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Lifestyle Change in a Large National Healthcare System

By

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Division of Biological and Biomedical Sciences
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# Lifestyle Change in a Large National Healthcare System

By

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MPH, Emory University, 2009

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Advisor: Lawrence S. Phillips, M.D.

An Abstract of

A dissertation submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University

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ABSTRACT

Lifestyle Change in a Large National Healthcare System

By Sandra Jackson

**Background**: Lifestyle change programs are recommended for weight management and chronic disease prevention. However, little is known regarding their impact in healthcare settings, where participants are *patients* to whom lifestyle change is *recommended*, rather than volunteer research subjects. The Veterans Health Administration (VA) developed MOVE! (Managing Overweight / Obesity in Veterans Everywhere), which is the largest lifestyle change program in the US. Our objectives were to examine the association between MOVE! participation and (a) diabetes incidence, (b) cardiovascular disease (CVD) incidence, and (c) diabetes management.

**Methods**: We used national VA databases to identify approximately 2 million patients eligible for MOVE! (obese or overweight with a weight-related health condition). Cox proportional hazards models were used to analyze incidence of (a) diabetes (based on ICD-9 codes or prescription of a diabetes medication); (b) CVD including coronary artery disease (CAD), cerebrovascular disease (CBD), peripheral vascular disease (PVD), and heart failure (HF); and (c) diabetes complications (eye disease and renal disease) and medication intensification.

**Results**: Patients were approximately 92% male, 76% white, with mean age 52 years and BMI 32. MOVE! participants had modest weight loss over 3 years, while non-participants gained weight. Adjusting for age, race, sex, BMI, and baseline comorbidity, MOVE! participation was associated with lower incidence of diabetes: HR 0.67 (95% CI 0.61-0.74) for "intense and sustained" participants (who engaged in $\geq$8 sessions over $\geq$129 days) vs. non-participants, and HR 0.80 (0.77-0.83) for less active participants. Any amount of MOVE! participation was also associated with lower incidence of total CVD (hazard ratio 0.83, 95% CI 0.80-0.86), CAD (HR 0.81, 0.77-0.86), CBD (HR 0.87, 0.82-0.92), PVD (HR 0.89, 0.84-0.94) and HF (HR 0.78, 0.74-0.82). Among patients with diabetes at baseline, any MOVE! participation was associated with improved glycemic control despite lower medication intensification (HR 0.81, 0.79-0.83), as well as lower incidence of diabetic eye disease (HR 0.80, 0.76-0.85) and renal disease (HR 0.90, 0.86-0.93).

**Conclusions**: This study of the VA's MOVE! program provides evidence that participation in a large-scale, healthcare system-based lifestyle change program is associated with lower incidence of diabetes and cardiovascular disease, as well as improved diabetes management.

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# Chapter 1: Introduction

Obesity has been described as the greatest public health challenge of our time,(1) yet we know little about how to bring help to the millions of affected Americans. In the US, the prevalence of obesity has risen dramatically in recent decades,(2) and two thirds of adults are now overweight or obese.(3) Obesity has been associated with a wide range of negative social, emotional, and health consequences including stigma and discrimination,(4) increased risk of mental illnesses such as depression,(5) and increased risk of cancer, sleep apnea, and osteoarthritis.(6) Obesity has also been linked to lower life expectancy, and an estimated 112,000 excess deaths were attributed to obesity in 2000.(7-9) In addition to a substantial burden of morbidity and mortality, obesity also increases costs. Medical expenses are approximately 42% higher among obese compared to normal weight persons, and the total medical cost of obesity was estimated at $147 billion in 2008.(10)

Obesity substantially increases the risk of developing diabetes and cardiovascular disease, (11-12) and these conditions carry a considerable burden of morbidity, mortality, and cost. The lifetime risk of diabetes in the US is estimated at 33-53%,(13) although the risk varies considerably across BMI categories. At age 18, the remaining lifetime risk of developing diabetes for a normal weight man is under 20%, whereas for a very obese man, the remaining lifetime risk is over 70%.(14) Other findings also point to the profound influence of obesity on diabetes: in genetically similar Pima Indian populations in the US and Mexico, the US Pima Indians have a 5-fold greater prevalence of diabetes compared the Mexican Pima Indians, which has been attributed to the greater obesity

prevalence among US Pimas, as well as Western diet and less physical activity.(15) In addition, evidence from the Health Professionals' Follow Up Study demonstrated that among those with genetic susceptibility to diabetes, a Western diet exacerbates disease risk.(16) Among US adults, diabetes is the leading cause of blindness, kidney failure, and nontraumatic lower-limb amputations, and diabetes is one of the top 10 causes of death.(17) The disease is quite costly: total expenses related to diabetes were estimated at $245 billion in 2012.(18) Obesity and diabetes both contribute to cardiovascular diseases (CVD), which are also major causes of mortality and healthcare cost in the US. One third of deaths are attributable to CVD, (19-20) and the total cost of CVD, including healthcare costs and lost productivity due to premature mortality, was estimated at $312.6 billion in 2009.(21)

Lifestyle change programs are recommended for weight management and for prevention or delay of the development of chronic diseases.(22) They can be highly effective; in the landmark US Diabetes Prevention Program (DPP), participants exhibited 7% weight loss and a 58% reduction in diabetes incidence.(23) In recognition of the substantial burden of obesity and chronic disease affecting the veteran population,(24-26) the Veterans Health Administration (VA) implemented a lifestyle change program called MOVE!. To date, it is the largest lifestyle change program in the US, with over 400,000 participants since 2005.(27) A regional evaluation of the program demonstrated modest weight loss,(28) but little is known about other potential health benefits associated with participation. Studying the MOVE! program offers a unique opportunity to examine a healthcare system-based lifestyle change program that has been implemented on a national scale.

The following chapter examines obesity, diabetes, and cardiovascular disease epidemiology in the US and the use of lifestyle change programs as a component of preventive care, including the VA's MOVE! program (Chapter 2). Chapter 3 provides an overview of the VA's national data and methodological issues specific to our analyses. The next three chapters describe substantive results:

- In Chapter 4, we describe the characteristics of MOVE! program participants compared to eligible non-participants, as well as the associations between participation and both weight change and diabetes incidence.

- In Chapter 5, we examine the association between MOVE! program participation and change in CVD incidence, including total CVD, coronary artery disease (CAD), cerebrovascular disease (CBD), peripheral vascular disease (PVD), and heart failure (HF).

- In Chapter 6, we examine MOVE!-eligible patients with diabetes, and the association between participation and aspects of diabetes management such as glucose control, incidence of diabetes complications (eye disease and renal disease), and medication intensification.

The final chapter summarizes the main findings and explores the limitations, strengths, and implications of this research.

Although several landmark studies have established the ability of lifestyle change programs to decrease diabetes incidence, (23, 29-31) there is limited understanding of the

potential impact of a lifestyle change program implemented in a healthcare setting, as has been recommended for widespread translation.(32-33) Our **first aim** is to examine the association of MOVE! participation with diabetes incidence, among eligible patients without diabetes. In addition to the knowledge gap regarding healthcare-based implementation, there is mixed evidence regarding the impact of lifestyle change programs on cardiovascular disease incidence, and relatively few studies have had sufficient sample size to examine cardiovascular endpoints.(34-37) Our **second aim** is to examine the association between MOVE! and cardiovascular disease incidence, among VA patients without CVD at baseline. Lastly, evidence is scarce regarding the impact of lifestyle change programs on diabetes management, and particularly microvascular outcomes.(34) Our **third aim** is to investigate the association between MOVE! and diabetes management, including glucose control, incidence of eye disease, incidence of renal disease, and medication intensification.

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# Chapter 2: Literature Review

## *Epidemiology of Overweight and Obesity*

The national prevalence of obesity has increased dramatically since the 1970s.(1) Current estimates suggest that 68% of US adults are overweight or obese, defined as body mass index (BMI) 25-29.9 $kg/m^2$ or BMI $\geq$30$kg/m^2$, respectively.(2) Among all adults, 35% are obese, and – particularly among women – prevalence is higher among racial/ethnic minorities: 54% of non-Hispanic black women and 45% of Mexican-American women are obese, compared to 33% of non-Hispanic white women.(3) Explanations for the recent rise in obesity include increased sedentary activity such as television viewing, increased consumption of sugar-sweetened beverages, and increased overall caloric consumption.(4-5) For example, between 1971 and 2004, average total caloric consumption increased by 22% among women and 10% among men.(3) Additional factors contributing to the rise of obesity have been proposed, including demographic shifts (such as the aging of the population and increased proportion of minorities), reduced sleep, increased exposure to endocrine disruptors, increased climate control reducing daily energy expenditure, reduced smoking, and epigenetic mechanisms.(6)

If linear trends were to continue, Wang et al. projected that by 2048, the entire US population would be either overweight or obese,(7) while more conservative estimates have predicted that the obesity prevalence will reach 42% by 2030.(8) The rising obesity prevalence has had a profound impact on medical costs. The rise in obesity and obesity-

related spending between 1987 and 2001 may explain 27% of the rise in inflation-adjusted per capita medical costs during the same period.(9) Medical spending for obese persons is an estimated 42% higher than for normal weight individuals, and the total medical cost of obesity was estimated at $147 billion in 2008.(10)

Obesity is associated with lower quality of life, and an extensive range of social, emotional, and health consequences.(11) Socially, obese individuals experience stigma and discrimination.(12) Overweight and obese individuals are at greater risk of mental illness such as depression,(13) as well as conditions such as Alzheimer's disease and dementia.(14) Obesity is also associated with numerous physical comorbidities, such as cancer, sleep apnea, musculoskeletal conditions including osteoarthritis (a chronic condition in which a joint's cartilage deteriorates) and plantar fasciitis (characterized by inflammation and structural deterioration in the foot), nonalcoholic fatty liver disease, dermatologic conditions, and reproductive disorders in both women and men.(15)

In addition to a substantial burden of morbidity, obesity is associated with increased mortality. An estimated 112,000 excess deaths were attributable to obesity in the United States in 2000.(16) Specifically, obesity has been associated with increased CVD mortality, and overweight and obesity together have been associated with increased mortality from diabetes and kidney disease.(17) In the Framingham Heart Study, 40-year-old men and women lost 3 years of life expectancy due to overweight, while men lost 6 years and women lost 7 years due to obesity.(18)

***Epidemiology of Diabetes***

Diabetes mellitus is a set of metabolic diseases characterized by elevated blood glucose levels. While insufficient insulin production by the pancreas is the root cause, most commonly insulin secretion is present but insufficient to compensate for increased insulin resistance. Type 2 diabetes mellitus accounts for over 90% of diabetes cases among adults in the US,(19) and for the purposes of this dissertation, the term "diabetes" will be used to refer to type 2 diabetes mellitus. The lifetime risk for development of diabetes has been estimated at 33-53%.(20) Obesity is strongly associated with the development of diabetes; the Nurses' Health Study found that for each 5-unit increase in BMI, the risk of diabetes doubled.(21) As obesity has increased in the US in recent decades, the prevalence of diabetes has also increased sharply.(22) The prevalence of diabetes mellitus was estimated at 11.3% in 2011,(23) with an additional 38.3% of adults having prediabetes.(3) Prediabetes is defined as an intermediate form of dysglycemia, in which blood glucose or hemoglobin A1c (HbA1c) levels are above the threshold considered to be "normal", but have not yet reached levels required for diagnosis of diabetes. According to the American Diabetes Association (ADA), prediabetes includes impaired fasting glucose (IFG) of 100 to 125 mg/dL (fasting plasma glucose) and/or impaired glucose tolerance (IGT) of 140 to 199 mg/dL (plasma glucose measured two hours after administration of a 75-gram oral glucose tolerance test), and diabetes is diagnosed above these thresholds ($\geq$ 126 mg/dL fasting, and/or $\geq$ 200 mg/dL post-challenge). By ADA criteria for HbA1c, prediabetes is defined as 5.7% to 6.4%, and diabetes is $\geq$ 6.5%.

Complications of diabetes are a major cause of morbidity in the US. Diabetic nephropathy occurs in 20-40% of persons with diabetes,(24) and diabetes is the leading cause of kidney failure in adults.(25) Diabetic nephropathy occurs when high glucose concentration, which is toxic to cells of the vascular endothelium, causes damage over time (angiopathy) in the capillaries of the kidney glomeruli, which filter blood. This damage can impair filtration and lead to the leakage of proteins, like albumin, into the urine (proteinuria). Kidney disease can be diagnosed early, when small amounts of albumin leak into the urine (microalbuminuria), or it can be diagnosed later, when the concentration of albumin in the urine is greater (macroalbuminuria). As kidney disease progresses, the kidneys lose their ability to filter waste products from the blood, and patients in end stage renal disease (ESRD) who suffer kidney failure require either kidney transplant or dialysis.

Among US adults, diabetes is also the leading cause of new cases of blindness,(25) due to progression of diabetic eye disease. Eye disease is a common complication of diabetes; in one population, retinopathy affected over three quarters of patients who had diabetes for at least 15 years.(26) Diabetic retinopathy occurs when hyperglycemia damages blood vessels in the retina, which is the light-sensing lining at the back of the eye. The retina is a highly metabolically active tissue, and requires a regular oxygen supply. Diabetes can damage blood supply in the eye and cause hypoxia, which is thought to be the mechanism underlying many eye disease complications associated with the disease.(27) As damage progresses, the growth of new blood vessels can occur (proliferative retinopathy). These vessels often leak blood and other fluid in the eye, causing swelling or clouded vision. Excess fluid in the lens of the eye can also

change the eye's ability to focus and create blurred vision. Diabetes is also associated with increased risk of cataracts (clouding or fogging of the lens of the eye) and glaucoma (excess pressure in the eye which can damage nerves and increase blood pressure in the eye).

In addition to diabetic kidney disease and eye disease, another complication of diabetes is neuropathy. Diabetes is the leading cause of non-traumatic lower-limb amputations in adults,(25) which can result when nerve damage and poor circulation lead to non-healing ulcers. Other forms of morbidity associated with diabetes include increased risk of dental disease, nervous system damage, hypertension, heart disease, and stroke.(25) Diabetes is also associated with lower quality of life,(28) and increased risk of mortality. Diabetes was the seventh leading cause of death in the US in 2007, according to death certificates, and it may be substantially underreported.(25) The risk of death is twice as high among people with diabetes as among similarly-aged persons without the disease.(25)

Diabetes substantially increases medical costs. It has been estimated that persons with diabetes have average medical expenditures 2.3 times higher than persons without the disease.(25) In 2012, the total cost of diabetes was estimated at $245 billion,(29) and health care costs attributable to prediabetes and diabetes are projected to yield a cumulative cost of $3.5 trillion over the next decade.(30)

***Epidemiology of CVD***

Cardiovascular diseases include disorders of the coronary, cerebral, and peripheral circulation as well as heart failure, and are major causes of morbidity, mortality, and healthcare cost in the US.(31-32) CVD accounts for one third of deaths in the US, and coronary artery disease is the largest contributor, accounting for approximately one in six US deaths in 2009.(3) Coronary artery disease prevalence was estimated at 6.4% among adults in 2007-2010 based on National Health and Nutrition Examination Survey (NHANES) data,(3) and the lifetime risk of developing CAD after 40 years was estimated at 1 in 2 for men and 1 in 3 for women.(33) Stroke prevalence was estimated at 2.8% in 2007-2010 NHANES data, (3) and the lifetime risk for stroke among persons age 55 to 75 was approximately 1 in 5 among women and 1 in 6 among men.(34) Peripheral artery disease prevalence was estimated at 4.6% (age- and sex-standardized) in NHANES 1999-2004 data, and the risk was increased among the elderly, non-Hispanic blacks, and women.(35) The prevalence of heart failure was 2.2% among US adults in NHANES 2007-2010, and at age 40, the lifetime risk of heart failure is one in five.(3)

The total cost of CVD and stroke was estimated at $312.6 billion in 2009, including healthcare costs and lost productivity due to premature mortality.(3) Of the twenty most costly diagnoses in 2008, heart conditions ranked highest (with $95.6 billion in direct costs), followed by hypertension (ranked 7$^{th}$, $47.4 billion), stroke (ranked 16$^{th}$, $18.8 billion) and other circulatory conditions (19$^{th}$, $17.6 billion).(3)

Many individuals are at increased risk of cardiovascular events due to risk factors that could largely be modified by changes in behavior. For example, according to NHANES data from 2005-2010, 23% of US adults were current smokers, 54% had higher than optimal cholesterol levels (≥200 mg/dL), 57% had higher than optimal blood pressure (≥120/80 mmHg), and 32% did not engage in any leisure-time physical activity.(36) Modifiable factors account for a substantial proportion of CVD mortality; it was estimated that the population attributable fraction (the proportional reduction in mortality that would be expected if the risk factor were eliminated from the population) of CVD mortality was 41% for elevated blood pressure, 14% for smoking, 13% for poor diet, 12% for lack of physical activity, and 9% for high glucose levels.(36) Obesity has been associated with increased coronary artery disease,(37) cerebrovascular disease,(38) peripheral vascular disease,(39) and heart failure.(40-41)

***Obesity, Diabetes, and CVD in the VA***

The Veterans Health Administration (VA) is the largest integrated single-payer healthcare system in the US. Its network in 2013 included 151 hospitals and 825 community-based outpatient clinics (CBOCs).(42) The VA serves a population of 8.8 million veterans,(43) of whom approximately 6 million receive healthcare services each year.(44) In 2012, there were 83.6 million outpatient visits in the VA system, and 703,500 inpatient admissions.(45)

Eligibility for VA care is based on service-connected disability or poverty, and the veteran population served by the VA is generally disadvantaged and in poorer health

compared to patients receiving care in other settings. Compared to veterans who receive care outside of the VA, veterans who use VA services for their health care are more likely to be poor (23% with annual income under $15,000 vs. 6% of veterans receiving care outside of the VA), less-educated (16% with less than high school education vs. 7%), and minorities (15% black and 8% Hispanic vs. 7% and 5%, respectively).(46) In addition, veterans receiving care at the VA have poorer health than other veterans: they were more likely to have "fair or poor" health status (37% vs. 16%), to be disabled (19% vs. 7%), and to be smokers (34% vs. 22%).(46) VA patients also tend to have poorer health when compared against general civilian populations.(47) Veterans receiving care at the VA have substantially worse health-related quality of life compared to general populations receiving care in non-VA settings, including dimensions of physical functioning, role limitations due to physical or emotional problems, pain, general health perceptions, vitality, and social functioning.(48) VA patients also have a substantial burden of mental illness, including depression and PTSD. (48) (49)

Obesity presents a considerable burden for the VA system. Nearly three quarters of VA patients are overweight or obese,(50) and veterans receiving care at the VA have a higher prevalence of obesity than veterans receiving care elsewhere and non-veterans.(51) As a greater prevalence of obesity is observed among racial/ethnic minorities,(52) those with lower socioeconomic status,(52) persons with disabilities,(53-54) persons with mental illness,(55-57) and older adults,(58) the demographics and health characteristics of the VA population likely contribute to its high prevalence of obesity.

