SHAPE Study Results

One in three women will die from cardiovascular disease (CVD), making CVD the number one cause of death in women. After menopause, women have a higher risk for heart disease, possibly due to the loss of the female hormone estrogen. One potential reason for this is that decreasing levels of estrogen have been shown to cause the cells that line the arteries to become damaged and the arteries surrounding the heart to “stiffen.” These changes in artery health can lead to the development of CVD.

The purpose of the SHAPE (Sex Hormones and Atherosclerosis Prevention in Premenopausal Women) study was to find out how decreases in the female sex hormone estrogen with the menopause transition cause arteries to become unhealthy. We used ultrasound imaging to assess the health of the carotid (in the neck) and brachial (in the arm) arteries in women who were premenopausal (normal menstrual cycles), perimenopausal (irregular menstrual cycles), or postmenopausal (no menstrual cycles in over a year). SHAPE found that carotid and brachial artery health was progressively impaired across the menopause transition groups, with premenopausal women having the healthiest arteries and postmenopausal the least healthy. SHAPE also found that artery health became impaired in premenopausal and perimenopausal women when estrogen levels were lowered with a medication, suggesting that estrogen has a beneficial effect on artery health. To understand how estrogen benefits artery health, SHAPE examined whether giving the antioxidant vitamin C improved vascular health. Vitamin C improved vascular health in late perimenopausal and postmenopausal women, meaning that the decline in vascular health with decline in estrogen was related in part to oxidative stress. Oxidative stress occurs when the production of molecules that can damage cells in the body outpaces the body’s ability to neutralize them.

NEW STAFF ANNOUNCEMENT

Kelly Downing earned her PhD in Nutritional Sciences from the University of Kentucky and completed a one-year postdoctoral fellowship at Stanford University before moving to Colorado to continue her postdoctoral work under the mentorship of Dr. Kerrie Moreau. Dr. Downing has previously used mouse models to study risk factors for cardiovascular disease and is excited to join the IMAGE group to gain valuable translational and clinical research experience. Drs. Downing and Moreau will work together on the SHAPE-2 study to investigate the effects of estrogen and oxidative stress on vascular function.

SHAPE 2

The results from SHAPE have led to a new study called SHAPE-2. SHAPE-2 will test whether low levels of tetrahydrobiopterin (BH4), a natural substance in the body that can cause the arteries to expand, explain how oxidative stress damages arteries in women with low levels of estrogen. To answer this question, SHAPE-2 will examine whether giving a medication that increases BH4 level improves vascular health in perimenopausal and postmenopausal women. These studies will contribute to the understanding of how decreases in estrogen levels as women go through menopause may contribute to the development of CVD. SHAPE-2 is currently enrolling healthy women aged 18 to 70 years of age. For more details and contact information, please see SHAPE-2 under “Studies for Women” on page 2.
STUDIES FOR WOMEN & MEN:  

**SPARX** is a study to determine whether individuals recently diagnosed with Parkinson’s disease, and have not yet started drug treatment, can successfully take part in an aerobic exercise program. Individuals with PD are randomized to a control group that does not exercise, or to a group that exercises on a treadmill at a moderate or high intensity. Participants will exercise 4 days a week, for 30 minutes a day, for 6 months. If you or someone you know has been diagnosed with Parkinson’s disease and is interested in participating in this clinical research, please contact at 720-848-6376 or Toby.Wellington@ucdenver.edu. (COMIRB #11-1237)

The Determination of Pain Phenotypes in Older Adults with Knee Osteoarthritis study is exploring what causes pain with knee osteoarthritis. We are looking for people aged 50 to 85 years with and without knee pain to attend a single testing session at the Anschutz Medical Campus (~2 hours) to explore factors that contribute to knee pain. Monetary compensation provided. To learn more, please email KNEEpain@ucdenver.edu or call 303-724-9590 (COMIRB#12-1188).

