce diabetes risk and reverse its prevalence in over half of exercising subjects. Hence, treadmill training offers a new approach for rehabilitation of older stroke victims that improves their health and function, and decreases the risk for diabetes and recurrent stroke.

Excellence: What makes this project exceptional?

This program is exceptional because it provides a unique interface between basic science and clinical medicine to advance knowledge into new approaches for the diagnosis and treatment of CVD risk factors and disability conditions prevalent in older people. There is an enriched environment of interdisciplinary collaboration in “bench to bedside” research among GRECC investigators that examines the cellular, molecular and genetic mechanisms by which lifestyle interventions reduce CVD risk and improve functionality. This in turn prevents obesity and diabetes-associated CVD and stroke-associated disability. The conceptual model posits that multiple physiological systems and genes interact to determine the long-term cardiovascular health and functional independence of older individuals. This multidisciplinary approach leverages resources across multiple NIH and VA centers of excellence to bring a basic science outlook to the design of novel structured physical activity and exercise rehabilitation interventions. Our goal is to prevent and treat diabetes, cardiovascular disease and disability conditions to promote recovery in older Americans living with chronic diseases and disability.

Significance: How is this research relevant to older persons, populations and/or an aging society?

Aging and a sedentary lifestyle are associated with an increasing prevalence of overweight and obesity. These place older adults at greater risk for the development of

diabetes, CVD, functional impairments and disability. Innovative research that translates interventions to the community will increase physical activity and promote weight loss. This has the potential to decrease morbidity and mortality and improve quality of life in older adults with chronic CVD. GRECC genetic research demonstrates the value of genetic screening to identify susceptibility to disease. It also identifies who are most likely to experience health benefits from exercise and diet interventions. This will advance the science of rehabilitation research in aging, leading to new discoveries to identify, prevent and treat disease to reduce risk for frailty and prolonged disability requiring long-term care. Our programs provide hope and empower older Americans living with diabetes, CVD and stroke to combat their chronic disability and improve their health and well-being through exercise and dietary lifestyle modification..

Effectiveness: What is the impact and/or application of this research to older persons?

Our exercise training models are highly effective in improving cardiovascular fitness, strength and muscle mass, and glucose regulation to reduce CVD risk in older Americans living with diabetes, obesity and stroke. We thereby are enhancing the maintenance of functional independence even years after diagnosis. Routine clinical management of older adults with obesity, diabetes, CVD risk factors and disability associated with stroke do not provide resources for sustained or disease-specific exercise or nutritional interventions that are needed to improve long-term health outcomes in the elderly. Our research shows a synergy between exercise and dietary interventions to optimize CVD risk modification for diabetes, obesity and aging-related disability conditions. This research provides data for evidence-based translation into the clinical setting to develop national guidelines for disease, disability and age-specific exercise and dietary recommendations for older Americans.

Innovativeness: Why is this research exciting or newsworthy?

GRECC researchers have presented novel findings at the Institute of Medicine that task-oriented treadmill training which combines “motor learning” with aerobic exercise mediates brain plasticity to enhance mobility function, while improving fitness and reversing diabetes in older chronic stroke patients, even decades after the stroke. In 2008, these findings will be incorporated in National Academies of Science, Evidence-Based Guidelines for Physical Activity for All Americans. These guidelines requested by the Secretary for Health and Human Services, include the evidence for effectiveness of physical activity in aging, chronic diseases including diabetes and obesity, and disability including stroke, will form the basis for new models of care.

Genetic screening may allow us to target disease-specific interventions to subjects most likely to respond with improvements in functional performance and cardio metabolic health, even older people with multiple chronic medical comorbidities and stroke.

GRECC scientists investigate basic science mechanisms at the cellular and molecular level for these physiologic adaptations. This will generate new knowledge and technologies to provide the scientific foundation and rationale for the incorporation of disease- specific exercise and dietary approaches for the prevention and treatment of CVD and related disabilities into clinical practice.