Nearly one in five VA patients had diabetes in 2000, and the burden of disease is steadily increasing with a yearly incidence of 2%.(59) The VA prevalence of 19.6% is higher than that of the general adult population, due in large part to the higher proportion of older persons in the VA. Prevalence rises from approximately 4% among veterans aged 18-44y to a peak of 27% among those 65-74 years.(59) As nearly half of VA patients are over age 64, the age distribution of the VA population is a strong contributor to the high prevalence of disease.(59) In addition, other characteristics of the VA population may contribute to the high prevalence of diabetes, including the proportion of minorities, persons in poverty, and persons with disabilities.(60) For example, the age-adjusted prevalence of diabetes in 2008 was 44% higher among blacks than among whites, 113% higher among the poorest compared to the richest, and 166% higher among those with a disability compared to those without.(60)

In part due to high prevalence of diabetes, veterans receiving care at the VA are also at high risk of cardiovascular disease. In the VA, 58% of patients have dyslipidemia or hypertension, and 30% have both conditions.(61) Demographic characteristics of the VA population may play a role in the prevalence of CVD risk factors: older age, African American race, lower educational attainment, lower income, and disability were all associated with increased prevalence of hypertension in NHANES 2005-2008.(62) In the VA's 1999 fiscal year, the prevalence of ischemic heart disease was estimated at 16.4%, cerebrovascular disease 2.1%, peripheral vascular disease 3.9%, and congestive heart failure 4.7%.(63)

Diabetes and cardiovascular disease substantially increase costs and resource use for the VA. Total costs for VA services among veterans with diabetes were estimated at

$1.67 billion in 1998, including $1.45 billion for inpatient care and $215 million for outpatient care.(64) In 2000, patients with diabetes accounted for 30% of all VA pharmacy prescriptions, although they represented only 18% of patients.(65) Pharmacy costs were 79% higher among veterans with diabetes.(65) In addition to the costs of diabetes, cardiovascular diseases also increase costs. For example, in fiscal year 1999, the annual marginal cost (above the average patient cost of $4,947 per year) was $4,942 per patient for ischemic heart disease, $3,406 per patient for cerebrovascular disease, $9,268 per patient for peripheral vascular disease, and $8,340 per patient for congestive heart failure.(63)

### *Pathophysiology of Obesity's Contributions to Diabetes and CVD*

Obesity is associated with increased risk of diabetes, and the two maladies have overlapping and far-reaching health effects, including substantially increased risk of stroke and cardiovascular disease.(66-67) Several key mechanisms have been proposed to explain the ways in which excess weight affects cardiovascular and metabolic health. Adipose tissue – particularly visceral fat in the abdominal region – functions as an endocrine organ, releasing inflammatory adipokines that increase risk for atherosclerosis and thrombosis (contributing to cardiovascular disease), and insulin resistance (contributing to diabetes).(15, 68) In addition, visceral fat produces free fatty acids that may impair endothelial and vascular function (contributing to cardiovascular disease) and may decrease insulin sensitivity (contributing to diabetes).(69) Oxidative stress has been proposed as one mechanism by which insulin resistance may lead to dysfunction in the beta cells and the endothelium, and eventually to diabetes and CVD.(70)

Increasing insulin resistance may reveal latent beta cell dysfunction, when beta cells become unable to compensate for insulin resistance by increasing insulin secretion. The combination of insulin resistance and inadequate beta cell function can contribute to a broad group of pathophysiologic characteristics that occur in diabetes, including: increased glucose release from the liver, decreased glucose uptake by muscles, decreased insulin secretion from the β-cells of the pancreas, increased lipolysis in fat cells, excess glucagon secretion from the α-cells of the pancreas, increased glucose reabsorption by the kidney, and neurotransmitter dysfunction related to insulin resistance in the brain.(71) In turn, diabetes impairs vascular function and increases risk of CVD via numerous mechanisms, such as: impaired platelet function, impaired vascular smooth muscle function, increased oxidative stress (due to a hyperglycemic environment), inactivation of endothelium-derived nitric oxide (an important molecule synthesized by endothelial cells that allows for vasodilation), increased free fatty acid levels (due to increased lipolysis in fat cells), and impaired endothelium-dependent vasodilation (due to insulin resistance).(72)

Finally, obesity and diabetes are both associated with dyslipidemia, which increases cardiovascular risk. This form of abnormal lipid metabolism is characterized by smaller, denser, and more numerous low-density lipoprotein (LDL) particles, increased very low-density lipoprotein (VLDL) particles, increased triglycerides, and reduced high-density lipoprotein (HDL) particles.(15) Atherosclerosis occurs as LDL particles enter the arterial wall via a damaged endothelium and accumulate with white blood cells to form plaques. (73) As atherosclerosis worsens, distinct forms of cardiovascular disease may occur. Coronary artery disease occurs when stable plaques build up in the heart’s

arteries. These can be painless or can cause chest pain (angina), and if they rupture, clots can block arteries and cause heart attacks.(74) Prolonged damage to the heart can lead to heart failure, in which the heart can no longer pump sufficient blood to meet the body's needs.(75) Cerebrovascular disease (stroke) occurs when blood supply is blocked or a plaque ruptures in an artery of the brain causing permanent brain damage.(76) If a blockage leads to only temporary stroke-like symptoms, it is called a transient ischemic attack, and these are associated with substantially increased risk of subsequent stroke. Peripheral vascular disease occurs when arteries are hardened or blocked in the legs or arms, leading to pain, poor circulation, and poor wound healing.(75)

### *Lifestyle Change Programs*

#### Impact on Weight Loss and Diabetes Incidence

Lifestyle change programs are recommended for weight management,(77) as well as for the prevention or delay of diabetes.(24) These recommendations are based on the results of several landmark trials that have demonstrated the effectiveness of such interventions. For example, participants in the multicenter, randomized US Diabetes Prevention Program (DPP) exhibited 7kg weight loss in the first year of the intervention (approximately 7% of body weight), and approximately 4kg weight loss at 3 years (~4%).(78) The DPP, which enrolled 3,234 subjects with impaired glucose tolerance, tested an intensive lifestyle intervention arm in which 1,079 participants engaged in 16 core educational sessions and were encouraged by individual "lifestyle coaches" to lose 7% of their body weight and achieve 150 minutes of weekly physical activity.(79) Among lifestyle change participants, diabetes incidence was reduced by 58% after 3

years,(78) with a sustained reduction of 34% over 10 years observed in the follow-up US Diabetes Prevention Program Outcomes Study (DPPOS).(80)

Similarly, the Da Qing IGT and Diabetes Study observed 51% reduction in diabetes incidence among diet-and-exercise participants during the intervention, and the follow-up study reported a 43% reduction over 20 years.(81) In this 6-year intervention from 1986-1992, 577 adults with IGT were randomized to control, diet, exercise, or diet plus exercise. (82) The intervention consisted of weekly counseling for 1 month, followed by monthly counseling for 3 months, and then counseling once every three months for the rest of the intervention. Dietary group participants were encouraged to undertake caloric restriction among overweight participants with a targeted loss of 0.5-1 kg/month, and both normal weight and overweight participants were encouraged to improve dietary composition (increase vegetable intake, decrease alcohol intake, and decrease simple sugar intake), while physical activity group participants were encouraged to undertake a moderate increase in daily exercise (such as 30 minutes of walking).

The lifestyle change program of the Finnish Diabetes Prevention Study reduced diabetes incidence by 58% over 3 years,(83) and 43% over 7 years of follow-up.(84) The study enrolled middle-aged, overweight subjects with IGT, who were randomized to usual care or an intensive lifestyle intervention consisting of (a) individualized dietary counseling from a nutritionist to promote weight loss, reduced fat intake, and increased fiber intake; (b) resistance exercise training; and (c) encouragement to increase physical activity. Intervention participants lost 4.5 kg of weight at 1 year, and maintained a loss of 3.5 kg by year 3, while control participants lost approximately 1kg and maintained the loss.

A meta-analysis of lifestyle change program trials conducted among high-risk individuals demonstrated an overall 50% reduction in diabetes incidence.(85) Given the strength of these findings, lifestyle change programs have been adapted and translated more broadly. Specifically, the DPP has been adapted for group-based delivery, and has been implemented in community settings.(86) A review of community-based DPP translations observed an average of approximately 4% weight loss over 12 months.(87)

With a cost of $12,878 per quality-adjusted life year (QALY), the lifestyle change program in the DPP was found to be cost-effective over 10 years.(88) After assessing the benefits and cost-effectiveness of lifestyle change programs, the American Heart Association recommended that lifestyle change programs should be covered by third-party payers.(24) Healthcare system-based implementation is being employed in Europe, with promising initial results from the Finnish National Program for the Prevention of Type 2 Diabetes (FIN-D2D).(89) However, evidence of the impact of healthcare-based lifestyle change programs in the US is lacking.

Impact on CVD Risk Factors and CVD Incidence

Much of the burden of cardiovascular disease can be reduced through management of clinical and lifestyle risk factors, including blood pressure, lipid levels, smoking status, weight, and physical activity.(90-91) Lifestyle change, such as improved diet and exercise behavior, is a recommended strategy for the prevention or delay of the development of cardiovascular disease.(92) However, evidence of the impact of lifestyle

change programs on cardiovascular disease risk factors is mixed, and few studies have had sufficient sample size to study cardiovascular disease incidence.(93-98)

Some studies indicate a benefit of lifestyle change programs for cardiovascular risk factors, particularly among high-risk groups. The DPP Outcomes Study demonstrated reductions in CVD risk factors, including improvements in systolic and diastolic blood pressure, LDL cholesterol, triglycerides, and HDL cholesterol among all groups, even though lipid and blood pressure medication use was lower among lifestyle change participants.(97) In addition, four-year results of the multicenter Look AHEAD study in diabetes patients revealed improvements in HbA1c levels, blood pressure, and HDL.(93) A small randomized trial among severely obese (Class II and III) participants reduced blood pressure, waist circumference, and insulin resistance.(99) A review demonstrated very modest but significant changes in blood pressure and cholesterol among general population participants.(100)

Evidence regarding impact on CVD is limited and mixed. The Look AHEAD trial of lifestyle change among diabetes patients did not reduce CVD incidence,(101) although it has been suggested that differential statin use, and weight loss in the controls (-3.5% by the end of the trial), may have confounded results.(101-102) A recent Cochrane review indicated that multifactorial lifestyle change programs have not affected CVD mortality among general populations, but did demonstrate benefit among trials restricted to high-risk participants with diabetes or hypertension (OR 0.71 for total mortality, 95% CI 0.61 to 0.83; OR for fatal and nonfatal CVD events 0.78, 95% CI 0.68 to 0.89).(100)

Impact on Diabetes Management

There is limited evidence supporting the potential for lifestyle change programs to positively impact diabetes management and to reduce diabetes complications.(95) Clinical guidelines recommend improving glucose control, blood pressure, and lipid levels in order to reduce diabetic nephropathy and diabetic retinopathy.(24) To the extent that lifestyle change programs can affect glucose control, blood pressure, and lipid levels, it is conceivable that they could reduce these common complications of diabetes. However, there have been few studies of the impact of lifestyle change programs on microvascular outcomes.(95) At this time, microvascular results are still forthcoming from the Look AHEAD trial: initial findings presented at the 2013 American Diabetes Association meeting indicated that lifestyle change participants had 31% lower incidence of advanced renal disease and 14% lower incidence of retinopathy (103-104). The China Da Qing Diabetes Prevention Outcomes study found that lifestyle intervention was associated with a lower incidence of severe retinopathy (HR 0.53, 0.29-0.99) but not nephropathy (HR 1.05, 0.16-7.05).(105) The multidimensional Steno-2 trial, which incorporated both lifestyle change and pharmacotherapy, reported a reduction in progression of retinopathy (OR 0.45, 0.21-0.95) and nephropathy (OR O.27, 0.10-0.75) among participants with diabetes.(106) Unfortunately, this intervention included pharmacotherapy, so the results may not be representative of lifestyle change programs incorporating only diet, exercise, and motivational components. On the other hand, weight loss may be an important component in preventing or delaying diabetes complications: a recent review has linked weight loss in chronic kidney disease patients

to improved renal function, including decreased proteinuria and higher glomerular filtration rate (GFR) (107).

Although there are few studies of lifestyle change programs that examined diabetes outcomes, more studies have investigated intermediate outcomes. For example, lifestyle change programs have been associated with modest indications of benefit in weight and glucose control among patients with diabetes.(108-109) One small-scale (147 subjects) healthcare-based randomized trial among obese persons with diabetes showed reduced weight (-3.0kg at 12 months) and HbA1c, although impact on HbA1c was modest and no longer statistically significant at 12 months (-0.2%, p=.45) (110). Lifestyle change programs have also demonstrated reduced medication usage among participants with diabetes (110-111).

Unfortunately, some evidence suggests that lifestyle change participants with diabetes may not lose weight as well as participants without diabetes, or may not sustain changes beyond the end of lifestyle interventions.(95, 112-113) Patients with diabetes may have greater difficulty adhering to dietary and exercise regimens,(114) and they face numerous barriers to lifestyle change.(115) In particular, weight loss or maintenance may be more difficult among persons with diabetes, due to the weight gain associated with use of some antidiabetes medications and insulin, the risk of hypoglycemia with weight loss (particularly if medications are not adjusted proactively), and the mental and emotional effects of previous failed weight loss attempts.(116-118) Further research is needed to determine the extent to which lifestyle change program participation can favorably impact diabetes management among patients with diabetes.

### *The VA's MOVE! Program*

In recognition of the substantial burden of obesity, diabetes, and cardiovascular disease among the VA population, the VA has implemented policies to improve chronic disease care such as the use of relevant performance measures. The quality of VA diabetes care now consistently compares favorably against other care systems including private healthcare,(119-121) academic institutions,(122) and Medicare.(123-124) However, the VA has also taken steps to enhance disease prevention efforts. In 2002, the National Center for Health Promotion and Disease Prevention began developing the MOVE!® program. The acronym, MOVE!, stands for Managing Overweight and/or Obesity in Veterans Everywhere, although use of the original name has since been dropped in favor of the abbreviation.

The program is based on the National Heart, Lung, and Blood Institute's *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults*.(125) MOVE! was developed for rapid adoption across VA facilities: it includes a toolkit of curriculum modules, patient handouts, promotional materials, staff training, and administrative manuals. MOVE! was piloted in 2003 and 2004, then revised based on patient and staff feedback, and began being fully rolled out in 2005.(126) It was mandated to be implemented across VA facilities in 2006,(127) and by 2009, nearly all (98.7%) VA facilities had implemented MOVE!.(126) Currently, MOVE! is the largest lifestyle change program in the US, with over 400,000 participants since 2005.(128)

Primary care patients in the VA are screened for obesity at least every two years.(126) MOVE! is offered to veterans who are obese (BMI $\geq$ 30), or who are overweight (BMI 25-29.9) with at least one weight-related health condition such as

diabetes, hypertension, dyslipidemia, osteoarthritis, or sleep apnea, if the physician deems weight loss to be appropriate. Patients with serious illness or limited life expectancy are excluded.(126) MOVE! is targeted to veterans under age 70, due to uncertainty about adverse effects of overweight among those beyond this age.(129-130)

The MOVE! program typically involves 8-12 group-based educational sessions on nutrition, physical activity, goal-setting, and maintenance.(126) The standard MOVE! curriculum includes an orientation session and 10 core modules emphasizing reading food labels and selecting healthy choices, reducing fat intake, balancing energy intake with energy output and evaluating portion sizes, walking with a pedometer and physical activity modifications for wheelchair users, setting physical activity goals and overcoming barriers, exercising safely, the importance of planning ahead, modifying one's environment for success, resolving difficulties, and staying motivated. The MOVE! curriculum uses an intake questionnaire (originally a 23-item questionnaire, called Move!23, but recently shortened and revised to the Move!11), which assesses medical history, weight-management history, barriers to lifestyle change, and readiness to change.(126) The questionnaire is used to offer tailored support and the MOVE! curriculum includes handouts that can be given in response to particular issues that participants identify as areas in which they struggle, such as eating in restaurants, exercising on a budget, and quitting smoking. As of the time of writing, there were 31 handouts pertaining to nutrition issues, 39 for physical activity, 36 for behavioral health and motivation, and 9 miscellaneous handouts (including topics such as handling weight loss plateaus, keeping a food diary, and the benefits of losing 10% body weight).

Unlike the US Diabetes Prevention Program, MOVE! sessions are generally offered on a rolling admissions basis, and sessions are structured as independent units (which can be taken in any order) rather than as a successively building curriculum. MOVE! also incorporates elements of motivational interviewing,(131) encouraging participants to set their own targets for physical activity, nutrition, and weight loss, rather than following program-prescribed goals. MOVE! staff assist patients in setting 1-3 short term behavior change goals, and also provide diet and physical activity logs for participants to use to monitor their behavior.(126) Implementation may vary across VA facilities in terms of procedures for enrollment, organization, delivery format (group-based, individual, or phone), and curriculum.(127, 132-133)

Impact of the Program

Relatively few studies have examined the effects of MOVE!, and most have been restricted to local settings. One of the largest studies evaluated the results of MOVE! in four Western states, and observed modest weight loss at six months and one year (-1.3 lb in participants compared to non-participants at six months, and -0.9 lb at one year).(134) However, half of the participants were found to have only attended a single session. Weight loss was greater among participants who engaged more actively with the program; those with at least 6 MOVE! encounters lost more weight (-3.7 lb).(134)

Despite only modest changes in weight, MOVE! participation has been associated with improvement in health-related quality of life.(135) In the absence of substantial weight loss, some of the benefit of MOVE! may derive from halting an upward trend of weight gain among participants. In a study of MOVE! participants in Miami, veterans

gained approximately 2 kg/year prior to MOVE! enrollment, but this slope of weight change was significantly different after initiation of MOVE! attendance.(136) Participants who only attended an initial MOVE! session (completing an intake questionnaire and receiving tailored handouts and a telephone follow-up) halted the trend of weight gain, and participants who engaged in more MOVE! group sessions achieved an average weight loss of 1.6 kg/year.(136) A study of MOVE! in Los Angeles (restricted to patients who participated in at least 3 MOVE! sessions) observed similar findings, in which patients gained approximately 1.4 kg/year prior to MOVE! enrollment, and lost an average of 2.2 kg after enrollment (with a significant difference in pre-enrollment vs. post-enrollment slope of weight change).(137)

***Summary***

In summary, obesity, diabetes, and CVD are considerable public health challenges. Lifestyle change programs have demonstrated the potential to reduce weight and diabetes incidence – particularly in high-risk patients with prediabetes – and may impact microvascular and macrovascular health outcomes. Implementing such programs in healthcare settings may offer a powerful strategy to scale up, given that 85% of population has health insurance.(138) However, little is known about implementation in healthcare settings. The VA's MOVE! program is the largest such program in the US, and offers a unique opportunity for examining a national, healthcare-based lifestyle change program. To our knowledge, no prior studies have been conducted to examine the association between MOVE! participation and cardiometabolic health outcomes, including diabetes incidence, CVD incidence, and management of existing diabetes.

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# Chapter 3: Methods

Methods and statistical analyses for Aims 1-3 are described in each of the following three chapters (Chapters 4-6). In this chapter, we offer additional details about VA data and special data considerations for our analyses.

### *National VA data*

These analyses used data from the VA's Corporate Data Warehouse (CDW), a national repository of information from multiple Veterans Health Administration clinical and administrative systems.(1) Data are available from October 1, 1999, and are hosted in SQL Server in a relational database. CDW "Production Data" are extracted from the data warehouse, have undergone indexing and some cleaning, and are updated daily. Available CDW Production data include patient and staff demographics, patient vital signs, outpatient encounters, inpatient admissions and records, pharmacy data, consult records, "health factors" (text data, including answers to clinical reminder questions such as, "Have you smoked in the last year?"), immunization records, laboratory results, diagnoses, and procedures.

CDW "Raw Data" are extracted directly from the Veterans Health Information Systems and Technology Architecture (VistA), which is the electronic medical record system used by the VA to support day-to-day patient care at VA facilities.(1) CDW Raw data are not filtered, edited, modeled, or standardized, and have not been restructured for enhanced performance. They reflect the structure of the source data, and are updated weekly or monthly (less frequently than "Production" data). CDW Raw data include fee

basis, bill claims, intravenous medications, allergies and adverse events, and radiology. The vast majority of data used in the present work was pulled from CDW Production Data, with the exception of "fee basis" data, which was extracted in order to access certain procedure codes (used in combination with ICD-9 codes and CPT codes to more fully capture health outcomes, such as cardiovascular disease and diabetes complications).

In CDW data, patients are assigned a unique "Patient Surrogate ID" (PatientSID) number. However, PatientSIDs are specific to each facility at which a patient receives care, so data must be joined across PatientSIDs to collect full history on patients who have used more than one VA facility. This was done using VA-created scrambled social security numbers.

One limitation of CDW data is that data are not cleaned for out-of-range values – any values entered in error in the source (VistA) are generally present in CDW data.(1) For this reason, data were carefully cleaned for implausible values, using cutoffs based on the literature when available. For example, weights under 75 pounds or over 700 pounds were excluded, as were heights under 48 inches or over 84 inches. (2) Similarly, we eliminated systolic blood pressure (SBP) less than 60 or greater than 250, HDL cholesterol less than 10 or greater than 120, non-HDL cholesterol less than 10 or greater than 1000, random plasma glucose (RPG) less than 30, and HbA1c values less than 2.5% or greater than 25%.(3-4) Where inconsistencies occurred in patient demographic data, we used the most frequent (e.g. race, gender) or most recent (e.g. zipcode) characteristics.

Another concern with the use of VA data is that some veterans receive care outside of the VA, making it possible that some diagnoses, procedures, and medications may not be reported within the VA health system. To address this, we restricted our analyses to patients with recorded primary care visits during at least 3 consecutive years during our study period (2005-2012). This requirement assured that each included patient had multiple opportunities for reporting diagnoses made outside the VA, and made it more likely that the study population was receiving a substantial amount of their care from the VA.

***VINCI environment***

All data were accessed through the VA Informatics and Computing Infrastructure (VINCI) data processing environment. This secure analytical workspace was created by VA to safeguard Protected Health Information (PHI) and to allow regulated data access for research. It includes large, high-speed data storage, access to high performance servers, regular data backup and archiving, and tools for data analysis and management. The VINCI Data Center is located in Austin, Texas, and most VINCI staff members are located in Salt Lake City, Utah. VINCI represents a partnership between the VHA Health Services Research and Development Service, VA Office of Informatics and Analytics, and the VA Office of Information and Technology's Business Intelligence Service Line.(5)

***Defining outcomes of interest***

To define health outcomes of interest, we used a combination of ICD-9 codes, procedure codes, CPT codes, and pharmacy data. Diabetes was identified by use of the 250.xx ICD-9 code or prescription of a diabetes drug. The use of similar indicators has been validated.(6-7) In sensitivity analyses, we employed a more stringent definition of diabetes (requiring two uses of the ICD-9 code or use of a diabetes drug), which yielded a slightly smaller number of diagnoses but equivalent results.

For cardiovascular diseases, we defined coronary artery disease as ICD-9 codes 410.0-414.9 and procedure codes 36.xx. Cerebrovascular disease was identified by ICD-9 codes 430-436 and procedure codes 38.01, 38.02, 38.11, 38.12, 38.31, 38.32, 38.41, 38.42, 38.61, 38.62, 39.22, 39.28, 39.72, and 39.74. Peripheral vascular disease was defined as ICD-9 codes 440.20-440.4, 443.9 and procedure codes 38.08, 38.18, 38.38, 38.48, 38.68, and 39.25. Heart failure was identified by the ICD-9 code 428.xx.

For diabetes complications, we defined diabetic eye disease as use of ICD-9 codes 250.5x or 362.0x (the latter includes background retinopathy, proliferative and nonproliferative retinopathy, and macular edema), as well as diabetes (250.xx) plus: retinal edema (362.83); vitreous hemorrhage (379.23); retinal detachment (361.xx); cranial nerve palsy (951.0, 951.1, 951.3); blindness (369.xx); and procedure codes (14.21–14.25) and CPT codes (67210, 67227–8, 67145) for laser surgery; procedure codes (14.7x) and CPT codes (67030–1, 67036, 67038–40) for vitrectomy; procedure codes (14.4x, 14.5x) and CPT codes (67110, 67105, 67107–8, 67110, 67112) for retinal detachment repair; and procedure codes (16.4) and CPT codes (65101, 65103, 65105,

65093) for enucleation. Sensitivity analyses included ICD-9 codes for glaucoma (365.xx) and cataract (366.xx), as well as procedure codes (12.6x) and CPT codes (65855, 66150–66180) for glaucoma trabeculectomy, and procedure codes (13.2x–13.5x) and CPT codes (66850–66984) for cataract extraction.