**Sita Study:** Do you have type 2 diabetes? This research study will evaluate the effects of two FDA-approved diabetes medications on cardiovascular function during exercise. Qualified participants will receive study medication, as well as free lab screenings, physical exams and exercise testing. Financial compensation is provided. If you are between the ages of 22 and 70 years old with type 2 diabetes who takes metformin only for your diabetes, you may qualify for this study. If interested, email Shawna.mcMillin@ucdenver.edu or call Shawna at 303-724-2255 or (P.I. Regensteiner, COMIRB# 13-2015).

**Leg Blood Flow Study** This is a study evaluating men and women with or without type 2 diabetes during single leg calf exercise. We are evaluating the function of heart and blood vessels during exercise. Eligible participants are healthy men and women with type 2 diabetes (not using insulin) between the ages 30-70 years who are non-smokers and currently exercising no more than once per week. The study involves 8 study visits and two weeks of supervised exercise training over the course of two months. If you are interested in participating in this study, please contact Shawna McMillin by email Shawna.mcMillin@ucdenver.edu or call 303-724-2255 or (P.I. Regensteiner, COMIRB# 06-0062).

**AcT2:** The AcT2 study is looking at a medication called acipimox and its effects on type 2 diabetes and exercise capacity. Study participants will be financially compensated and receive no cost lab screenings, physical exams, exercise testing and more. Participants will be asked to take the investigational drug or placebo for 7-9 days on separate occasions. If you are a non-smoker, age 30-60 with type 2 diabetes that does not require insulin, and exercise less than 1 hour per week, then this study could be for you! If interested, contact Shawna McMillin at 303-724-2255. (COMIRB# 10-1393)

The B-WELL study is to test whether decreasing time spent sitting and adding short intervals of walking improves the health of older adults. We are looking for non-smoking sedentary men or women between 60 and 85 years old without orthopedic conditions that limit ability to walk briskly. To learn more please contact Mary Peterson at Mary.Peterson@ucdenver.edu or call (720) 848-6474. (COMIRB# 13-2094).

**STUDIES FOR WOMEN:**

The **FAME study** is examining how the loss of estrogen changes metabolism and risk of disease in women. Eligible participants are healthy women between the ages of 45 and 70 years who are not using hormone therapy and who are either within 6 years of menopause or more than 10 years past menopause. Volunteers will be asked to wear estrogen patches for one week prior to one of two visits. The study is designed to measure insulin metabolism. Up to $400 in compensation will be provided for participation in the study. To learn more, please email Tracy.Swbaas@ucdenver.edu or call 720-848-6418. (COMIRB# 11-0788)

The **TEMPUS study** will examine whether one week of estrogen has different effects on insulin metabolism in women who are only a few years past menopause compared to women who are many years past menopause. Eligible participants are healthy women between the ages of 45 and 70 years who are not using hormone therapy and who are either within 6 years of menopause or more than 10 years past menopause. Volunteers will be asked to wear estrogen patches for one week prior to one of two study visits. The study is designed to measure insulin metabolism. Up to $400 in compensation will be provided for your time (up to $300). To learn more, please call 720-848-6399 or email: Kimberly.Hamer@ucdenver.edu. (COMIRB# 12-1157)

The **GEM study** investigates the relationship between volume of aerobic exercise and positive changes in DNA methylation over four months among previously sedentary women 20-70 years (Non-smokers). Volunteers should NOT be currently exercising more than 20 minutes a day, for 6 months. Eligible participants should not be exercising regularly but should be willing to participate in an exercise program 4 times per week for 16 weeks. Monetary compensation will be provided for participation in the study. To learn more, please call 303-492-9549 or email: GEM.CUstudy@gmail.com. (COMIRB# 13-2314)

**SHAPE 2** The purpose of this study is to investigate how the menopause transition and the loss of estrogen impacts the health and function of arteries in women. We are looking for Premenopausal women 18-49 years, Perimenopausal women 40-55 years and Postmenopausal women 45-70 years (Non-smokers). Volunteers should NOT be taking Birth Control or Hormone Replacement Therapy (HRT), or exercising vigorously more than 2 days per week. To learn more, please call Lila Sibarzo 720-848-6419 or email shape.study@ucdenver.edu. (P.I. Kerrie Moreau COMIRB# 06-0537)