We defined diabetic renal disease as use of ICD-9 code 250.4x, as well as diabetes 250.xx plus proteinuria (791.0); kidney disease (580, 581, 582, 583); acute renal failure (584), end-stage renal disease (ESRD) or uremia (585, 586); hemodialysis (procedure code 39.95 or CPT codes 90935, 90937); peritoneal dialysis (procedure code 54.98 or CPT codes 90945, 90947); or transplantation (procedure code 55.6).

Assessment of laboratory data posed some unique challenges. At present, much of the laboratory data in the VA CDW has not yet been standardized across clinics, so similar tests (e.g., "plasma glucose") may be given a different name according to each laboratory. The VA is currently advancing standardization efforts through the use of Logical Observation Identifiers Names and Codes (LOINC). We obtained LOINC codes for variables of interest and assessed usage within the VA. We were able to use LOINC codes to identify high density lipoprotein (HDL) cholesterol and total cholesterol, from which we calculated non-HDL cholesterol. For glucose measurements, we manually searched for relevant variable names and combined relevant data. Random plasma glucose (RPG) was defined as any outpatient blood or plasma glucose measure, excluding capillary or arterial values and excluding glucose challenge test measurements.

***Construction of complex covariates***

Smoking Status

We determined that smoking status was an important covariate to include in our analyses, given that smoking has been linked to greater risk of diabetes and cardiovascular disease.(8) However, the ICD-9 code for smoking is subject to underreporting,(9) and there is no other direct indicator of smoking status within VA CDW data. Fortunately, Dr. Kathleen McGinnis and her colleagues in the Veterans Aging Cohort Study Team validated an approach to assess smoking status using text-based "Health Factor" data available within the VA CDW. (10) Health Factor data are created when responses are recorded from various clinical reminders, established by individual VA facilities and regions. For example, in some clinics, a clinical reminder might prompt a physician to ask the question, "Do you currently use tobacco?", and based on the patient's response, a Health Factor phrase might be recorded in the patient's medical record as "CURRENT TOBACCO USER". McGinnis and colleagues collected Health Factor data pertaining to smoking, and used face validity to map individual phrases to one of three indications of smoking status: "Current Smoker", "Former Smoker", or "Never Smoker / Lifetime Non-Smoker," or the Health Factor phrase was mapped as "Unknown." Patients were classified into the 3 smoking categories based on frequency of responses in their medical records (e.g., if a patient had 3 Health Factors that mapped to "Current Smoker" and one that mapped to "Never Smoker / Lifetime Non-Smoker", the patient was classified as "Current Smoker"). This approach was then validated using existing survey data that included self-assessment of smoking status among subgroups of veterans. Agreement between the Health Factor assessment of

smoking and the two survey sources was found to be substantial, with sensitivity for identifying current smokers ranging from 88% to 95%, and specificity ranging from 79% to 84%.(10)

Mapping for 963 smoking codes identified by McGinnis et al. is publicly available. (10) However, new Health Factors pertaining to smoking have been created in subsequent years. Upon selecting relevant Health Factors, we identified an additional 528 phrases, yielding a total of 1,491. For the purposes of this dissertation, the mapping strategy of McGinnis et al. was updated and extrapolated to include these new smoking-related Health Factors. For example, the original mapping strategy translated the Health Factor "V16 TOBACCO CESSATION PROGRAM DECLINED" as the smoking status "Current Smoker" (inferring that the patient was a current smoker who was offered tobacco cessation counseling referral, and declined it), so we interpreted the new Health Factor code "REFUSED SMOKING CESSATION REFFERAL" in the same manner, as "Current Smoker". In some cases, we noted discrepancies in the original mapping strategy. For example, "V7-DECLINED MEDS FOR TOBACCO CESSATION" was mapped as "Current Smoker", while "DECLINES TOBACCO CESSATION MEDICATION" was mapped as "Unknown". Personal communication with the study's corresponding author indicated that these could indicate an oversight in category assignment, as multiple researchers and clinicians worked on the mapping strategy and there were multiple entries per person.(11) In these cases, we adapted the mapping strategy to be as consistent as possible.

Distance to MOVE!

In addition to constructing an indicator for smoking status, we also chose to construct an indicator for distance to each patient's nearest MOVE! facility, as was done in a prior study of MOVE!.(3) We requested and were granted permission to access patient zipcode data, and calculated the distance between the midpoint of each patient's zipcode and the nearest facility offering MOVE!. To do this, we obtained the geographic coordinates of each zipcode's centroid (using the sashelp.zipcode file), as well as the coordinates of the facilities offering MOVE! (using available VA Geographic Information System [GIS] data), and used the SAS macro %geodist to calculate minimum distances.(12)

***MOVE! participation***

In Chapter 4, we defined MOVE! participation as a 3-level categorical variable based on previous work,(13) examining "intense and sustained" participants (who attended at least 8 sessions within 6 months ["intense"] with a span of at least 129 days between the first and the last session ["sustained"], "less active" participants (those who engaged in at least one session of the program but did not meet criteria for "intense and sustained" participation), and "eligible non-participants" (who met eligibility criteria for MOVE! but did not participate during our study window, 2005-2012). Intense and sustained participation has been associated with substantially greater weight loss compared to lesser amounts of participation,(13) and has been identified by the VA as a targeted level of participation.

However, one critique of MOVE! is that relatively few participants (<10%) achieve this intense and sustained level of participation. For this reason, in Chapters 5 and 6, we focused our primary analyses on the most inclusive definition of participation (attending at least one session of MOVE), and examined "intense and sustained" participation as a sensitivity analysis.

***Statistical analyses***

Baseline was assigned for non-participants as the date of the first visit with a recorded weight after January 1, 2005 (the first year of MOVE! rollout), and for participants as the date of first MOVE! visit. This strategy allowed for control of baseline factors among participants at the time of MOVE! participation (for example, exact age and weight at the beginning of participation). Sensitivity analyses were conducted to adjust for a categorical measure of baseline year, to allow for any influence of changes in clinical procedures such as screening.

Given the observational nature of this investigation, MOVE! participants were self-selecting, and observed results may be confounded by characteristics that might affect a patient's decision to enroll in MOVE! (for example, baseline BMI, a recent diagnosis such as hypertension, or more abstract characteristics such as how strongly the patient prioritizes his or her health). Although it is impossible to rule out confounding by unmeasured factors, we employed three main strategies to address confounding by measured variables: (**i**) an extensive set of ***clinical inclusion/exclusion criteria***, and sensitivity analyses to evaluate the effects of these criteria; (**ii**) an ***extensive set of control variables***, including baseline comorbidities, demographic and clinical characteristics, and

factors such as glucose levels, smoking status, whether a patient is taking medications with weight gain risk, and how frequently a patient interacts with the VA health system, and (**iii**) a ***propensity score*** to adjust for likelihood of participation in MOVE! (used in chapters 5 and 6).

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# Chapter 4: Weight Loss and Diabetes Incidence with the VA Lifestyle Change Program

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***Abstract***

**Importance**: Lifestyle modification programs are aimed to improve health, yet little is known about their impact in clinical settings, where participants are *patients* to whom participation is *recommended*, rather than volunteer research subjects.

**Objective:** To compare patterns of weight change among MOVE! participants and eligible non-participants, and to determine whether participation is associated with reduced diabetes incidence.

**Design**: We used Veterans Health Administration (VA) databases to examine patients with at least three years of continuous outpatient care during 2005-2012. Generalized estimating equations were used to examine characteristics associated with MOVE! participation, and Cox proportional hazards regression was used to analyze the association between participation and diabetes incidence.

**Setting:** The VA's MOVE! program is the largest lifestyle change program in the US

**Participants:** Eligible individuals were obese or overweight with a weight-related health condition. Of 1.8 million eligible individuals, 238,540 participated in MOVE! between 2005-2012.

**Exposure:** We examined two levels of MOVE! participation: "intense and sustained" participation ($\geq$8 sessions within 6 months, and $\geq$129 days between first and last sessions) and "less active" participation (participation in at least 1 MOVE! session, but insufficient participation to be designated "intense and sustained"), and compared against non-participation.

**Main Outcomes and Measures:** Main outcome measures were % change in body weight and diabetes incidence, as defined by use of diabetes ICD-9 code or a diabetes drug.

**Results:** Intense and sustained participation was associated with greater weight loss at 3 years compared to less active participation and nonparticipation (-2.2% vs. -0.64% and +0.46%, respectively, both $p<0.01$). Among patients who did not have diabetes at baseline, MOVE! participation was associated with lower diabetes incidence: the hazard ratio comparing less active participants to non-participants was 0.80 (95% CI, 0.77-0.83), and comparing intense and sustained participants to non-participants was 0.67 (95% CI, 0.61-0.74). These patterns were consistent across sex, race/ethnicity, and age. Participation appeared to be most beneficial among patients with higher BMI or random plasma glucose (p-values <0.001).

**Conclusions and Relevance:** This study of the VA's MOVE! program provides evidence that participation in a large-scale, healthcare-based lifestyle change program is associated with weight loss and lower diabetes incidence.

***Introduction***

Obesity and diabetes are public health problems of epidemic proportions, for which lifestyle change is primary management.(1-3) Randomized trials have shown that lifestyle change programs can facilitate weight loss and reduce diabetes incidence. For example, participants with prediabetes who were randomized to the lifestyle change arm in the United States Diabetes Prevention Program (DPP) exhibited 7% weight loss, and their progression to diabetes was reduced by 58% at 3 years. Over 10 years, this group had a sustained reduction in diabetes incidence of 34%.(4-5) Similar results were obtained in other large studies,(6-7) and in small-scale, community-based adaptations of the DPP, which yielded about 4% weight loss.(8) Implementation of lifestyle interventions within healthcare systems has been recommended as a strategy to scale up the reach of such programs, given that 85% of the US population has health insurance.(9-11) This strategy is being employed in Europe, with promising initial results from the Finnish National Program for the Prevention of Type 2 Diabetes (FIN-D2D).(12) However, evidence of the impact of healthcare-based lifestyle change programs in the United States is lacking.

The Veterans Health Administration (VA) is the largest integrated healthcare system in the US, serving over 8 million patients each year.(13) In the VA, two-thirds of veterans are overweight or obese,(14) and nearly one in five had diabetes in 2000.(15) Addressing these health issues is a priority, and the VA developed the Managing Overweight and/or Obesity in Veterans Everywhere (MOVE!®) program.(16) Since 2005, over 400,000 veterans have participated in MOVE, making it the largest lifestyle change program nationwide. A preliminary study evaluating the results of MOVE! found that

weight loss was modest but sustained over one year.(17) Our objective was to compare patterns of weight change among participants and eligible non-participants, and to determine whether participation in MOVE! is associated with reduced diabetes incidence.

## *Methods*

The MOVE! program**,** similar to group-based translations of the DPP, involves educational sessions pertaining to nutrition, physical activity, and goal-setting.(18) The standard MOVE! curriculum includes an orientation session and 10 core modules emphasizing reading food labels and selecting healthy choices, reducing fat intake, balancing energy intake with energy output and evaluating portion sizes, walking with a pedometer and physical activity modifications for wheelchair users, setting physical activity goals and overcoming barriers, exercising safely, the importance of planning ahead, modifying one's environment for success, resolving difficulties, and staying motivated. However, there is considerable variability in implementation across VA facilities in terms of organization and delivery format (most sessions are in-person and group-based, but some are offered individually or by phone).(19) MOVE! sessions take place on a rolling admissions basis. In administrative databases, MOVE! encounters are recorded for each patient. Level of participation was determined by counting the number of MOVE! visits that occurred on unique days.

### Databases

This secondary data analysis was approved by the Emory University Institutional Review Board and the Atlanta VA Medical Center's Research and Development

Committee. We utilized data from the VA's Corporate Data Warehouse (CDW), a national repository of information from clinical and administrative systems. Data are available from 1999, and include patient demographics, vital signs, diagnoses, procedures, and prescriptions. All data were accessed through the VA Informatics and Computing Infrastructure (VINCI) data processing environment.

**Study Population**

From nearly 10 million veterans receiving care between 2005-2012 (Figure 4.1), we selected 4.5 million veterans with at least one outpatient visit per year for at least 3 consecutive years, between 2005-2012, who were eligible to participate in MOVE: patients who were either obese (body mass index [BMI] $\geq$30 kg/m$^2$), or overweight (BMI $\geq$25) with a weight-related health condition (diabetes, coronary artery disease, hypertension, dyslipidemia, sleep apnea, or osteoarthritis). From these, we excluded patients over age 70 because MOVE! is not targeted at individuals above this age, due to uncertainty about adverse effects of overweight.(20-21) To allow comparisons with a previous study of MOVE,(17) we also excluded veterans who would be unlikely to be able to participate in a weight loss program due to contraindications, or who would be likely to experience weight change for reasons unrelated to MOVE. Consistent with prior study, such patients included those with recent sepsis, pregnancy, cancer other than skin cancer, neurodegenerative disease, human immunodeficiency virus (HIV), and anorexia, or those receiving hospice or nursing home care. Lastly, we excluded veterans missing data for key demographic and clinical indicators, leaving 1,844,797 patients eligible for analysis.

**Measurements**

*Demographic characteristics:* Information in the VA CDW includes age, sex, race/ethnicity, marital status, and VA facility. Race/ethnicity was defined as White, African American, and Other, the latter combining Hispanics, Asian/Pacific Islanders, and American Indians/Alaska Natives (each <2% of the population). A simple measure of socioeconomic status (SES) and disability status (based on whether the veteran qualifies for care based on disability or low SES) has been used previously (22-23) and was employed in these analyses.

*Weight-related illnesses and comorbidities:* Illnesses were assessed using ICD-9 codes and procedure codes. The Charlson Comorbidity Index (CCI) was employed using the enhanced ICD-9 coding algorithm developed by Quan et al.(24)

*Diabetes incidence:* Baseline was assigned as a veteran's first MOVE! visit for participants and as the first visit at which weight was recorded after January 1, 2005 (the initial year of MOVE! roll-out) for non-participants. All regressions were adjusted for baseline year as a categorical variable, to allow for potential differences in management across years. Among patients who did not have diabetes at baseline, diabetes incidence was defined as a new use of the 250.xx ICD-9 code or prescription of a diabetes drug. The use of similar indicators has been validated;(15, 25) in sensitivity analyses, a more stringent definition of diabetes (requiring two uses of the ICD-9 code or use of a diabetes drug) yielded a slightly smaller sample but equivalent results.

*Random Plasma Glucose (RPG):* Laboratory glucose values were available for a subset of patients (N=814,387), and were used to conduct subgroup analyses examining

the association between MOVE! participation and diabetes incidence across levels of baseline RPG. We used the most recent outpatient glucose value measured within six months prior to a patient's baseline visit.

*BMI:* BMI was assessed using clinically recorded weight and height, after excluding implausible values (approximately 0.1%).(26) Height was taken as the average height recorded for the patient, if multiple measures were available. Weight was recorded as the patient's baseline weight, and follow-up weights as average weight within subsequent time windows (6 mo: 3-9 mo; 12 mo: 9-15 mo; 24 mo: 21-27 mo; 36 mo: 33-39 mo).

*Distance to MOVE*: Distance to the nearest VA facility offering MOVE! was calculated for each patient, based on geographic distance between the geographic midpoint of the patient's zipcode and the coordinates of the nearest VA facility offering MOVE.

*Smoking:* Text-based information was used to classify patients as "Current Smoker", "Former Smoker", or "Never / Lifetime Non-Smoker," as previously described and validated by McGinniss et al.(27)

**Statistical Analysis**

Level of participation was defined as a categorical variable based on previous work.(28) "Intense and sustained" participation, defined as attending ≥8 sessions within 6 months ("intense") with a span of ≥129 days between the first and the last session ("sustained"), has been associated with substantially greater weight loss compared to lesser amounts of participation.(28) We defined "less active" participants as those who

engaged in at least one session of the program but did not meet criteria for "intense and sustained" participation.

Descriptive characteristics were calculated across levels of MOVE! participation) and bivariate associations were analyzed using ANOVA (continuous variables) and Cochran-Armitage tests for trend (binomial variables). To examine patterns of weight change over three years, individuals with available weight data across four time points (6, 12, 24, and 36 months) were compared across levels of participation (N= 562,023).

In regression analysis, we conducted stepwise model selection and assessed model fit based on the *Akaike information criterion* (AIC) and the quasi-likelihood adaptation, QIC.(29-30) We used generalized estimating equations (GEE) to account for clustering within clinics in models examining characteristics associated with enrollment (any participation vs. none) and extent of participation (intense and sustained vs. less active). Cox proportional-hazards models were constructed to estimate hazard ratios for diabetes incidence among participants who had not been diagnosed with diabetes at baseline. Robust sandwich covariance matrix estimates were used to adjust for clustering at the clinic level.(31) Post-hoc analyses were performed to examine the association between participation and diabetes incidence among subgroups likely to have different diabetes risk (age, sex, race/ethnicity, BMI, and RPG).

Sensitivity analyses included an examination of the impact of our health status exclusion criteria, in which we conducted analyses with both more strict criteria [excluding patients with additional conditions such as heart failure (17)] and more inclusive criteria, such as including veterans older than 70 years. All analyses were conducted using SAS® version 9.2 (Cary, NC).(32)

## *Results*

### Characteristics of MOVE! participants

Of 1.8 million patients eligible for MOVE, nearly 13% participated in at least one session. On average, participants were older, heavier, and sicker than non-participants (Table 4.1). Baseline prevalence of diabetes was nearly twice as high among participants as among non-participants. Participants included greater proportions of women and blacks than non-participants, and fewer current smokers. In GEE models, characteristics associated with likelihood of participation included being female or African American, or having mental health conditions, greater BMI, greater CCI, or more years of care in the VA (Table 4.2). Those with a high percentage of service connection (an indicator of disability) were less likely to participate than those without a service connected disability.

### Intense and sustained compared with less active participation

Among MOVE! participants, only 8% participated actively enough to meet criteria for "intense and sustained" participation. Nearly one third of intense and sustained participants had BMIs in the range of Class III Obesity (BMI $\geq$40), compared to 22% of less active participants and only 6% of non-participants (Table 4.1). Multivariable regression comparing characteristics of intense and sustained participants vs. less active participants revealed that women were more likely to meet criteria for intense and sustained participation than men (Table 4.2). Those with a prescription for a weight loss medication were also more likely to engage in intense and sustained participation.

**Patterns of Weight Change**

Among veterans with available weight data across all four time points (6, 12, 24, and 36 months), any participation in MOVE! was associated with modest but sustained weight loss (Figure 4.2). Intense and sustained participants lost approximately 2.7% of their body weight in the first six months, and maintained a loss of 2.2% over three years.

**Diabetes Incidence**

Among eligible patients without diabetes at baseline, participation in MOVE! was associated with lower diabetes incidence in Cox proportional hazards models (Table 4.3). In the multivariable model, the adjusted hazard ratio for diabetes incidence among intense and sustained participants in MOVE, as compared to those who did not participate, was 0.67 (95% CI, 0.61-0.74). For less active participants compared to non-participants, the hazard ratio was 0.80 (95% CI, 0.77-0.83). Greater age and BMI were also associated with increased risk of diabetes incidence, as were minority race/ethnicity and service-connected disabilities. Results remained robust in sensitivity analyses using more strict, and more sensitive, inclusion criteria.

**Subgroup Analyses**

The results of stratified analyses by selected socio-demographic characteristics revealed no significant heterogeneity in the association between intense and sustained participation in MOVE! and diabetes incidence by gender, race/ethnicity, and age categories (Figure 4.3). However, there were statistically significant differences in the association between participation and diabetes incidence across baseline BMI categories

and glucose levels, suggesting greater benefit of participation among those at higher risk for diabetes (with higher BMI or RPG, both $p<0.001$ for interaction).

### *Discussion*

We examined patterns of weight loss and diabetes incidence associated with participation in a national healthcare system-based lifestyle change program. There was a significant, dose-dependent inverse association between diabetes incidence and participation in the VA's MOVE! program. Compared with lack of participation, intense and sustained participation was associated with 33% lower diabetes incidence, and less active participation was associated with 20% lower incidence. Subgroup analyses suggested that while results were consistent across gender, race/ethnicity, and age categories, participation may be particularly beneficial for patients at higher risk of diabetes – those with higher BMI, and those with higher RPG.

Our findings are consistent with other studies that have demonstrated that participating in lifestyle change programs is associated with weight loss.(5, 8, 33) The observed weight loss associated with MOVE! participation was much lower than the ~4% observed in translations of the DPP,(8) which may be due to fewer sessions attended. Among DPP translation studies with $\geq$9 months follow-up, each core session attended was associated with an additional weight change of -0.22 percentage points.(8) The mean number of sessions attended among intense and sustained MOVE! participants was 12.9, which would correspond to an expected weight change of -2.8%, while less active participants attended 2.5 sessions, which would correspond to an expected loss of -0.6%. The observed weight changes among participants with 12-month data were -2.8% and -

0.7%, respectively. Given the consistency of these findings with expected results, MOVE! may be as effective as other lifestyle change programs on a per-session-attended basis.

The observed association between MOVE! participation and diabetes incidence was also consistent with – but more modest than – the impact achieved in clinical trials emphasizing lifestyle modification, such as the DPP,(5) the Da Qing IGT and Diabetes Study,(6) and the Finnish Diabetes Prevention Study.(7) This may be due in part to the lesser amount of weight loss associated with MOVE! participation, as weight change is a strong predictor of diabetes incidence.(34) In addition, if MOVE! participants attended fewer sessions than participants in other studies, then they may have been less likely to change diet and physical activity behaviors, which can impact insulin sensitivity and glycemic control independent of weight loss.(35-37) Lastly, the above trials were targeted to individuals with prediabetes, whereas enrollment in MOVE! is based on weight status, and thus MOVE! may include lower-risk individuals. In subgroup analyses, we observed the strongest effects of participation among patients with elevated RPG, and it is conceivable that restricting MOVE! enrollment to individuals with high-risk prediabetes would increase the strength of the association between MOVE! participation and reduction in diabetes incidence.

As compared to clinical and community-based lifestyle change trials, this study is important because participants were not *subjects who volunteered for a research trial*, but *patients recommended by their primary care providers to engage in lifestyle change*. Only a modest percentage of patients eligible for MOVE! participated. Although patients usually adhere to provider recommendations in some areas, such as cancer screening and

taking medications, patient compliance with lifestyle change recommendations for the prevention and management of chronic diseases is notoriously low.(38) This may be due, in part, to the relative difficulty of behavior change required for weight loss. Compliance may also be affected by the nature of the interaction between physicians and obese patients; it has been suggested that physicians build less emotional rapport with obese patients, which may impact adherence to recommendations.(39)

The strengths of this analysis include a large study population and the use of national data to examine a real-world, large-scale lifestyle change program within a healthcare setting. However, the study has limitations. Due to the observational nature of the analyses, confounding is a concern. Although it is impossible to rule out confounding by unmeasured factors, the available data allowed adjustment for recognized confounding factors and health conditions that may impact lifestyle program participation and outcomes related to weight loss and diabetes incidence, such as smoking status, mental health conditions, physical limitations, underlying health conditions such as hypothyroidism, and use of prescription medications for weight loss, or medications with a reported risk of weight gain. To reduce the possibility of measurement error, such as in the use of clinically measured weights and heights,(26) we excluded implausible values and utilized averages when multiple values were available within appropriate time windows. Oral glucose tolerance tests (OGTTs) could not be used to define diabetes incidence precisely; it is likely that more incident diabetes would have been detected with OGTT-based criteria, as compared to the use of ICD-9 codes. While many veterans receive some care outside of the VA, making it possible that some diagnoses may not be reported within the VA health system, our requirement for 3 years of consistent

outpatient care at the VA assured multiple opportunities for reporting diagnoses made outside the VA, and made it more likely that the study population was receiving the majority of their care from the VA. We also conducted sensitivity analyses restricted to veterans receiving three consecutive years of *primary* care (a more stringent requirement than any outpatient care), and results remained robust.

In conclusion, we found that participation in the VA's MOVE! lifestyle change program was associated with modest but sustained weight loss and reduced diabetes incidence. These results are consistent with numerous clinical trials that demonstrated the potential of lifestyle change programs to reduce diabetes incidence. Since many Americans participate in healthcare systems, and there is increased emphasis on prevention in the Affordable Care Act,(40) implementation of MOVE-type lifestyle change programs through such systems might be beneficial to improving the health of people nationwide.

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**Figure 4.1 Study Population**

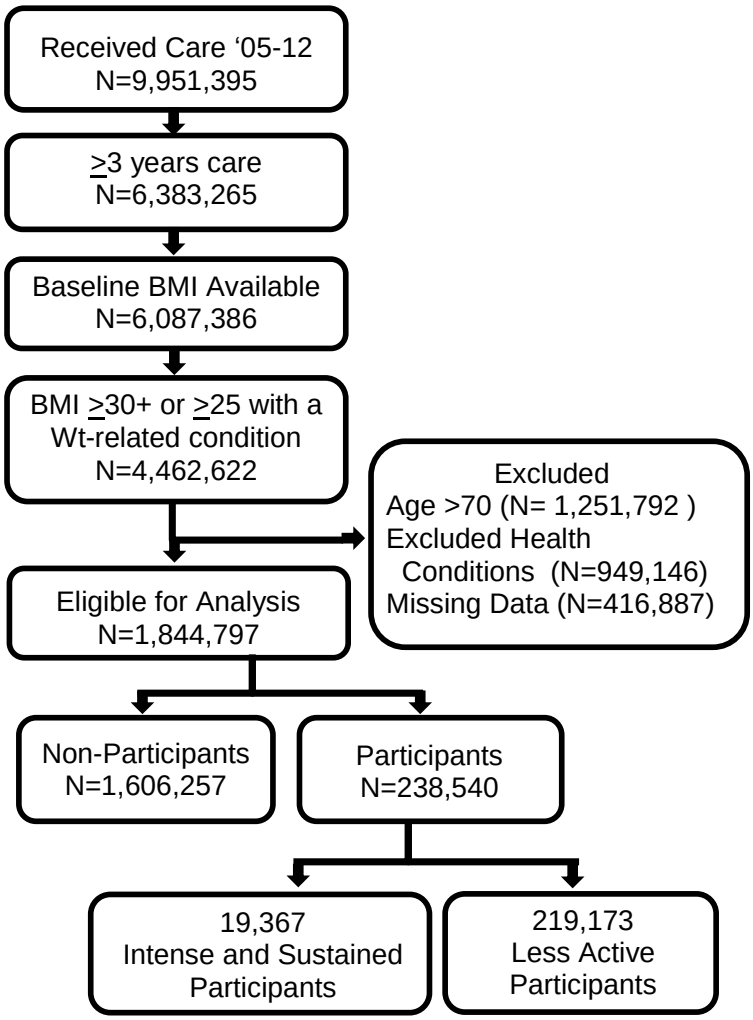
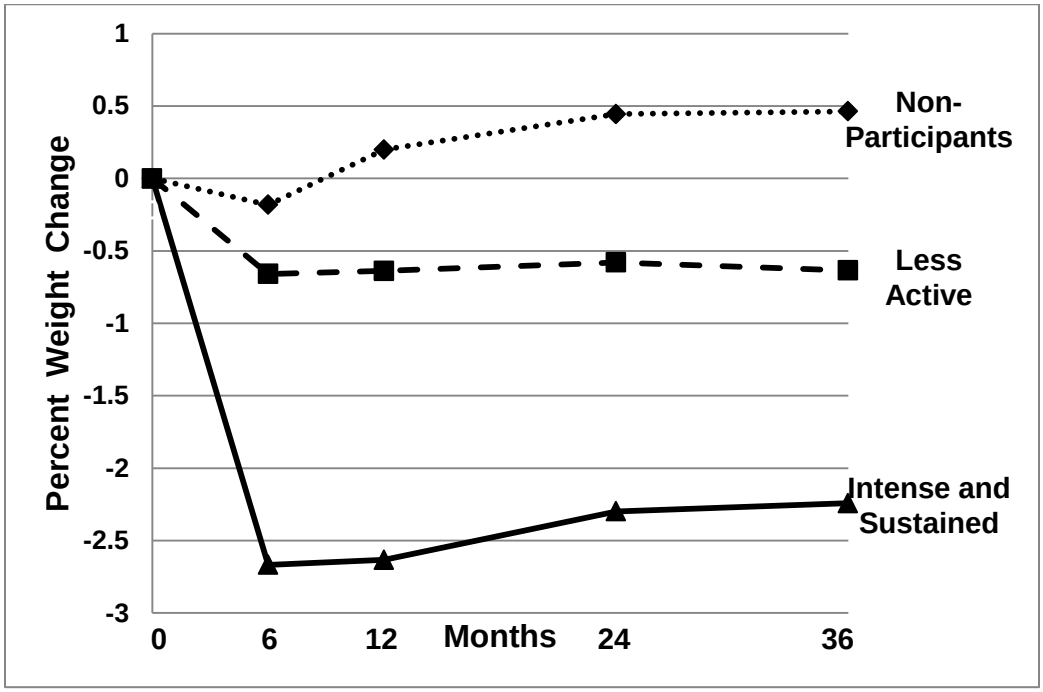
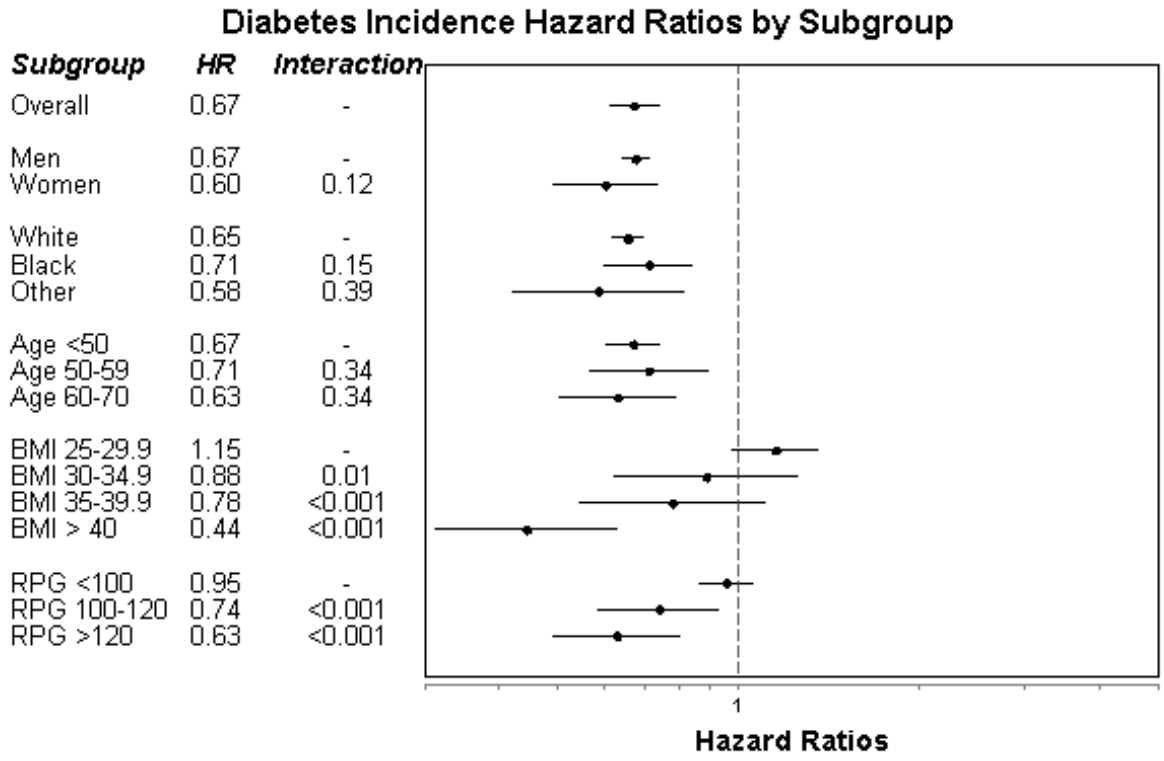


**Figure 4.2 Weight Change (%) Over Three Years among Participants and Eligible Non-participants**




N= 562,023. Calculations of percent weight loss were performed among veterans with data available across all four time points (6 months, 12 months, 24 months, and 36 months).

**Figure 4.3 Hazard Ratios for Diabetes Incidence among Intense and Sustained Participants Compared to Non-participants, by Subgroup**




N=1,400,935. Examination of RPG was performed among a subgroup of patients with available laboratory data, N=814,387. Cox proportional hazards models included covariates as described in Table 4.3. Wald p-values for interaction terms are shown.

**Table 4.1. Characteristics of Participants and Eligible Non-participants, 2005-2012***

| | Non-participants | MOVE! Participants | | |
|---|---|---|---|---|
| | | All | Less Active | Intense & Sustained |
| N | 1,606,257 | 238,540 | 219,173 | 19,367 |
| Age at baseline | 53.5±11.4 | 54.4±10.7 | 54.2±10.8 | 56.9±9.0 |
| Sex | | | | |
| Male | 94.1% | 87.3% | 87.3% | 86.5% |
| Female | 5.9% | 12.7% | 12.7% | 13.5% |
| Race | | | | |
| White | 78.7% | 72.1% | 71.8% | 75.8% |
| African American | 17.2% | 23.8% | 24.1% | 20.7% |
| Other | 4.1% | 4.1% | 4.2% | 3.4% |
| BMI at baseline, mean | 31.5±5.3 | 36.0±6.4 | 35.9±6.3 | 37.6±7.0 |
| 25-29.9 | 44.3% | 14.7% | 15.1% | 10.1% |
| 30-34.9 | 36.6% | 36.1% | 36.5% | 31.6% |
| 35.0-39.9 | 13.4% | 26.9% | 26.8% | 27.8% |
| ≥40 | 5.8% | 22.4% | 21.7% | 30.4% |
| Charlson Comorbidity Index | | | | |
| 0 Point | 85.5% | 65.2% | 65.5% | 61.7% |
| 1 Point | 10.8% | 23.4% | 23.3% | 24.7% |
| 2+ Points | 3.7% | 11.4% | 11.2% | 13.6% |
| Weight-related conditions | | | | |
| Diabetes | 21.1% | 37.8% | 37.3% | 43.3% |
| Coronary Artery Disease | 10.2% | 14.1% | 14.0% | 15.9% |
| Hypertension | 52.8% | 70.8% | 70.4% | 75.5% |

| | | | | |
|---|---|---|---|---|
| Osteoarthritis | 20.2% | 36.7% | 36.4% | 40.1% |
| Dyslipidemia | 44.9% | 66.0% | 65.6% | 70.6% |
| Sleep Apnea | 0.4% | 8.0% | 7.8% | 10.4% |
| Mental health conditions | | | | |
| Depression | 19.0% | 42.2% | 42.1% | 43.2% |
| Psychoses | 16.6% | 37.7% | 37.6% | 39.0% |
| PTSD | 9.2% | 22.1% | 22.0% | 23.0% |
| Drug abuse | 4.9% | 10.8% | 10.9% | 9.7% |
| Alcohol abuse | 7.7% | 14.0% | 14.1% | 12.5% |
| Smoking Status | | | | |
| Current Smoker | 36.6% | 29.6% | 30.2% | 22.2% |
| Former Smoker | 30.5% | 33.1% | 32.5% | 39.6% |
| Lifetime Non-smoker | 33.0% | 37.3% | 37.3% | 38.2% |
| Rx for weight loss medication | 5.0% | 10.4% | 9.8% | 16.7% |
| Rx with weight gain risk | 69.9% | 82.6% | 82.4% | 84.5% |
| Married | 58.5% | 53.5% | 53.4% | 54.5% |
| Not Service Connected | 52.9% | 43.8% | 43.9% | 42.9% |
| No. primary care visits/year | 3.4±2.2 | 4.2±2.6 | 4.2±2.6 | 4.8±3.1 |
| No. years with a visit | 8.7±3.5 | 9.2±3.4 | 9.2±3.4 | 9.5±3.4 |
| Distance to MOVE! >30 mi | 60.0% | 53.7% | 53.7% | 53.1% |

*± values are means ±SD. All associations between patient characteristics and level of MOVE! participation were significant ($p < 0.001$), according to chi-squared tests and Cochran-Armitage tests for trend (categorical variables) and ANOVA (continuous variables).

**Table 4.2. Characteristics Associated with Any Participation (All Participants vs. Eligible Non-participants) and Intense and Sustained Participation (Intense and Sustained Participants vs. Less Active Participants).**

| | **All Participants vs. Eligible Non-Participants** | | **Intense and Sustained Participants vs. Less Active Participants** | |
|---|---|---|---|---|
| | N=1,844,797 | | N=238,540 | |
| | OR | 95% CI | OR | 95% CI |
| Age at baseline | 0.99 | (0.99-0.99) | 1.03 | (1.03-1.04) |
| Female | 2.02 | (1.90-2.14) | 1.40 | (1.30-1.50) |
| Race (ref=White) | | | | |
| African American | 1.35 | (1.20-1.51) | 0.93 | (0.81-1.07) |
| Other | 1.05 | (0.92-1.19) | 0.84 | (0.73-0.97) |
| BMI at baseline, mean | 1.13 | (1.12-1.14) | 1.04 | (1.03-1.04) |
| Charlson Comorbidity Index (ref=none) | | | | |
| 1 Point | 2.78 | (2.62-2.94) | 1.04 | (0.98-1.10) |
| 2 or More Points | 6.27 | (5.67-6.94) | 1.05 | (0.97-1.14) |
| Weight-related conditions | | | | |
| Diabetes | 0.41 | (0.38-0.43) | 0.85 | (0.80-0.91) |
| Coronary Artery Disease | 0.88 | (0.85-0.92) | 0.92 | (0.86-0.99) |
| Hypertension | 1.30 | (1.27-1.34) | 0.92 | (0.88-0.96) |
| Osteoarthritis | 1.47 | (1.42-1.52) | 0.97 | (0.93-1.02) |
| Dyslipidemia | 1.42 | (1.39-1.45) | 1.02 | (1.00-1.05) |
| Sleep Apnea | 4.86 | (4.34-5.45) | 1.15 | (1.06-1.25) |
| Mental health conditions | | | | |

| | | | | |
|---|---|---|---|---|
| Depression | 1.42 | (1.37-1.48) | 0.97 | (0.93-1.02) |
| Psychoses | 1.44 | (1.38-1.50) | 0.94 | (0.89-1.00) |
| PTSD | 1.48 | (1.41-1.54) | 1.02 | (0.95-1.08) |
| Drug abuse | 1.33 | (1.23-1.43) | 1.01 | (0.91-1.11) |
| Alcohol abuse | 1.24 | (1.19-1.30) | 0.98 | (0.92-1.05) |
| Smoking Status | | | | |
| Current Smoker (ref=Never) | 0.79 | (0.76-0.81) | 0.81 | (0.78-0.85) |
| Former Smoker (ref=Never) | 1.11 | (1.05-1.17) | 1.14 | (1.08-1.21) |
| Prescription medication for weight loss | 1.60 | (1.44-1.79) | 1.53 | (1.25-1.88) |
| Prescription medication with weight gain risk | 1.27 | (1.22-1.33) | 0.99 | (0.94-1.05) |
| Service Connection (ref=not service connected) | | | | |
| 0-20% | 1.04 | (1.01-1.08) | 1.07 | (1.01-1.13) |
| 30-60% | 0.99 | (0.95-1.03) | 1.10 | (1.03-1.17) |
| 70-100% | 0.85 | (0.80-0.91) | 1.16 | (1.08-1.25) |
| No. primary care visits/year | 1.07 | (1.06-1.09) | 1.06 | (1.05-1.08) |
| No. years with a visit | 1.35 | (1.33-1.37) | 1.00 | (0.99-1.02) |

*GEE models adjusted for clustering by clinic. Additional covariates included baseline year (categorical), distance to a facility offering MOVE, marital status, and other comorbidities that may affect weight status and ability to be physically active such as hypothyroidism, COPD, heart failure, liver disease, and renal disease. Continuous variable odds ratios are calculated per 1-unit increase.

**Table 4.3, Diabetes incidence in multivariable Cox proportional hazards model**

| | Diabetes Incidence | |
|---|---|---|
| | HR | 95% CI |
| MOVE! Participation | | |
| Less active | 0.80 | (0.77-0.83) |
| Intense / Sustained | 0.67 | (0.61-0.74) |
| Age at baseline | 1.04 | (1.03-1.04) |
| Female | 0.82 | (0.80-0.84) |
| Race (ref=White) | | |
| African American | 1.35 | (1.31-1.40) |
| Other | 1.32 | (1.26-1.37) |
| BMI at baseline, mean | 1.05 | (1.04-1.05) |
| Weight-related conditions | | |
| Coronary Artery Disease | 1.14 | (1.13-1.16) |
| Hypertension | 1.19 | (1.17-1.21) |
| Osteoarthritis | 0.85 | (0.84-0.87) |
| Dyslipidemia | 1.02 | (1.01-1.04) |
| Mental health conditions | | |
| Depression | 0.94 | (0.93-0.96) |
| Psychoses | 0.97 | (0.95-0.98) |
| PTSD | 0.87 | (0.85-0.89) |
| Alcohol abuse | 0.95 | (0.93-0.96) |
| Smoking Status | | |
| Current Smoker (ref=Never) | 1.20 | (1.17-1.22) |
| Former Smoker (ref=Never) | 1.06 | (1.03-1.09) |

| | | |
|---|---|---|
| Prescription medication for weight loss | 3.68 | (3.14-4.30) |
| Prescription medication with weight gain risk | 1.58 | (1.55-1.62) |
| Service Connection (ref=not service connected) | | |
| 0-20% | 1.17 | (1.14-1.21) |
| 30-60% | 1.24 | (1.22-1.26) |
| 70-100% | 1.43 | (1.40-1.47) |
| No. visits/year | 1.08 | (1.08-1.09) |
| No. years with a visit | 0.97 | (0.97-0.98) |

*N=1,400,935. Cox proportional hazards model also adjusted for baseline year (categorical), marital status, weight-related comorbidities, and distance to a facility offering MOVE. Charlson comorbidity index, sleep apnea, COPD, and drug abuse were considered for inclusion but eliminated through model selection based on AIC. Continuous variable odds ratios are calculated per 1-unit increase. The model was stratified by BMI category due to the presence of interaction and was adjusted for clustering by clinic.

# Chapter 5: Reduced Cardiovascular Disease Associated with Participation in a National VA Lifestyle Change Program

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***Abstract***

**Background**: Lifestyle change programs can reduce weight and cardiovascular disease (CVD) risk factors, but their impact on CVD remains unestablished. The VA's MOVE!® program is the largest in the US.

**Methods**: In national VA databases, we identified patients eligible for MOVE! (2005-2012) – obese or overweight with a weight-related health condition. We analyzed associations between participation and CVD incidence (ICD-9 and procedure codes for coronary artery disease, CAD, cerebrovascular disease, CBD, peripheral vascular disease, PVD, and heart failure, HF) using Cox proportional hazards models.

**Results**: There were 1,463,003 eligible patients without baseline CVD, including 169,248 (12%) MOVE! participants. Patients were 92% male, 76% white, with mean age 52 years and BMI 32. Participants received lifestyle change counseling and decreased weight by -0.9% and -0.6% at 12 months and 3 years, while non-participants increased weight by 0.2% and 0.6% (each $p<0.001$). Adjusting for age, race, sex, BMI, and baseline comorbidity, over a mean 4.9 years of follow up, MOVE! participation was associated with lower incidence of total CVD (hazard ratio 0.83, 95% CI 0.80-0.86), CAD (HR 0.81, 0.77-0.86), CBD (HR 0.87, 0.82-0.92), PVD (HR 0.89, 0.84-0.94) and HF (HR 0.78, 0.74-0.82). In 701,930 patients with available data, the association with CVD was attenuated after further adjustment for baseline SBP, HDL cholesterol, non-HDL cholesterol, and RPG (HR 0.88, 95% CI 0.84-0.92).

**Conclusions**: The VA's MOVE! program demonstrates that modest lifestyle change can be achieved in a large-scale healthcare setting, and participation is associated with reduced development of cardiovascular disease.

***Introduction***

Obesity and cardiovascular disease (CVD) are major causes of morbidity, mortality, and healthcare cost in the US.(1-2) Much of the burden of CVD is avoidable through risk factor management, and lifestyle change programs that offer nutrition and physical activity counseling are a recommended strategy for prevention.(3-4) Several large randomized trials have demonstrated that lifestyle change programs can achieve weight loss and reductions in diabetes incidence.(5-7) However, evidence of impact on CVD risk factors is mixed, and few studies have had sufficient size to study CVD incidence.(8-13)

The Veterans Health Administration (VA) is the largest integrated healthcare system in the US, serving over 8 million patients annually.(14) Nearly three quarters of the patients are overweight or obese(15) and 58% have dyslipidemia, hypertension, or both.(16) The VA's lifestyle change program, MOVE!®, is the largest such program in the country, with over 400,000 participants since 2005.(17) A preliminary study evaluating the results of MOVE! found that weight loss was modest but sustained over one year.(18) In the present study, our objective was to examine the association between MOVE! participation and CVD incidence, including coronary artery disease (CAD), cerebrovascular disease (CBD), peripheral vascular disease (PVD), and heart failure (HF).

## *Methods*

### Databases

The VA's Corporate Data Warehouse (CDW) contains data on all veterans receiving care in VA facilities, from 1999-present, including demographics, vital signs, diagnoses, procedures, and prescriptions. We accessed these data through the VA Informatics and Computing Infrastructure (VINCI) data processing environment.(19) This secondary data analysis was approved by the Emory University Institutional Review Board and the Atlanta VA Medical Center's Research and Development Committee.

### MOVE! Program

The MOVE! program typically involves 8-12 group-based educational sessions on nutrition, physical activity, goal-setting, and maintenance.(20) Although there is a standard 10-session core curriculum, implementation may vary across VA facilities in terms of organization and delivery.(21) We defined participants as those who attended at least one session.

### Study Population

From nearly 10 million veterans receiving care between 2005-2012 (Figure 5.1), we selected 4.5 million veterans who had at least one outpatient visit per year for at least 3 consecutive years, who were eligible to participate in MOVE: patients who were either obese (body mass index [BMI] $\geq$30 kg/m$^2$), or overweight (BMI $\geq$25) with a weight-related health condition (diabetes, hypertension, dyslipidemia, sleep apnea, or osteoarthritis). From these, we excluded patients over age 70 because MOVE! is not

targeted at individuals above this age, due to uncertainty about adverse effects of overweight.(22-23) Consistent with a previous study of MOVE,(18) we also excluded veterans who would be unlikely to be able to participate due to contraindications. We excluded veterans with missing data for key demographic and clinical indicators, and restricted our study population to veterans without CVD at baseline, leaving 1,463,003 patients eligible for analysis.

**Measurements**

*Demographic characteristics:* Available data included age, sex, race/ethnicity, marital status, and VA facility. Race/ethnicity was defined as White, African American, and Other, the latter combining Hispanics, Asian/Pacific Islanders, and American Indians/Alaska Natives (each <2% of the population). The VA's "service-connected disability" indicator was used as a simple measure of socioeconomic status (SES) and disability status, consistent with prior studies.(24-25). This variable indicates whether veterans are eligible for VA care based on disability status, "service connected disability," or based on low SES, "no service connected disability."

*Weight-related illnesses and comorbidities:* Illnesses were assessed using ICD-9 codes and procedure codes. The Charlson Comorbidity Index (CCI) was employed using the enhanced ICD-9 coding algorithm developed by Quan et al.(26)

*Cardiovascular disease incidence:* Incident CVD was identified with ICD-9 and procedure codes for coronary artery disease, CAD, cerebrovascular disease, CBD, peripheral vascular disease, PVD, and heart failure, HF. Total CVD was defined as incidence of any of these four conditions.

*CVD Risk Factors:* Additional laboratory and clinical values (systolic blood pressure, SBP, random plasma glucose, RPG, high density lipoprotein cholesterol, HDL, non-high density lipoprotein cholesterol, non-HDL cholesterol) were available for a subset of patients (N=701,930). These measures were recorded as the most recent value within 12 months prior to baseline visits. Follow-up measures were recorded as average values captured within subsequent time windows (6 mo: 3-9 mo; 12 mo: 9-15 mo; 24 mo: 21-27 mo; 36 mo: 33-39 mo).

*BMI:* Body mass index (BMI) was assessed using clinically recorded weight and height, after excluding implausible values (approximately 0.1%).(27) Height was taken as the average height recorded for the patient, if multiple measures were available. Weight was recorded as the patient's baseline weight, with follow-up measures as above.

*Distance to MOVE*: Distance to the nearest VA facility offering MOVE! was calculated for each patient, based on geographic distance between the geographic midpoint of the patient's zipcode and the coordinates of the nearest VA facility offering MOVE.

*Smoking:* Text-based information was used to classify patients as "Current Smoker", "Former Smoker", or "Never / Lifetime Non-Smoker," as previously described and validated by McGinniss et al.(28)

**Statistical Analysis**

Descriptive characteristics were calculated for MOVE! participants and non-participants, and bivariate associations were analyzed using ANOVA (continuous variables) and chi-squared tests (categorical variables). Least square means were used to

obtain average SBP, HDL cholesterol, non-HDL cholesterol, and RPG among participants compared to non-participants, controlling for baseline value, BMI, age, sex, race/ethnicity, and diabetes status.

In regression analysis, we conducted stepwise model selection and assessed model fit based on the *Akaike information criterion* (AIC).(29) After evaluating model assumptions, Cox proportional-hazards models were constructed to estimate hazard ratios for cardiovascular disease incidence. Robust sandwich covariance matrix estimates were used to adjust for clustering at the clinic level, and models were stratified by baseline diabetes status.(30) Models were further adjusted for a propensity score that reflected likelihood of participating in MOVE.(31) Post-hoc analyses were performed to examine the association between participation and CVD incidence among subgroups likely to have different CVD risk. Baseline was assigned as a veteran's first MOVE! visit for participants and as the first visit at which weight was recorded after January 1, 2005 (the initial year of MOVE! roll-out) for non-participants. Sensitivity analyses were adjusted for baseline year as a categorical variable, to allow for potential differences in management across years. We also performed sensitivity analyses examining those who met the VA criteria for "intense and sustained" participation in MOVE! (attending $\geq 8$ sessions within 6 months), which is a level of participation that has been previously associated with greater weight loss.(32) All analyses were conducted using SAS® version 9.2 (Cary, NC).(33)

## *Results*

### Baseline Subject Characteristics

Compared to eligible non-participants, participants were more likely to be female (16% vs. 7%), African American (25% vs. 19%), and obese (85% vs. 55%) (Table 5.1). At baseline, participants had more diagnosed illnesses and risk factors than non-participants, including diabetes (31% vs. 17%), hypertension (64% vs. 47%), dyslipidemia (59% vs. 38%), and depression (41% vs. 18%) (each $p<0.001$). However, participants were less likely to be current smokers than non-participants (29% vs. 37%) ($p<0.001$). In a subset of patients with laboratory data, participants had slightly lower HDL cholesterol, non-HDL cholesterol, and SBP than non-participants, after stratifying by baseline diabetes status (all $p<0.001$, Table 5.2).

### MOVE! Attendance and CVD Risk Factors

The median number of MOVE! sessions attended was 2, with 54% of participants engaging in only 1 or 2 sessions. Twenty-six percent of participants attended 3-7 sessions, and 20% engaged in at least 8 sessions. Among those with recorded weights available, participants decreased weight by -0.9% and -0.6% at 12 months (N=118,118) and 3 years (N=61,823), respectively, while non-participants increased weight by 0.2% (N=917,563) and 0.6% (N=713,110). "Intense and sustained" participants lost substantially more weight (-3.0% at 12 months, N=10,857, and -2.1% at 3 years, N=5,381) compared to less active participants (-0.7% at 12 months, N=107,261, and -0.5% at 3 years, N=56,442).

At 6 months, MOVE! participation was associated with slightly lower SBP (-0.63 mmHG), non-HDL cholesterol (-1.59 mg/dL), and RPG (-1.49mg/dL), after controlling for baseline value, BMI, age, sex, race/ethnicity, and diabetes status (all $p<0.001$). These differences generally decreased over time between 6 and 36 months. As baseline diabetes was strongly related to risk factors (particularly RPG and non-HDL cholesterol), results are stratified by diabetes status (Table 5.3). In sensitivity analyses, "intense and sustained" participants at 6 months had substantially lower SBP (-2.72 mmHG), non-HDL cholesterol (-4.98 mg/dL), and RPG (-5.61 mg/dL) compared to non-participants.

**CVD Incidence**

In this population without baseline CVD, the observed incidence rate of total CVD was 35 per 1000 person-years. Individually, incidence rates of CAD, CBD, PVD, and HF were 21, 8, 7, and 5, respectively, per 1000 person-years. Average per-patient observation time was 59 months (range 1 to 95). In multivariable Cox proportional hazards models adjusting for demographic and clinical factors including age, race, sex, BMI, and baseline comorbidities (Table 5.4), MOVE! participation was associated with a lower incidence of total CVD (hazard ratio 0.83, 95% CI 0.80-0.86), as well as CAD (HR 0.81, 0.77-0.86), CBD (HR 0.87, 0.82-0.92), PVD (HR 0.89, 0.84-0.94) and HF (HR 0.78, 0.74-0.82). In sensitivity analyses, a slight dose response effect was observed (total CVD HR 0.79, 0.73-0.85 for "intense and sustained" participants compared to non-participants; HR 0.83, 0.80-0.87 for less active participants compared to non-participants).

In the multivariable model described above for total CVD (Table 5.4), other factors associated with greater incidence of CVD included male sex (women vs. men: HR 0.76, 95% CI 0.73-0.79), current smoking status (HR 1.42, 1.38-1.46), higher baseline age (each additional year of age: HR 1.05, 1.05-1.06), hypertension (HR 1.15, 1.14-1.17), and substantial service-connected disabilities (those with 70-100% service-connected disability compared to no disability: HR 1.35, 1.32-1.39).

In 701,930 patients with available data (Table 5.5), the association with total CVD was attenuated, but not eliminated, after further adjustment for SBP, HDL cholesterol, non-HDL cholesterol, and RPG (HR 0.88, 95% CI 0.84-0.92).

**Subgroup Analyses**

Subgroup analyses were performed to examine possible heterogeneity of effects across socio-demographic and clinical characteristics (Figure 5.2). Across categories for sex, age, race/ethnicity, BMI, smoking status, hypertension, and diabetes, an inverse association between MOVE! participation and CVD incidence was observed. While no subgroups indicated harm (HR >1), there were variations in degree of benefit associated with MOVE! participation in some subgroups. Wald p-values for interaction terms were significant for sex, diabetes status, BMI $\geq 40$, smoking status, hypertension, and age $\geq 60$. The inverse association between MOVE! and CVD incidence appeared stronger for men (HR 0.82, 95% CI 0.79-0.85) than women (HR 0.93, 0.83-1.05), among whom the association was not significant. The association between MOVE! participation and CVD incidence appeared more marked among those without baseline diabetes (HR 0.78, 0.75-0.82) compared to those with diabetes (HR 0.90, 0.83-0.97), although the association

remained significant even in those with diabetes. MOVE! participation may be less strongly associated with CVD incidence among those with BMI ≥40 (HR 0.87, 0.77-0.99) compared to those who were overweight (HR 0.81, 0.76-0.86), or obese with BMI 30-39.9 (HR 0.82, 0.73-0.93). We observed a stronger association between MOVE! participation and CVD incidence among current smokers (HR 0.77, 0.70-0.86) and former smokers (HR 0.83, 0.75-0.93) compared to nonsmokers (HR 0.88, 0.84-0.94).

***Discussion***

We observed a significant association between participation in a national, healthcare system-based lifestyle change program and lower cardiovascular disease incidence. Participation in MOVE! was associated with 17% lower total CVD incidence. In individual cardiovascular diseases, participation was associated with 19% lower CAD incidence, 13% lower CBD incidence, 11% lower PVD incidence, and 22% lower HF incidence. The association of MOVE! participation with reduced CVD incidence was attenuated, but remained significant, after adjustment for clinical, demographic, and baseline CVD risk factors.

These results are consistent with several clinical trials that have demonstrated modest improvements in cardiovascular risk factors among lifestyle change participants. For example, a small randomized trial among severely obese participants reduced blood pressure, waist circumference, and insulin resistance.(34) The DPP Outcomes Study, conducted among participants with prediabetes, demonstrated improved CVD risk factors, including systolic and diastolic blood pressure, LDL cholesterol, triglycerides, and HDL cholesterol among all groups, even though lipid and blood pressure medication

use was lower among lifestyle change participants.(12) Four-year results of the Look AHEAD study in diabetes patients revealed improved HbA1c, blood pressure, and HDL cholesterol.(8) A review demonstrated modest but significant changes in blood pressure and cholesterol associated with lifestyle change program participation among general population participants.(35)

Despite apparent benefit for cardiovascular risk factors, few studies have shown an association between lifestyle change program participation and CVD incidence. Specifically, our results contrast those of the Look AHEAD study, in which participants achieved substantial weight loss of 8.6%, and improved their CVD risk factor levels, but did not have reduced CVD incidence.(36) It has been suggested that Look AHEAD findings may have been confounded by differential statin use, and weight loss in the controls (3.5% by the end of the trial).(36-37) However, Look AHEAD was also conducted entirely among participants with diabetes, and we observed a more modest association between MOVE! participation and CVD incidence among VA patients with diabetes (HR 0.90) than among those without diabetes (HR 0.78). Researchers have noted that lifestyle change is more difficult among persons with diabetes due to a multitude of potential reasons, such as the tendency of some antidiabetic medications to promote weight gain, the risk of hypoglycemia with weight loss, and the mental and emotional effects of previous unsuccessful weight loss attempts.(38-39)

More research is needed to determine whether lifestyle change can reduce CVD events among patients with diabetes and other high-risk groups (such as those with prediabetes or hypertension), as compared with the general population. A recent Cochrane review questioned the ability of multifactorial lifestyle change programs to

affect total or CVD mortality among a general population, but did demonstrate benefit among trials restricted to high-risk participants with diabetes or hypertension (OR for fatal and nonfatal CVD events 0.78, 95% CI 0.68 to 0.89).(35) Although we observed a stronger association between MOVE! participation and CVD incidence among those without diabetes, our population was high-risk (average BMI 32; approximately 50% with diagnosed hypertension).

The strengths of our study include a study population large enough to examine CVD as an outcome, as well as the use of national-level data to examine a lifestyle change program within a healthcare setting. One limitation of the study is the potential for confounding, due to the observational nature of the data. Although it is impossible to rule out confounding by unmeasured factors, detailed electronic health record data allowed for adjustment of known cardiovascular risk factors, and a propensity score approach was used to further minimize confounding by measured variables. Another limitation is that veterans may receive care outside of the VA, and cardiovascular events may not be recorded in VA databases. To minimize this potential source of misclassification, we restricted analyses to veterans receiving at least 3 continuous years of outpatient care in the VA, in order to ensure that included patients had substantial and consistent contact with the VA system.

A potential limitation of the study is the differential assignment of baseline, in which baseline was assigned for non-participants as the first visit with a recorded weight after 2005 (the first year of MOVE! rollout), and for participants as their first MOVE! visit. This strategy had the benefit of allowing for control of baseline factors among participants at the time of MOVE! participation (for example, exact age and weight at the

beginning of participation). In sensitivity analysis, results remained largely unchanged after adjusting for baseline year, both in the propensity score and in regression models. One alternative approach would be to assign baseline as the first visit after 2005 among all patients, and examine associations with MOVE! participation as a time-varying covariate. However, since such an approach would also require accounting for covariates at the time of MOVE! participation, the proportional hazards model would necessitate adjustment for numerous time-varying covariates and would become quite complex. Another alternative approach would compare participants against 'baseline-matched' non-participants by proportionally assigning non-participant baseline years in comparable ratios to the baseline years of MOVE! participants.

In conclusion, this large observational study demonstrates that participation in the VA national, healthcare system-based lifestyle change program was associated with a reduction in CVD incidence. If further research demonstrates benefit and cost-effectiveness, lifestyle change programs may be an attractive strategy for healthcare systems to consider implementing as an adjunct to conventional pharmacotherapy approaches for control of CVD risk factors.

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Sandra Jackson (Emory University GDBBS) and Lawrence Phillips (Atlanta VA Medical Center and Emory University School of Medicine) had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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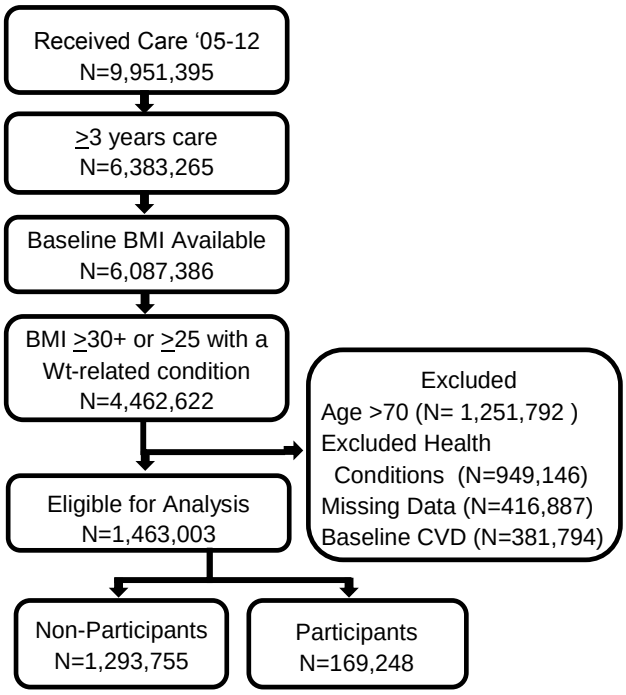
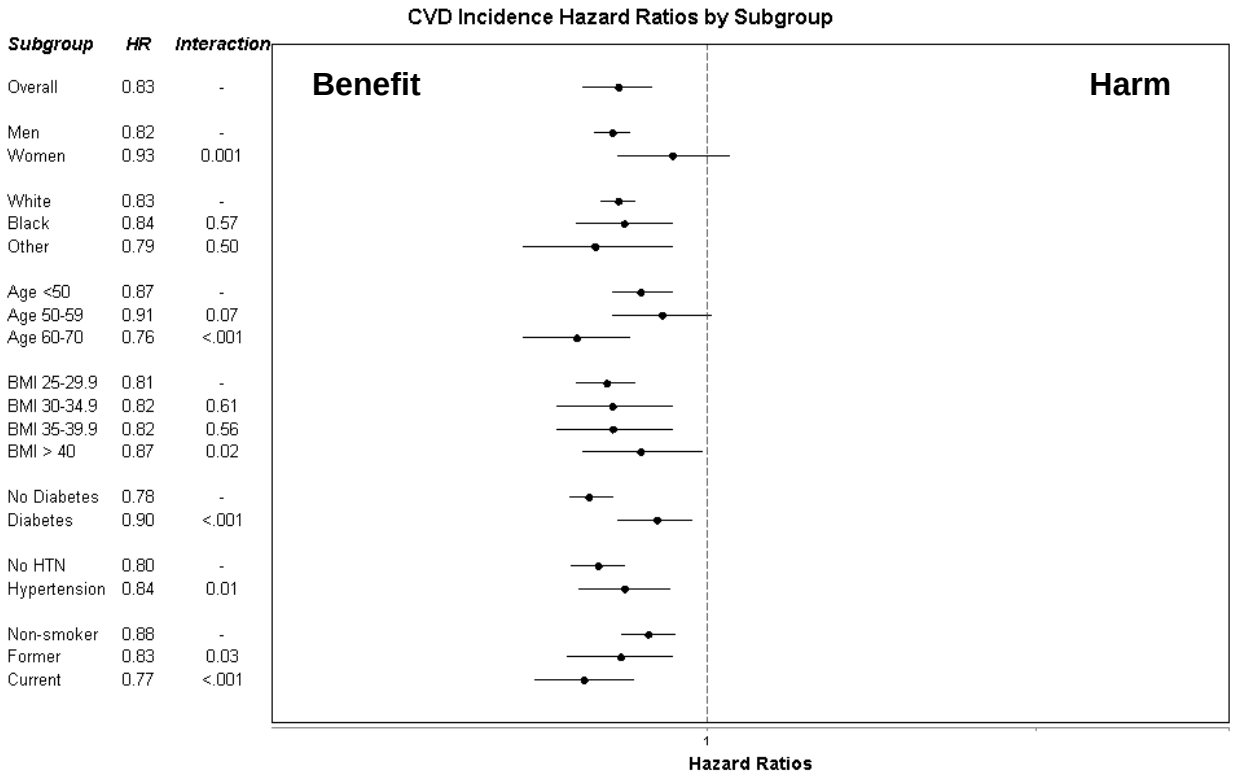
**Figure 5.1: Study Population**




Weight-related health conditions included diabetes, hypertension, dyslipidemia, sleep apnea, or osteoarthritis. Excluded health conditions, consistent with a prior study of MOVE, included diagnoses of sepsis, pregnancy, cancer other than skin cancer, neurodegenerative disease, HIV, or anorexia, or receipt of hospice or nursing home care.

**Figure 5.2. Hazard Ratios for Total CVD Incidence among Participants Compared to Non-Participants, by Subgroup**




*N=1,463,003. Cox proportional hazards models included covariates: baseline age, BMI, sex, race/ethnicity, CCI, hypertension, dyslipidemia, COPD, smoking status, prescriptions for weight loss, prescriptions with a risk of weight gain, service connected disability status, osteoarthritis, kidney disease, sleep apnea, mental health conditions, service connected disability status, marital status, distance to MOVE! clinic, number of primary care visits per year, and years of care in the VA system. Wald p-values for interaction terms are shown. Hazard ratios less than 1 (to the left of the dashed axis) indicate that MOVE! participation was associated with reduced CVD incidence. Significant p-values indicate possible heterogeneity of effects across subgroups.

**Table 5.1. Characteristics of Participants and Eligible Non-Participants, 2005-2012**

| | All | Non-Participants | Participants |
|---|---|---|---|
| | N=1,463,003 | N=1,293,755 | N=169,248 |
| Age at baseline | 51.97 ± 11.71 | 51.91 ± 11.77 | 52.39 ± 11.18 |
| Sex | | | |
| Male | 92.14% | 93.16% | 84.42% |
| Female | 7.86% | 6.84% | 15.58% |
| Race | | | |
| White | 76.24% | 77.03% | 70.13% |
| African American | 19.40% | 18.62% | 25.40% |
| Other | 4.36% | 4.35% | 4.47% |
| BMI at baseline, mean | 31.89 ± 5.15 | 31.38 ± 4.76 | 35.80 ± 6.27 |
| 25-29.9 | 41.22% | 44.66% | 14.97% |
| 30-34.9 | 36.91% | 36.86% | 37.25% |
| 35.0-39.9 | 14.67% | 13.09% | 26.79% |
| ≥40 | 7.19% | 5.39% | 20.98% |
| Charlson Comorbidity Index | | | |
| 0 Point | 89.46% | 91.16% | 76.46% |
| 1 Point | 8.88% | 7.57% | 18.94% |
| 2+ Points | 1.66% | 1.28% | 4.59% |
| Diabetes | 18.77% | 17.21% | 30.72% |

| | | | |
|---|---|---|---|
| Hypertension | 49.00% | 47.05% | 63.91% |
| Dyslipidemia | 40.76% | 38.33% | 59.33% |
| Mental health conditions | | | |
| Depression | 20.94% | 18.32% | 40.99% |
| Psychoses | 18.49% | 16.09% | 36.80% |
| PTSD | 10.69% | 9.26% | 21.64% |
| Smoking Status | | | |
| Current Smoker | 35.84% | 36.70% | 29.25% |
| Former Smoker | 28.71% | 28.46% | 30.63% |
| Lifetime Non-smoker | 35.45% | 34.84% | 40.12% |
| Rx for weight loss medication | 4.30% | 3.79% | 8.14% |
| Rx with weight gain risk | 69.93% | 68.55% | 80.44% |
| Married | 56.79% | 57.40% | 52.17% |
| No Service Connected Disability | 50.51% | 51.42% | 43.52% |
| No. primary care visits/year | 3.34 ± 2.08 | 3.26 ± 2.02 | 3.97 ± 2.45 |
| No. years with a visit | 8.40 ± 3.41 | 8.35 ± 3.41 | 8.81 ± 3.35 |
| Distance to MOVE! Clinic | 43.50 ± 33.52 | 43.91 ± 33.61 | 40.38 ± 32.60 |

*± values are means ±SD. All associations between patient characteristics and MOVE! participation were significant ($p < 0.001$), according to chi-squared tests (categorical variables) and ANOVA (continuous variables).

**Table 5.2, CVD Risk Factors at Baseline**

| | Without Baseline Diabetes | | | With Baseline Diabetes | | |
|---|---|---|---|---|---|---|
| | All | Participants | Non-Participants | All | Participants | Non-Participants |
| **N** | 542,494 | 86,434 | 456,060 | 159,436 | 43,582 | 115,854 |
| SBP | 132.48 ± 15.86 | 130.23 ± 13.95 | 132.91 ± 16.16 | 134.34 ± 16.54 | 131.56 ± 14.77 | 135.38 ± 17.04 |
| HDL | 43.77 ± 12.81 | 42.46 ± 11.89 | 44.01 ± 12.96 | 40.48 ± 11.50 | 39.38 ± 10.61 | 40.89 ± 11.78 |
| Non-HDL-Cholesterol | 155.43 ± 40.07 | 150.96 ± 38.22 | 156.27 ± 40.36 | 140.67 ± 44.46 | 134.14 ± 42.38 | 143.13 ± 44.98 |
| RPG | 100.39 ± 19.30 | 101.15 ± 16.70 | 100.24 ± 19.76 | 155.85 ± 69.13 | 152.30 ± 65.46 | 157.19 ± 70.41 |

* N=701,930 at baseline. ± values are means ±SD. All associations between CVD risk factors and MOVE! participation were significant ($p < 0.001$), controlling for baseline diabetes status.

**Table 5.3. Population Marginal Mean Cardiovascular Risk Factors over 6-36 Months, Stratified by Participation and Diabetes Status**

| | 6 Months | 12 Months | 24 Months | 36 Months |
|---|---|---|---|---|
| **Systolic Blood Pressure** | | | | |
| Non-Participants, No DM | 131.29 | 130.81 | 130.36 | 130.21 |
| Participants, No DM | 130.59 | 130.34 | 130.34 | 130.37 |
| Non-participants, DM | 133.90 | 133.66 | 132.93 | 132.92 |
| Participants, DM | 133.06 | 132.81 | 132.69 | 132.99 |
| **HDL Cholesterol** | | | | |
| Non-Participants, No DM | 44.42 | 44.98 | 44.87 | 44.86 |
| Participants, No DM | 44.48 | 45.14 | 45.59 | 45.92 |
| Non-participants, DM | 41.13 | 41.70 | 41.47 | 41.20 |
| Participants, DM | 41.19 | 41.72 | 42.13 | 42.46 |
| **Non-HDL Cholesterol** | | | | |
| Non-Participants, No DM | 151.76 | 148.08 | 145.93 | 144.67 |
| Participants, No DM | 150.57 | 147.58 | 144.64 | 143.12 |
| Non-participants, DM | 135.40 | 132.92 | 130.84 | 129.12 |
| Participants, DM | 133.10 | 131.28 | 128.89 | 127.14 |
| **Random Plasma Glucose** | | | | |
| Non-Participants, No DM | 103.14 | 102.56 | 103.70 | 103.94 |
| Participants, No DM | 101.80 | 101.54 | 102.52 | 103.26 |
| Non-participants, DM | 147.65 | 148.59 | 149.08 | 149.27 |

| | | | | |
|---|---|---|---|---|
| Participants, DM | 146.20 | 146.99 | 148.61 | 149.31 |

** Least square means compute averages controlled for baseline value, baseline BMI, baseline age, sex, and race/ethnicity. Sample sizes vary by laboratory value and decrease over time; available upon request.

**Table 5.4, Multivariable Cox Proportional Hazards Results for CVD Incidence**

| | Total CVD | | CAD | | CBD | | PVD | | HF | |
|---|---|---|---|---|---|---|---|---|---|---|
| | HR | CI | HR | CI | HR | CI | HR | CI | HR | CI |
| MOVE! Participation | 0.83 | 0.80-0.86 | 0.81 | 0.77-0.86 | 0.87 | 0.82-0.92 | 0.89 | 0.84-0.94 | 0.78 | 0.74-0.82 |
| Age at baseline | 1.05 | 1.05-1.06 | 1.05 | 1.05-1.05 | 1.06 | 1.06-1.06 | 1.07 | 1.06-1.07 | 1.06 | 1.06-1.06 |
| Female | 0.76 | 0.73-0.79 | 0.69 | 0.66-0.73 | 1.01 | 0.97-1.06 | 0.74 | 0.69-0.79 | 0.64 | 0.59-0.67 |
| Race (ref=White) | | | | | | | | | | |
| African American | 0.97 | 0.92-1.03 | 0.90 | 0.83-.97 | 0.97 | 0.92-1.01 | 0.99 | 0.92-1.07 | 1.38 | 1.30-1.46 |
| Other | 0.83 | 0.79-0.86 | 0.82 | 0.78-0.87 | 0.80 | 0.75-0.86 | 0.83 | 0.76-0.91 | 0.81 | 0.75-0.87 |
| BMI at baseline | 1.01 | 1.01-1.01 | 1.01 | 1.01-1.02 | 0.98 | 0.98-0.99 | 1.00 | 0.99-1.00 | 1.06 | 1.06-1.07 |
| CCI (ref=none) | | | | | | | | | | |
| One | 1.07 | 1.05-1.09 | 1.04 | 1.01-1.06 | 1.08 | 1.05-1.12 | 1.05 | 1.02-1.09 | 1.28 | 1.22-1.35 |
| Two+ | 1.12 | 1.07-1.17 | 1.03 | 0.98-1.09 | 1.28 | 1.19-1.37 | 1.11 | 1.02-1.21 | 1.22 | 1.12-1.33 |
| Hypertension | 1.15 | 1.14- | 1.10 | 1.09- | 1.29 | 1.26- | 1.16 | 1.14- | 1.28 | 1.24- |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | 1.17 | | 1.12 | | 1.32 | | 1.19 | | 1.32 |
| Dyslipidemia | 0.96 | 0.95-0.98 | 1.01 | 0.99-1.04 | 0.99 | 0.97-1.01 | 0.91 | 0.88-0.93 | 0.80 | 0.77-0.82 |
| COPD | 1.07 | 1.05-1.10 | 1.11 | 1.08-1.14 | 0.99 | 0.94-1.03 | 1.00 | 0.95-1.05 | 1.29 | 1.23-1.35 |
| Smoking Status | | | | | | | | | | |
| Current Smoker (ref=Never) | 1.42 | 1.38-1.46 | 1.28 | 1.23-1.33 | 1.46 | 1.39-1.52 | 2.35 | 2.18-2.53 | 1.42 | 1.35-1.49 |
| Former Smoker (ref=Never) | 1.08 | 1.04-1.13 | 1.07 | 1.02-1.14 | 1.07 | 0.99-1.14 | 1.21 | 1.12-1.30 | 1.07 | 1.01-1.14 |
| Rx for weight loss | 1.14 | 1.11-1.16 | 1.14 | 1.10-1.17 | 1.11 | 1.06-1.15 | 1.23 | 1.17-1.28 | 1.18 | 1.13-1.23 |
| Rx with weight gain risk | 1.44 | 1.42-1.47 | 1.38 | 1.33-1.40 | 1.50 | 1.45-1.55 | 1.81 | 1.75-1.86 | 1.86 | 1.79-1.93 |
| Service Connected Disability (ref=none) | | | | | | | | | | |
| 0-20% | 0.93 | 0.91-0.95 | 0.94 | 0.92-0.96 | 0.93 | 0.90-0.97 | 0.94 | 0.91-0.97 | 0.81 | 0.78-0.85 |
| 30-60% | 1.03 | 1.01-1.06 | 1.07 | 1.04-1.10 | 0.97 | 0.94-1.00 | 1.06 | 1.02-1.10 | 0.82 | 0.78-0.85 |
| 70-100% | 1.35 | 1.32-1.39 | 1.46 | 1.42-1.50 | 1.18 | 1.14-1.22 | 1.45 | 1.40-1.50 | 1.31 | 1.25-1.37 |

N=1,463,003. Models also controlled for osteoarthritis, distance from a patient's zipcode to a facility offering MOVE, marital status, kidney disease, sleep apnea, mental health conditions (depression, psychoses, and PTSD), number of primary care visits per year, and years of care in the VA system. Other factors considered for inclusion in analysis but omitted through AIC model selection included alcohol abuse and drug abuse. Models were stratified by baseline diabetes status using the strata option in the SAS phreg procedure. Models were adjusted for clustering by clinic, and included propensity scores to adjust for likelihood of MOVE! participation.

**Table 5.5, CVD Incidence in subset with additional baseline CVD risk factor data**

| | Total CVD | | CAD | | CBD | | PVD | | HF | |
|---|---|---|---|---|---|---|---|---|---|---|
| | HR | CI | HR | CI | HR | CI | HR | CI | HR | CI |
| MOVE! Participation | 0.88 | 0.84-0.92 | 0.86 | 0.81-0.92 | 0.93 | 0.87-0.99 | 0.95 | 0.88-1.02 | 0.83 | 0.77-0.89 |
| sBP* | 1.05 | 1.04-1.05 | 1.03 | 1.03-1.04 | 1.07 | 1.06-1.08 | 1.07 | 1.06-1.08 | 1.08 | 1.07-1.09 |
| HDL cholesterol* | 0.94 | 0.93-0.95 | 0.92 | 0.91-0.93 | 0.96 | 0.94-0.97 | 0.94 | 0.92-0.96 | 1.01 | 0.99-1.02 |
| Non-HDL cholesterol* | 1.01 | 1.01-1.01 | 1.02 | 1.01-1.02 | 1.01 | 1.01-1.02 | 1.01 | 1.01-1.02 | 0.99 | 0.99-1.00 |
| RPG* | 1.01 | 1.01-1.01 | 1.01 | 1.01-1.01 | 1.01 | 1.01-1.01 | 1.02 | 1.01-1.02 | 1.02 | 1.02-1.03 |

Models identical to Table 3 above, but including additional adjustment (sBP, HDL cholesterol, non-HDL cholesterol, and RPG) and restricted to patients with available data for these laboratory and clinical measures (N=701,930). *Hazard ratios for clinical measures are per 10-unit increase.

# Chapter 6: Participation in a National VA Lifestyle Change Program is Associated with Improved Diabetes Management

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***Abstract***

**Objective**: Healthcare system-based lifestyle change programs have the potential to assist many diabetes patients, and the VA's The VA's MOVE!® program is the largest in the US. We sought to examine the association between MOVE participation and diabetes management.

**Research Design and Methods:** We used VA databases to identify patients with diabetes eligible for MOVE (2005-2012) – BMI ≥30, or BMI ≥25 with a weight-related health condition. Least square means were used to calculate changes in weight, random plasma glucose (RPG), and HbA1c, adjusting for baseline differences between participants and nonparticipants. Cox proportional hazards models were constructed to analyze associations with diabetic eye disease and renal disease, as well as medication intensification (initiating a new oral antidiabetes medication or insulin).

**Results**: There were 400,170 eligible patients with diabetes, including 87,366 (22%) MOVE participants. The patients were 96% male, 77% white, with mean age 58 years and BMI 34. Controlling for baseline value, BMI, age, gender, race/ethnicity, and antidiabetes medications, MOVE participants had lower body weight (-0.6 kg), RPG (-2.8 mg/dL), and HbA1c (-0.1%) at 12 months compared to nonparticipants (each $p<0.001$). In multivariable Cox models adjusting for age, race, sex, BMI, and baseline comorbidities, MOVE participation was associated with lower incidence of eye disease (hazard ratio 0.80, 95% CI 0.76-0.85) and renal disease (0.90, 0.86-0.93), as well as less medication intensification (0.81, 0.79-0.83).

**Conclusions**: In this VA healthcare setting, lifestyle change program participation among patients with diabetes was associated with lower incidence of diabetes complications, despite less medication intensification.

***Introduction***

In parallel with recent increases in obesity, the prevalence of type 2 diabetes has increased sharply in the United States (1). Diabetes is a major cause of mortality and morbidity among adults, and is the leading cause of incident blindness and kidney failure (2). In 2012, the total cost of diabetes was estimated at $245 billion (3), and health care costs attributable to prediabetes and diabetes are projected to yield a cumulative expenditure of $3.5 trillion over the next decade (4). Lifestyle change programs have been shown to reduce diabetes incidence among those at risk for the disease (5), and evidence suggests that lifestyle change programs improve weight and glycemic control (6-7), reduce medication use (8-9), and may reduce microvascular complications (10-11) among those with diabetes. While lifestyle change is a recommended strategy for disease management among patients with diabetes (12), there is little understanding of how translating lifestyle change programs into a clinical setting may impact diabetes management (13).

The Veterans Health Administration (VA) is the largest integrated healthcare system in the US (14). In 2000, it was estimated that nearly 1 in 5 patients receiving care at the VA had diabetes (15), approximately twice the prevalence in the general adult population (16). The VA's MOVE!® lifestyle change program has enrolled over 400,000 participants since 2005, and the program has been associated with modest weight loss (17). We examined the association between MOVE participation and (a) change in hemoglobin A1c (HbA1c) and random plasma glucose (RPG), (b) incidence of diabetic eye disease and renal disease, and (c) intensification of antidiabetes medications.

## *Methods*

### Databases

We used data from the VA's Corporate Data Warehouse (CDW), which is a national repository of information from clinical and administrative systems. Data are available from 1999-present, and include patient demographics, vital signs, diagnoses, procedures, and prescriptions. We accessed these data through the Veterans Informatics and Computing Infrastructure (VINCI) data processing environment . This work was approved by the Emory University Institutional Review Board and the Atlanta VA Medical Center Research and Development Committee.

### MOVE Program

The VA's MOVE program typically offers group-based counseling on nutrition, physical activity, goal-setting, and maintenance. The standard MOVE curriculum includes an orientation session with an intake questionnaire, which is used to offer tailored feedback to patients. In addition, the curriculum includes 10 core modules emphasizing improving nutrition, reducing fat intake, evaluating portion sizes, walking with a pedometer and physical activity modifications for wheelchair users, setting goals and overcoming barriers, exercising safely, the importance of planning ahead, modifying one's environment for success, resolving difficulties, and staying motivated. Implementation may vary across VA facilities in terms of organization and delivery, although a study of best practices has emphasized the importance of using the standard MOVE curriculum and offering a group-based format (18). We defined participants as those who attended at least one session of the program.

**Study Population**

There were nearly 10 million veterans receiving care between the time of MOVE roll-out (2005) through the end of 2012 (Figure 1). From this group, we selected veterans with at least one VA outpatient visit per year for at least 3 consecutive years, who were eligible to participate in MOVE: patients who were either obese (body mass index [BMI] $\geq$30 kg/m$^2$), or overweight (BMI $\geq$25) with a weight-related health condition (diabetes, hypertension, dyslipidemia, sleep apnea, or osteoarthritis). From these 4.5 million veterans, we excluded patients over age 70 because MOVE is not targeted to individuals above this age, due to uncertainty about adverse effects of overweight among the elderly (19). To allow comparisons with a previous study of MOVE (17), we also excluded veterans who would be unlikely to be able to participate in a weight loss program due to contraindications, or who would be likely to experience weight change for reasons unrelated to MOVE (such as sepsis, pregnancy, cancer other than skin cancer, neurodegenerative disease, HIV, and anorexia, or those receiving hospice or nursing home care). In addition, we restricted our study population to veterans with diabetes at baseline, defined as use of the 250.xx ICD-9 code or prescription of a diabetes drug. The use of similar indicators has been validated (15). Lastly, we excluded veterans missing data for key demographic and clinical indicators, leaving 400,170 patients eligible for analysis.

**Measurements**

*Demographic characteristics:* Information in the VA CDW includes age, sex, race/ethnicity, marital status, and VA facility. Race/ethnicity was defined as White, African American, and Other, the latter combining Hispanics, Asian/Pacific Islanders, and American Indians/Alaska Natives (each <2% of the population). The VA's "service-connected disability" indicator was used as a simple measure of socioeconomic status (SES) and disability status, consistent with prior studies.(20-21). This variable indicates whether veterans are eligible for VA care based on disability status, "service connected disability," or based on low SES, "no service connected disability." Having few service-connected disabilities is a proxy for low SES.

*Weight-related illnesses and comorbidities:* Illnesses were assessed using ICD-9 codes and procedure codes. The Charlson Comorbidity Index (CCI) was employed using the enhanced ICD-9 coding algorithm developed by Quan et al. (22).

*Diabetes complications:* Diabetic eye disease and renal disease were identified with ICD-9 codes, procedure codes, and CPT codes. Diabetic eye disease was defined as ICD-9 code 250.5x or 362.0x, as well as diabetes plus codes for retinal edema, vitreous hemorrhage, retinal detachment, cranial nerve palsy, blindness, laser surgery, vitrectromy, retinal detachment repair, and enucleation, as used in previous studies of eye disease in the VHA. Sensitivity analyses were also conducted examining eye disease with inclusion of ICD-9 codes for glaucoma and cataracts, and procedure codes for glaucoma trabeculectomy and cataract extraction. Diabetic renal disease was defined as ICD-9 code 250.4x, or diabetes plus ICD-9 codes for proteinuria, kidney disease, acute renal failure, end-stage renal disease or uremia, or diabetes plus procedure codes or CPT codes for hemodialysis, peritoneal dialysis, or transplantation.

*Diabetes medications:* Initiation of oral antidiabetes medications and insulin were assessed based on date of first recorded prescription. Medication intensification was defined as prescription of a new oral antidiabetes medication or initiation of insulin (23).

*Laboratory Measures:* Additional laboratory and clinical values (systolic blood pressure, RPG, and hemoglobin HbA1c) were available for a subset of patients. Random plasma glucose was defined as any outpatient blood or plasma glucose measure, excluding capillary or arterial values and excluding glucose challenge test measurements. Laboratory measures were recorded as the most recent value within 12 months prior to baseline visits. Follow-up measures for RPG and HbA1c were recorded as average values captured within subsequent time windows (6 mo: 3-9 mo; 12 mo: 9-15 mo; 24 mo: 21-27 mo; 36 mo: 33-39 mo).

*BMI:* Body mass index (BMI) was assessed using clinically recorded weight and height, after excluding implausible values (approximately 0.1%). Height was taken as the average height recorded for the patient, if multiple measures were available. Weight was recorded as the patient's baseline weight, and follow-up weights as average weight within subsequent time windows, as above.

*VA Care*: Distance to the nearest VA facility offering MOVE was calculated for each patient, based on geographic distance between the geographic midpoint of the patient's zipcode and the coordinates of the nearest VA facility offering MOVE. Each patient's average number of primary care visits per year, and total number of years with recorded VA visits, were also calculated to assess frequency and longevity of interaction with the VA system.

*Smoking:* Text-based information was used to classify patients as "Current Smoker", "Former Smoker", or "Never / Lifetime Non-Smoker," as previously described and validated by McGinniss et al. (24).

**Statistical Analysis**

Bivariate associations were analyzed using ANOVA (continuous variables) and chi-squared tests (categorical variables) for descriptive characteristics among participants and nonparticipants. Least square means were used to calculate average body weight, RPG, and HbA1c among participants compared to non-participants, controlling for baseline value, BMI, age, gender, race/ethnicity, and baseline antidiabetes medications.

For regressions, we conducted stepwise model selection and assessed model fit based on the ***Akaike information criterion*** (AIC). Cox proportional-hazards models were constructed to estimate hazard ratios for diabetic eye disease (among those without eye disease at baseline) and diabetic renal disease (among those without renal disease at baseline), as well as medication intensification. Robust sandwich covariance matrix estimates were used to adjust for clustering at the clinic level (25). Models were further adjusted for a propensity score that reflected likelihood of participating in MOVE (26). Baseline was assigned as a veteran's first MOVE visit for participants and as the first visit at which weight was recorded after January 1, 2005 (the initial year of MOVE roll-out) for non-participants. Sensitivity analyses were adjusted for baseline year as a categorical variable, to allow for potential differences in management across years. We also performed sensitivity analyses examining those who met the VA criteria for "intense and sustained" participation (attending $\geq$ 8 sessions within 6 months), which is a level of

participation that has been previously associated with greater weight loss (27). All analyses were conducted using SAS® statistical software (version 9.2; SAS Institute, Cary, NC).

## *Results*

### Baseline Subject Characteristics

In this MOVE-eligible population with diabetes, MOVE participants were more likely than nonparticipants to be female (7% vs. 3%), African American (23% vs. 17%), and obese (89% vs. 67%) (Table 6.1). Patients had frequent (median approximately 4 primary care visits per year) and sustained (median 10 years) care in the VA system. Participants were more likely than nonparticipants to have baseline eye disease (25% vs. 15%) or baseline renal disease (13% vs. 5%), and were more likely to be taking oral antidiabetes medications (79% vs. 67%) or insulin (32% vs. 19%). Participants were more likely to have a service-connected disability (59% vs. 49%) but less likely to be current smokers (27% vs. 31%). All differences between participants and nonparticipants were statistically significant ($p<0.001$).

### Change in Weight, RPG, and HbA1c

Participation was associated with modestly lower body weight (-0.6 kg), random plasma glucose (-2.8 mg/dL), and HbA1c (-0.1%) at 12 months (Table 6.2A, all $p<0.001$), after adjusting for baseline value, baseline BMI, baseline age, gender, race/ethnicity, and baseline medication status (oral antidiabetes medications and/or insulin). Differences in measurements between participants and nonparticipants became

smaller over time from 12 to 36 months, but remained significant. In sensitivity analyses, participants who met VA criteria for "intense and sustained" participation (9.5% of participants), had substantially lower weight (-2.1 kg), RPG (-7.8 mg/dL), and HbA1c (-0.3%) compared to nonparticipants at 12 months (Table 6.2B, all $p<0.001$).

**Incidence of Diabetes Complications**

Median follow-up time was 69 months (range 1-95). Incidence of diabetic eye disease was 52 per 1000 person-year (among those with no eye disease at baseline) and incidence of renal disease was 30 per 1000 person-years (among those with no renal disease at baseline). In multivariable models, MOVE participation was associated with lower incidence of eye disease (HR 0.80, 95% CI 0.76-0.85) and renal disease (HR 0.90, 0.86-0.93) (Table 6.3). For eye disease, being African American was also associated with increased incidence (HR 1.19, 1.11-1.27), as was having a prescription for oral antidiabetes medications (HR 1.23, 1.20-1.26) or insulin (HR 2.10, 2.03-2.17) at baseline. For renal disease, being African American (1.45, 1.39-1.51), having diagnosed hypertension (HR 1.40, 1.37-1.44), and taking insulin at baseline (HR 1.67, 1.63-1.71) were associated with increased incidence.

In sensitivity analyses including glaucoma and cataract in the definition of eye disease, the effect of MOVE participation was reduced (HR 0.92, 95% CI 0.87-0.98). The inverse associations between MOVE participation and diabetic eye disease (HR 0.85, 95% CI 0.80-0.90) and renal disease (HR 0.94, 0.90-0.98) remained significant after further adjustment for baseline HbA1c and systolic blood pressure, among those with

available measures (N=218,935 for eye disease and N=251,295 for renal disease) (Table 6.4).

**Initiation and Intensification of Diabetes Medications**

Medication intensification occurred at a rate of 157 new medications per 1000 person-year of observation. MOVE participation was inversely associated with medication initiation (HR 0.81, 0.79-0.83) (Table 6.3). This association adjusted for baseline medication status, which was strongly linked to medication intensification: as expected, patients who already had a prescription for insulin at baseline were much less likely to have a new medication added (HR 0.30, 0.28-0.31) compared to patients who did not. The inverse association between MOVE participation and medication initiation remained significant (HR 0.88, 0.86-0.91) after further adjustment for baseline HbA1c and systolic blood pressure (Table 6.4). In sensitivity analyses examining level of MOVE participation, intense and sustained MOVE participation was associated with a stronger effect on medication intensification and renal disease, but not eye disease (Table 6.5).

In additional analyses separately examining oral antidiabetes medication initiation and insulin initiation, oral antidiabetes medication initiation occurred more frequently (141 per 1000 person-years) than insulin initiation (60 per 1000 person-years). MOVE participation appeared more strongly associated with reduced oral antidiabetes medication intensification (HR 0.78, 0.75-0.82) than insulin initiation (HR 0.96, 0.93-0.99) (Table 6.6).

***Discussion***

In this national population of patients with diabetes, we observed a significant association between participation in the VA lifestyle change program and lower incidence of diabetes complications and medication intensification. Participation in MOVE was associated with 20% lower incidence of diabetic eye disease, 10% lower renal disease, and 19% lower medication intensification. These inverse associations remained significant after adjustment for baseline demographic and clinical risk factors.

Our observations are consistent with other studies, including the multicenter randomized Look AHEAD trial, that have shown reduced medication usage among lifestyle change program participants with diabetes (8-9). However, there is less evidence regarding the potential for lifestyle change programs to impact microvascular outcomes in patients with diabetes (13). At this time, microvascular results are still forthcoming from the Look AHEAD trial: initial findings presented at the 2013 American Diabetes Association meeting indicated that lifestyle change participants had 31% lower incidence of advanced renal disease, and 14% lower incidence of retinopathy (10). The China Da Qing Diabetes Prevention Outcomes study found that lifestyle intervention was associated with a lower incidence of severe retinopathy (HR 0.53, 0.29-0.99) but not nephropathy (HR 1.05, 0.16-7.05) (28).The multidimensional Steno-2 trial, which incorporated both lifestyle change and pharmacotherapy, reported a reduction in progression of retinopathy (OR 0.45, 0.21-0.95) and nephropathy (OR O.27, 0.10-0.75) (11). However, due to the inclusion of pharmacotherapy, these results may not be representative of lifestyle change programs incorporating only diet, exercise, and motivational components. Although trials among patients with diabetes with

microvascular endpoints are scarce, a recent review has linked weight loss in chronic kidney disease patients with improved renal function, including decreased proteinuria and increased GFR (29).

Our study is also consistent with prior work that has demonstrated improvements in weight and glucose control with lifestyle change among patients with diabetes.(6-7) For example, a small-scale (147 patients) healthcare system-based randomized trial among obese persons with diabetes reduced weight (-3.0kg at 12 months) and A1c, although impact on HbA1c was modest and no longer statistically significant at 12 months (-0.2%, p=.45) (9). These metabolic changes were comparable to what we observed in "intense and sustained" MOVE participants (weight loss -2.1 kg, HbA1c -0.3% over 12 months, all $p<0.001$ compared to nonparticipants).

Clinical diabetes management is a complicated undertaking, of which patient education and lifestyle change counseling is only one component. In a managed care setting, implementation of a multifactorial diabetes disease management program, including provision of diabetes education and nutrition counseling with no copayments, as well as establishment of a diabetes registry, dissemination of clinical guidelines, and development of clinical reminders to improve processes of care, was associated with decreased HbA1c (-0.60%) (30). The multicenter TRIAD observational study of diabetes care hypothesized that system factors (including health system structure, disease management strategies, patient education, payment strategies, and data systems) impact processes of care such as HbA1c testing, clinical examinations, and medication prescriptions, and thereby impact patient health outcomes including glycemic control and diabetes complications (31). Perhaps due to greater awareness of these issues, clinical

management of diabetes has improved, although nearly half of patients with diabetes in 2007-2010 reported not receiving diabetes education (32).

If lifestyle change programs are implemented in healthcare settings, one must consider the broader context of the healthcare system in which they operate, and how health system factors may affect program participation and health impact. For example, the TRIAD study found that out-of-pocket costs influence patient participation in diabetes education programs (33), and in 2008, the VA eliminated copayments for health education in order to promote participation in MOVE. In addition to implementation of the MOVE program and provision of health education services without copayment, the VA compares favorably against commercial managed care in other aspects of diabetes management, including A1c testing, aspirin use counseling, eye and foot examinations, and lipid control (34).

One concern is that, among participants with diabetes, changes in behavior and weight loss may not be sustained beyond the end of lifestyle interventions (13). We observed modest differences in weight, RPG, and HbA1c between participants and nonparticipants that were attenuated over time. Prior research has suggested that lifestyle change program participants with diabetes have impaired weight loss and maintenance of losses over time compared to those without diabetes (35-36). Difficulties among patients with diabetes in adhering to dietary and exercise regimens have been previously noted (37), and such patients face numerous barriers to lifestyle change. In particular, weight loss or maintenance may be more difficult among persons with diabetes due to the weight gain associated with some antidiabetes medications and insulin, the risk of hypoglycemia with weight loss (particularly if medications are not adjusted proactively), and the mental

and emotional effects of previous failed weight loss attempts (38-40). If lifestyle change is more difficult in patients with diabetes, it highlights the importance of intervention early in the natural history of the disease.

The strengths of our study include the examination of a lifestyle change program within a national healthcare setting, and a study population large enough to examine associations with the development of diabetes complications. The limitations include the observational nature of the data, with a potential for confounding. However, detailed electronic health record data allowed for adjustment for differences in known clinical risk factors, and a propensity score approach was used to further minimize confounding by measured variables. In addition, some veterans receive care outside of the VA, and some diagnoses and medications may not be recorded in VA databases. To minimize this potential source of misclassification, we restricted analyses to veterans receiving at least 3 continuous years of outpatient care in the VA, in order to ensure that included patients had substantial and consistent contact with the VA system. We were also not able to account for increases in dosage in our examination of medication intensification. However, our definition of medication intensification as 'initiation of a new medication' is consistent with prior work (23).

In conclusion, this study demonstrates that participation of patients with diabetes in a healthcare system-based lifestyle change program was associated with a reduced incidence of diabetes complications. In addition, participation was associated with improved weight, blood pressure, and A1c levels despite reduced intensification of diabetes medications. Lifestyle change programs, which are already recommended to be

offered through healthcare systems for diabetes prevention among high-risk individuals, may also be beneficial for the growing population of diabetes patients in the US.

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**Figure 6.1. Study Population**

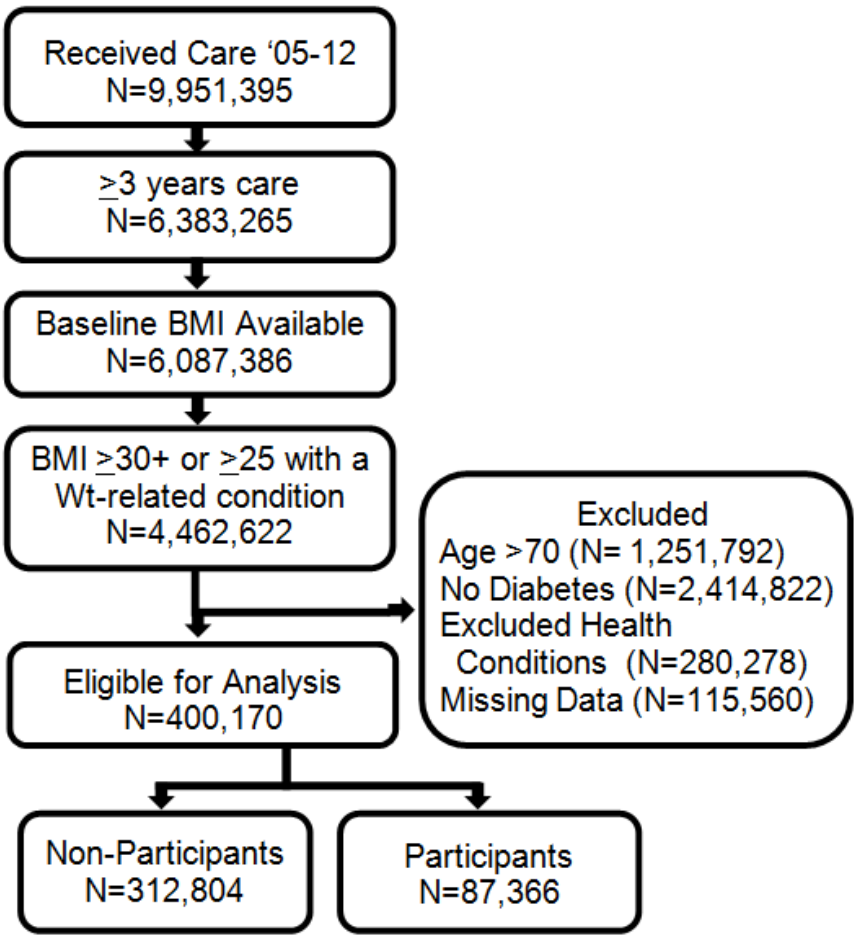

**Table 6.1. Characteristics of Participants and Eligible Non-Participants with DM, 2005-2012**

| | All | Non-Participants | Participants |
|---|---|---|---|
| | N=400,170 | N=312,804 | N=87,366 |
| Age at baseline | 58.44 ± 7.68 | 58.48 ± 7.68 | 58.30 ± 7.71 |
| Sex | | | |
| Male | 95.85% | 96.69% | 92.82% |
| Female | 4.15% | 3.31% | 7.18% |
| Race | | | |
| White | 77.14% | 78.36% | 72.77% |
| African American | 18.34% | 17.07% | 22.88% |
| Other | 4.52% | 4.57% | 4.34% |
| BMI at baseline, mean | 33.99 ± 6.16 | 33.06 ± 5.62 | 37.33 ± 6.82 |
| 25-29.9 | 28.51% | 33.31% | 11.34% |
| 30-34.9 | 35.36% | 36.71% | 30.53% |
| 35.0-39.9 | 21.16% | 19.07% | 28.65% |

| | | | |
|---|---|---|---|
| ≥40 | 14.97% | 10.91% | 29.48% |
| Baseline eye disease | 16.89% | 14.61%% | 25.07% |
| Baseline renal disease | 6.63% | 4.92% | 12.73% |
| Baseline Oral Antidiabetic Medication | 69.33% | 66.67% | 78.89% |
| Baseline Insulin | 22.02% | 19.15% | 32.28% |
| Baseline HbA1c* | 7.50% | 7.48% | 7.56% |
| Baseline RPG† | 156.08 | 157.25 | 152.66 |
| Charlson Comorbidity Index | | | |
| 0 Point | 72.10% | 76.47% | 56.46% |
| 1 Point | 17.65% | 15.43% | 25.59% |
| 2+ Points | 10.25% | 8.10% | 17.96% |
| Hypertension | 80.52% | 78.31% | 88.43% |
| Dyslipidemia | 70.07% | 67.02% | 80.99% |
| Mental health conditions | | | |
| Depression | 25.24% | 20.44% | 42.45% |
| Psychoses | 21.50% | 17.17% | 36.99% |

| | | | |
|---|---|---|---|
| PTSD | 12.01% | 9.17% | 22.18% |
| Smoking Status | | | |
| Current Smoker | 29.98% | 30.86% | 26.80% |
| Former Smoker | 37.53% | 37.27% | 38.48% |
| Lifetime Non-smoker | 32.49% | 31.87% | 34.71% |
| Rx for weight loss medication | 21.99% | 21.73% | 22.95% |
| Married | 62.18% | 63.50% | 57.46% |
| No Service Connected Disability | 49.13% | 51.27% | 41.48% |
| No. primary care visits/year | 4.26 ± 2.55 | 4.06 ± 2.41 | 4.97 ± 2.90 |
| No. years with a visit | 9.87 ± 3.32 | 9.84 ± 3.35 | 10.00 ± 3.21 |
| Average Distance to MOVE Clinic | 43.64 ± 32.74 | 44.45 ± 32.88 | 40.76 ± 32.08 |

*For baseline HbA1c, N=274,474 for all, N=200,209 for nonparticipants, and N=74,265 for participants. †For baseline RPG, N=319,964 for all, N=238,054 for nonparticipants, and N=81,910 for participants. ±values are means ±SD. All associations between patient characteristics and MOVE participation were significant ($p < 0.001$), according to chi-squared tests (categorical variables) and ANOVA (continuous variables).

**Table 6.2. Population Marginal Mean Random Plasma Glucose and Hemoglobin HbA1c over 6-36 Months, Stratified by Participation**

| **Table 6.2a: Participants vs. Non-participants** | | | | |
|---|---|---|---|---|
| | 6 Months | 12 Months | 24 Months | 36 Months |
| **Weight (kg)** | | | | |
| Non-participants | 105.84 | 105.49 | 104.84 | 103.83 |
| Participants | 105.38 | 104.91 | 104.25 | 103.54 |
| Difference | 0.46 | 0.58 | 0.59 | 0.29 |
| **RPG (mg/dL)** | | | | |
| Non-participants | 148.28 | 148.56 | 148.46 | 149.28 |
| Participants | 145.33 | 145.76 | 146.83 | 148.48 |
| Difference | 2.95 | 2.80 | 1.63 | 0.80 |
| **HbA1c (%)** | | | | |
| Non-participants | 7.45 | 7.53 | 7.54 | 7.62 |
| Participants | 7.38 | 7.43 | 7.50 | 7.57 |
| Difference | 0.07 | 0.10 | 0.04 | 0.05 |
| **Table 6.2b: "Intense and Sustained" and "Less Active" vs. Non-participants** | | | | |

| | 6 Months | 12 Months | 24 Months | 36 Months |
|---|---|---|---|---|
| **Weight (kg)** | | | | |
| Non-participants | 105.85 | 105.49 | 104.84 | 103.83 |
| Less Active | 105.58 | 105.10 | 104.40 | 103.67 |
| Intense and Sustained | 103.81 | 103.44 | 102.96 | 102.48 |
| **RPG (mg/dL)** | | | | |
| Non-participants | 148.31 | 148.59 | 148.48 | 149.29 |
| Less Active | 146.08 | 146.33 | 147.26 | 148.84 |
| Intense and Sustained | 138.76 | 140.83 | 143.12 | 145.34 |
| **HbA1c (%)** | | | | |
| Non-participants | 7.45 | 7.53 | 7.54 | 7.62 |
| Less Active | 7.41 | 7.45 | 7.52 | 7.58 |
| Intense and Sustained | 7.16 | 7.28 | 7.39 | 7.43 |

Least square means compute averages controlled for baseline value, baseline BMI, baseline age, gender, race/ethnicity, and baseline medication status (oral antidiabetes medications and/or insulin). For weight, N=15,885 at 6 months, 317,129 at 12 months, 280,996 at 24 months, and 242,766 at 36 months. For RPG, N=227,144 at 6 months, 230,508 at 12 months, 204,690 at 24 months, 177,611 at 36 months. For HbA1c,

N=187,810 at 6 months, 190,126 at 12 months, 167,636 at 24 months, and 144,876 at 36 months. All differences were significant between participants and nonparticipants ($p<.001$) in Table 2a, and across participation levels (non-participation, less active participation, and intense and sustained participation) in Table 2b ($p<.001$).

**Table 6.3. Incidence of Diabetes Complications and Medication Intensification**

| | Eye Disease | | Renal Disease | | Medication intensification | |
|---|---|---|---|---|---|---|
| | N=332,571 | | N=373,643 | | N=400,170 | |
| | HR | CI | HR | CI | HR | CI |
| MOVE Participation | 0.80 | 0.76-0.85 | 0.90 | 0.86-0.93 | 0.81 | 0.79-0.83 |
| Age at baseline | 1.01 | 1.01-1.01 | 1.03 | 1.03-1.03 | 0.99 | 0.99-0.99 |
| Female | 0.81 | 0.76-0.86 | 0.78 | 0.71-0.85 | 0.83 | 0.80-0.86 |
| Race (ref=White) | | | | | | |
| African American | 1.19 | 1.11-1.27 | 1.45 | 1.39-1.51 | 0.97 | 0.94-0.99 |
| Other | 1.11 | 1.03-1.20 | 1.02 | 0.96-1.09 | 0.96 | 0.92-1.00 |
| BMI at baseline | 0.99 | 0.99-1.00 | 1.02 | 1.01-1.02 | 1.00 | 1.00-1.00 |
| Baseline kidney disease | 1.13 | 1.10-1.18 | - | - | 0.88 | 0.86-0.90 |
| Baseline eye disease | - | - | 1.31 | 1.27-1.35 | 0.98 | 0.97-1.00 |
| Insulin at baseline | 2.10 | 2.03-2.17 | 1.67 | 1.63-1.71 | 0.30 | 0.28-0.31 |
| Oral Antidiabetes Rx at baseline | 1.23 | 1.20-1.26 | 1.08 | 1.05-1.10 | 0.86 | 0.83-0.88 |

| | | | | | | |
|---|---|---|---|---|---|---|
| Rx for weight loss | 1.29 | 1.25-1.33 | 1.33 | 1.29-1.37 | 2.51 | 2.43-2.60 |
| Hypertension (ICD-9) | 1.05 | 1.03-1.08 | 1.40 | 1.37-1.44 | 0.98 | 0.97-1.00 |
| Dyslipidemia (ICD-9) | 0.92 | 0.90-0.95 | 1.04 | 1.01-1.07 | 0.95 | 0.94-0.96 |
| Service connected disability (ref=none) | | | | | | |
| 0-20% | 1.04 | 1.01-1.07 | 0.85 | 0.82-0.88 | 0.96 | 0.95-0.98 |
| 30-60% | 1.08 | 1.05-1.12 | 0.86 | 0.84-0.89 | 1.00 | 0.98-1.02 |
| 70-100% | 1.25 | 1.20-1.29 | 1.11 | 1.07-1.14 | 1.08 | 1.05-1.10 |

Models also controlled for Charlson Comorbidity Index, smoking status, coronary artery disease, COPD, osteoarthritis, mental health conditions (depression and psychoses), distance from a patient's zipcode to a facility offering MOVE, marital status, number of primary care visits per year, and years of care in the VA system. Other factors considered for inclusion in analysis but omitted through AIC model selection included heart failure, PTSD, alcohol abuse, and drug abuse. Models were adjusted for clustering by clinic, and included propensity scores to adjust for likelihood of MOVE participation. Hazard ratios reflect 1-unit change for continuous variables.

**Table 6.4. Incidence of diabetes complications and medication adjustment, further adjusting for baseline HbA1c, among subsets with laboratory measurements available**

| | Eye Disease | | Renal Disease | | Medication intensification | |
|---|---|---|---|---|---|---|
| | N=218,935 | | N=251,295 | | N=272,589 | |
| | HR | CI | HR | CI | HR | CI |
| MOVE Participation | 0.85 | 0.80-0.90 | 0.94 | 0.90-0.98 | 0.88 | 0.86-0.91 |
| Baseline HbA1c | 1.16 | 1.15-1.17 | 1.06 | 1.05-1.06 | 1.19 | 1.18-1.20 |
| Baseline Systolic BP | 1.01 | 1.01-1.01 | 1.01 | 1.01-1.01 | 1.00 | 1.00-1.00 |

Models identical to Table 3, but including addition adjustment of HbA1c, and restricted to patients with available data for laboratory measures. Models also controlled for Charlson Comorbidity Index, smoking status, coronary artery disease, COPD, osteoarthritis, mental health conditions (depression and psychoses), distance from a patient's zipcode to a facility offering MOVE, marital status, number of primary care visits per year, and years of care in the VA system. Other factors considered for inclusion in analysis but omitted through AIC model selection included heart failure, PTSD, alcohol abuse, and drug abuse. Models were adjusted for clustering by clinic, and included propensity scores to adjust for likelihood of MOVE participation. Hazard ratios reflect 1-unit change for continuous variables.

**Table 6.5. Incidence of diabetes complications and medication intensification, by level of MOVE participation**

| | Eye Disease | | Renal Disease | | Medication intensification | |
|---|---|---|---|---|---|---|
| | N=332,571 | | N=373,643 | | N=400,170 | |
| | HR | CI | HR | CI | HR | CI |
| MOVE Participation | | | | | | |
| Less Active | 0.79 | 0.75-0.84 | 0.90 | 0.87-0.94 | 0.82 | 0.80-0.84 |
| Intense & Sustained | 0.85 | 0.78-0.93 | 0.84 | 0.76-0.92 | 0.70 | 0.66-0.74 |

Models identical to Table 3, but examining two levels of MOVE participation. Models also controlled for Charlson Comorbidity Index, smoking status, coronary artery disease, COPD, osteoarthritis, mental health conditions (depression and psychoses), distance from a patient's zipcode to a facility offering MOVE, marital status, number of primary care visits per year, and years of care in the VA system. Other factors considered for inclusion in analysis but omitted through AIC model selection included heart failure, PTSD, alcohol abuse, and drug abuse. Models were adjusted for clustering by clinic, and included propensity scores to adjust for likelihood of MOVE participation. Hazard ratios reflect 1-unit change for continuous variables.

**Table 6.6. Initiation of Oral Antidiabetes Medication and Insulin**

| | Initiation of oral medication | | Initiation of insulin | |
|---|---|---|---|---|
| | N=122,714 | | N=312,060 | |
| | HR | CI | HR | CI |
| MOVE Participation | 0.78 | 0.75-0.82 | 0.96 | 0.93-0.99 |

Models also controlled for Charlson Comorbidity Index, smoking status, coronary artery disease, COPD, osteoarthritis, mental health conditions (depression and psychoses), distance from a patient's zipcode to a facility offering MOVE, marital status, number of primary care visits per year, and years of care in the VA system. Other factors considered for inclusion in analysis but omitted through AIC model selection included heart failure, PTSD, alcohol abuse, and drug abuse. Models were adjusted for clustering by clinic, and included propensity scores to adjust for likelihood of MOVE participation. Hazard ratios reflect 1-unit change for continuous variables.

# Chapter 7: Summary and Conclusions

## *Summary of Findings*

Given the vast health and economic burden of obesity, diabetes, and cardiovascular disease in the US, this dissertation examined a large-scale, healthcare system-based lifestyle change program and its association with cardiometabolic health outcomes. We observed that participation in MOVE! was associated with a lower incidence of diabetes, a lower incidence of cardiovascular disease, and – among patients with diabetes – improved diabetes management despite lower medication intensification.

We first examined the association of program participation with patterns of weight loss and diabetes incidence. The most engaged participants, "intense and sustained" participants, lost -2.8% of their body weight at 12 months, while less active participants lost -0.7%, and eligible non-participants gained 0.2%. Among patients without diabetes at baseline, there was a significant, dose-dependent inverse association between participation in the VA's MOVE! program and diabetes incidence , which persisted after adjustment for demographic and clinical characteristics including baseline age, BMI, comorbidities, and frequency and duration of contact with the VA health system. Compared with lack of participation, intense and sustained participation was associated with 33% lower diabetes incidence, and less active participation was associated with 20% lower incidence. These observations are consistent with trials that have shown weight loss and lower diabetes incidence with lifestyle change.(1-3) In addition, our subgroup analyses suggested that while results were consistent across

gender, race/ethnicity, and age categories, lifestyle change program participation may be particularly beneficial for patients at higher risk of diabetes – those with higher BMI, and those with higher RPG.

While there is considerable evidence supporting the potential for lifestyle change programs to impact weight loss and diabetes incidence,(1, 4-5) few studies have examined their potential to impact cardiovascular disease, and existing evidence is mixed. (6-11) Given this knowledge gap, we next examined the association between MOVE! participation and cardiovascular disease incidence among patients without cardiovascular disease at baseline. Participation in MOVE! was associated with 17% lower total CVD incidence, 19% lower CAD incidence, 13% lower CBD incidence, 11% lower PVD incidence, and 22% lower HF incidence. Our findings were consistent with clinical trials that have demonstrated improvements in cardiovascular risk factors among lifestyle change program participants. However, our results contrasted with the findings in the Look AHEAD study, which demonstrated substantial weight loss and improvement of CVD risk factors, but did not demonstrate reduced CVD incidence.(12) However, Look AHEAD was conducted entirely among participants with diabetes, and we observed a more modest association between MOVE! participation and CVD incidence among participants with diabetes than those without diabetes. In addition, it has been suggested that the Look AHEAD findings may have been confounded by differential statin use and weight loss in the controls.(12-13)

For our third aim, given the large and growing population of US adults with diabetes, we examined whether MOVE! participation was associated with improved diabetes management among patients with diabetes at baseline. We observed that

participation was associated with a 20% lower incidence of eye disease, 10% lower incidence of renal disease, and lower HbA1c levels despite 19% lower medication intensification. Our observations are consistent with other studies that have shown reduced medication usage and other benefits among lifestyle change program participants with diabetes.(14-15) These findings add to the limited body of work examining the impact of lifestyle change on diabetes complications.(8)

Overall, this dissertation adds to the evidence supporting the health benefits of participation in lifestyle change programs. Although the MOVE! program faces challenges such as limited session attendance among participants, our inclusive definition of participation (attending at least one session) was associated with measureable benefit with regard to diabetes and cardiovascular disease incidence and diabetes management. This dissertation offers insight into the potential impact of a large-scale, healthcare-based lifestyle change program.

### *Limitations*

One limitation of this dissertation is the potential for confounding, due to the observational nature of the data. For these analyses, the ideal counterfactual would compare MOVE! participants with *similar persons* who did not participate. This would eliminate confounding due to the inherent differences involved in comparing participants who, to some extent, are self-selecting, to non-participants. In observational studies, confounding by indication occurs when prognostic factors influence treatment decisions. For example, if referral to or participation in MOVE! is more likely among patients who have been diagnosed with prediabetes or who have diabetes risk factors, then this

increased diabetes risk among participants compared to non-participants may confound the association between MOVE! and diabetes. Although it is impossible to rule out confounding by unmeasured factors, we employed three main strategies to address confounding by measured variables: (**i**) an extensive set of ***clinical inclusion/exclusion criteria***, and sensitivity analyses to evaluate the effects of these criteria; (**ii**) an ***extensive set of control variables***, including baseline comorbidities, demographic and clinical characteristics, and factors such as glucose levels, smoking status, whether a patient was taking medications with weight gain risk, and how frequently a patient interacted with the VA health system, and (**iii**) chapters 5 and 6 employed a ***propensity score*** approach to adjust for likelihood of participation in MOVE!.

Another limitation of these analyses is the potential for misclassification. Some veterans receive care outside of the VA, making it possible that some diagnoses, procedures, and medications may not be reported within the VA health system. However, our requirement for at least 3 years of consistent outpatient care at the VA assured multiple opportunities for reporting diagnoses made outside the VA, and made it more likely that the study population was receiving a substantial amount of their care from the VA. An alternative approach would be to combine both VA and Medicare data, which is an established approach,(16) but was beyond the scope of the current research.

In addition, these analyses did not examine mortality. This could lead to misclassification (for example, if a fatal CVD event was not coded with ICD-9 codes for CVD, and was thus missed by our analyses). Mortality could lead to bias if risk of death differed between participants and non-participants. However, our analyses did exclude patients at the highest risk of death (as indicated by hospice care, malignant cancer, and

other conditions considered exclusionary for MOVE! participation). In order to address mortality more specifically, VA vital status data could be examined, but that was beyond the scope of our study.

A further potential limitation of the study is the differential assignment of baseline, in which baseline was assigned for non-participants as the first visit with a recorded weight after 2005 (the first year of MOVE! rollout), and for participants as their first MOVE! visit. This strategy allowed for control of baseline factors among participants at the time of MOVE! participation (for example, exact age and weight at the beginning of participation). In sensitivity analysis, results remained largely unchanged after adjusting for baseline year. Adjusting for baseline year as a categorical variable allowed for potential nonlinear effects of changes in patient care over time, such as shifts in the use of rosiglitazone for diabetes. However, an alternative approach would be to assign baseline as the first visit after 2005 among all patients, and examine associations with MOVE! participation as a time-varying covariate. Such an approach would also require accounting for covariates at the time of MOVE! participation via inclusion of numerous time-varying covariates, and would become quite complex. Another alternative approach would be to compare participants against ‘baseline-matched’ non-participants by proportionally assigning non-participant baseline years in comparable ratios to the baseline years of MOVE! participants.

### *Strengths*

A key strength of this study was our ability to leverage existing data from the VA health system to evaluate the *largest national implementation* of a lifestyle change program, for which there were no previous reports of impact on diabetes-related or cardiovascular health outcomes. Integration of lifestyle interventions within the realm of clinical care has been recommended for weight management and prevention or delay of chronic diseases, yet real-world evidence has been lacking.(17-18) Another strength of this study was our ability to examine health outcomes, including cardiovascular disease and diabetes complications, given our large sample size and observation period of up to 8 years. Many studies of lifestyle change programs only examined associations with changes in cardiovascular risk factors, and studies including macrovascular or microvascular outcomes are relatively scarce. (6, 8-9, 11)

### *Implications*

This dissertation addressed a knowledge gap by examining a healthcare-based lifestyle change program that has been implemented on a national scale. Despite the scope of the VA's MOVE! program – implemented in over 100 healthcare facilities and with over 400,000 participants – to our knowledge, no other national-level studies have examined the potential impact of healthcare-based lifestyle change programs on cardiometabolic health outcomes.

Investigating MOVE! offered a unique opportunity to examine what can be achieved in a healthcare setting, in a program that was designed to be easily implemented

with limited resources. When VA facilities were mandated to implement MOVE!, they were provided with a "toolkit" of materials (curriculum, handouts, administrative documents, etc), but there were no additional financial resources allocated to assist facility implementation efforts. A study of best practices has indicated that facilities with better weight loss outcomes used the standard MOVE! curriculum and a group delivery format.(19) Other characteristics associated with better outcomes included high program complexity and high staff involvement, an active physician champion, use of quality-improvement strategies, and having sufficient class availability that a waiting list was not required for veterans to enroll.(19)

Increasing the program's reach and the number of sessions attended by participants has been identified as an ongoing challenge of the MOVE! program,(20) as greater weight loss has been observed among participants who engage more extensively.(21-22) Our results are consistent with prior work highlighting the importance of more extensive participation, as we observed greater weight loss among "intense and sustained" participants over three years, as well as a dose-response effect linking more intense participation to a greater reduction in diabetes and cardiovascular disease incidence. The VA has also recognized the importance of enhancing participation. In 2008, the VA amended their regulations to remove co-payments for individual and group-based weight management counseling, with the direct intent of increasing participation in MOVE!.(23) A subsequent study confirmed that implementation of this policy was followed by a modest increase in MOVE! participation. Interestingly, MOVE! participation increased by 2% among patients newly exempt from the copayment, and by 12% among patients who were already eligible for

free care.(24) In addition to the elimination of copayments, it is possible that the increases observed were due to better promotion of the program and new implementation of an obesity screening quality of care indicator.(24)

Limited participation may partially explain why weight loss and associations with diabetes incidence were more modest than have been reported in other studies.(1-3) As discussed in Chapter 4, on a per-session-attended basis, weight loss associated with MOVE! was comparable to the amounts observed in community-based translations of the DPP.(5) Unfortunately, effective strategies to increase the number of sessions attended remain elusive. Some researchers have proposed implementing financial incentives for participation,(24) and the VA has begun tracking percentage of "intense and sustained" MOVE! participants as a quality of care indicator. In response to national policy, the Atlanta VA Medical Center has restructured its enrollment procedures to encourage participants to attend multiple sessions, and has observed an increase in the proportion of patients meeting intense and sustained participation criteria.(25) However, the potential impact of such national and local policies on participation remains unknown. In addition, there may be many challenges to overcome if facilities attempt to increase the intensity of patient involvement in MOVE!: one facility that has done so reported a variety of hurdles, including allocating limited resources in a context of existing care backlogs, conflicts in scheduling program sessions around space availability and staff duty assignments, and communication difficulties due to staff turnover and trainee involvement.(26)

In addition to facility-level difficulties in implementing more "intense and sustained" participation, some questions remain regarding the benefit of this level of

engagement. Although we observed a strong dose-response effect for diabetes incidence across participation levels, only a slight dose-response effect was observed for cardiovascular disease. One explanation for this observation may be that, compared to the development of cardiovascular disease, the development of diabetes is more sensitive to incremental changes in physical activity and diet. Indeed, even in the absence of weight loss, changes in physical activity and dietary intake have been shown to increase insulin sensitivity.(27-29) In addition, instruction in proper dietary intake has been associated with improvement in HbA1c without change in weight.(30)

Despite uncertainties regarding optimal participation targets, it should be noted that even the current level of MOVE! participation was associated with clinically meaningful and statistically significant, if modest, reductions in weight, cardiometabolic risk factors, diabetes and cardiovascular disease incidence, and improved diabetes management. As compared to clinical and community-based lifestyle change trials, this study is important because participants were not *subjects who volunteered for a research trial,* but *patients recommended by their primary care providers to engage in lifestyle change*. It has been suggested that, compared to clinical trials, healthcare system-based translations of lifestyle change programs may need to be considerably less resource-intensive (requiring less time and commitment from both participants and service providers) in order to facilitate widespread implementation.(31-32)The amount of participation observed, and associated modest weight loss and health outcomes, may be indicative of achievable results in scaled-up programs. Patient compliance with lifestyle change recommendations for the prevention and management of chronic diseases is notoriously low,(33) and may be a challenge to the effectiveness of lifestyle change

programs if they are broadly implemented as recommended by the Affordable Care Act.(34) In addition, certain patient populations, such as those with diabetes, may face additional barriers to weight loss.(8, 35-37). For example, patients with diabetes may have greater difficulty achieving weight loss or maintenance due to the weight gain associated with use of some antidiabetes medications and insulin, the risk of hypoglycemia with weight loss, and the emotional effects of previous failed weight loss attempts.(38-40) Such considerations would need to be addressed if lifestyle change programs are to be broadly implemented.

In addition to further investigations of clinical benefit among target populations, there is also a need for cost-effectiveness analysis of lifestyle change programs such as MOVE!. Obesity, diabetes, and cardiovascular diseases are costly conditions, and programs that reduce disease incidence or improve disease management may have considerable cost implications. There is substantial interest in the cost effectiveness of lifestyle change programs and disease management programs in numerous contexts, including community-based interventions, health system-based programs, and workplace wellness programs.(41-43) While the highly effective and intensive Diabetes Prevention Program was cost-effective,(44) the potential cost effectiveness of the less intensive MOVE! program remains unknown. Future research could examine the association between MOVE! participation and VA outpatient, inpatient, and pharmacy costs in a number of ways. For example, one could investigate whether the observed association between MOVE! participation and lower incidence of diabetes complications and lower medication intensification corresponds to lower costs among MOVE! participants with diabetes compared to non-participants. As end-stage renal disease is one of the most

costly chronic conditions among VA patients, even a slight reduction in incidence may translate to considerable potential savings.(45) Information about the costs of the MOVE! program, any potential cost savings associated with the program, and associated clinical benefits could be useful both for VA evaluations of MOVE! and for other health systems considering implementation of lifestyle change programs.

In addition to cost-effectiveness analyses, there are numerous additional avenues for future research:

- There are some indications that lifestyle change programs may be less effective among minorities. For example, one local investigation of the MOVE! program found that African American participants lost less weight than others.(21) Although our results demonstrated a significant association between MOVE! participation and health outcomes across racial/ethnic groups, a future study could specifically investigate disparities in participation rates, weight loss, change in cardiometabolic risk factors, and health outcomes.

- Although our analyses did not include patients over age 70, due to MOVE! age targeting, future research could examine the effect of differences in age on health outcomes. This is particularly important, given that the DPP observed a strong effect of lifestyle change among elderly participants.

- Since participation is a key challenge of the program, a qualitative methods study could provide valuable insights that might support

development of strategies to enhance initial participation rates as well as to increase the intensity of engagement among participants. For example, such a study could investigate barriers to participation among eligible non-participants, as well as barriers to intense and sustained participation among less active participants in the program.

- Even among intense and sustained participants, we observed that a substantial percentage (approximately 40%) did not lose more than 1% body weight. A mixed methods study could investigate perceptions and experiences among "responders" who lose weight in the program compared to "nonresponders" who do not lose weight, as well as programmatic aspects associated with greater weight loss. In addition, future research could examine whether individual characteristics assessed with the MOVE!23 intake questionnaire, or the revised and shortened MOVE!11 questionnaire, could be used to identify likely responders vs. non-responders. Such information could be very useful for quality improvement efforts or program targeting.

- A quantitative study could examine the impact of amount of weight lost on incidence of diabetes, cardiovascular disease, and diabetes management. In addition, the impact of reduction in weight on levels of glucose or HbA1c could be evaluated.

- The association between MOVE! participation and other weight-related health conditions could also be examined, such as the incidence of sleep

apnea and osteoarthritis. In addition, the association between MOVE! participation and depression incidence, or use of antidepressant medications among participants with baseline depression, could be investigated. Lastly, the association between MOVE! participation and mortality could be examined.

- While our analyses were adjusted for clustering at the facility level, future research could explore facility-level variation in implementation and MOVE! outcomes, including an examination of geographic variation in implementation, variation in amount of weight lost by participants, and impact of MOVE! on health outcomes in facilities with high average weight loss (or high participation rates) compared to less effective facilities.

The public health implications of this dissertation research and any future studies about MOVE! are potentially far-reaching. Nearly three out of four veterans receiving care in the VA are overweight or obese,(46) so an estimated 6 million veterans could benefit from this research,(47) in addition to the many millions of patients in other healthcare systems that could implement similar programs.

### *Summary*

In summary, this dissertation addresses a gap in the literature by investigating a large-scale, healthcare system-based lifestyle change program. The key findings indicate that participation in MOVE! may offer broad health benefits; participation was associated

with lower diabetes and cardiovascular disease incidence among patients without these problems at baseline, and improved diabetes management among participants with diabetes at baseline. As over 85% of Americans have health insurance, (48) healthcare system-based implementation of lifestyle change programs may be an attractive opportunity to scale up and achieve wider reach. With the increased emphasis on prevention in the Affordable Care Act,(34) implementation of MOVE!-type lifestyle change programs through such systems might be beneficial to improving the health of people nationwide.

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