Changes in Glucose Homeostasis and Systemic Inflammation Following an 8-week Exercise Only and 8-week Exercise Plus Dietary Weight Management Intervention among Overweight and Obese African American Older Adults with Osteoarthritis

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Background. Obesity is associated with impaired fasting blood glucose, insulin resistance (IR) and low-grade inflammation, all of which are risk factors for chronic diseases including type 2 diabetes (T2D). Glucose metabolism and inflammation can be modified with lifestyle changes, although few studies have examined the impact of behavioral lifestyle interventions conducted in a "real world" community-based setting on these parameters in overweight and obese older African American (AA) adults with osteoarthritis (OA). The aim of this study was to examine the impact of an 8-week exercise only and 8- week exercise plus dietary weight management intervention on glucose metabolism and systemic inflammation in older overweight and obese AA adults with pre-existing lower extremity OA.

Methods. Participants were randomized to an 8-week exercise-only (n=59) or exercise plus dietary weight management (n=48) intervention. Baseline and post-intervention body measures (weight, BMI, and percent body fat) and fasting serum glucose, serum insulin, high sensitivity C-reactive protein and interleukin-6 were assessed. The homeostatic model assessment of insulin resistance (HOMA-IR) was also calculated. Demographic and health-related data were obtained via questionnaire at baseline. Generalized estimating equations to compare changes from baseline adjusted for BMI and Spearman's correlation examining the relationship between change in body measures and change in inflammation and glucose metabolism were also examined.

Results. The participants were predominately female (86%) with mean age of 67.1 (± 5.6) years and mean BMI of 34 kg/m^2 (95% Confidence Interval: 31.9 – 36.1 kg/m^2). Participants in the exercise plus dietary weight management group lost significantly more weight on average than those in the exercise-only group (-2.0 vs. -0.1 kg; $p < 0.001$). There was no significant between-groups change in markers of inflammation or glucose metabolism, although a clinically meaningful 5% (-5.1 mg/dl) decline in glucose from baseline was observed in the exercise plus dietary weight management group.

Conclusions. An 8-week exercise plus dietary weight management intervention has potential clinical relevance in regard to improving both body weight and glucose metabolism in a population at elevated risk for T2D and its related complications.

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A large percentage of United States (US) citizens are overweight and obese, including older adults. According to a recent national survey, almost 70% of all US adults over the age of 60 are overweight ($25 < BMI < 30$ kg/m^2) or obese ($BMI > 30$ kg/m^2) based on body mass index (BMI), with older African American adults disproportionately burdened.[1] Excess body weight is an established risk factor for a multitude of chronic diseases including cardiovascular disease, several cancers, and type 2 diabetes (T2D).[2] Obesity is also associated with increased risk for debilitating chronic musculoskeletal conditions including osteoarthritis (OA).[3,4] Thus, as the US demographic profile shifts to a larger population of older adults, the public health burden of overweight and obesity-related chronic diseases including OA and T2D will increase dramatically.[2]

Excess adiposity is the single best predictor of T2D risk.[5] Almost 90% of people with T2D are overweight or obese.[6] Further, African Americans are at greater risk for developing T2D compared to other racial/ethnic groups in the US.[7] Obesity is linked to T2D through several proposed biological mechanisms including increased systemic inflammation, changes to fatty acid metabolism that promotes visceral, hepatic, and skeletal muscle fat deposition, and mitochondrial dysfunction.[8,9] These obesity-related adverse changes, including systemic inflammation, promote insulin resistance and pancreatic β-cell dysfunction leading to the development of T2D.[8] Notably, obesity-related physical impairments stemming from disorders like OA can increase a person's risk for developing T2D,[10] the rationale being that OA can make it difficult to engage in healthy lifestyle behaviors including physical activity (PA) and exercise and consequently further promoting debilitation and weight gain.[3,11] Measuring fasting blood glucose is one of the most common screening and diagnostic methods to determine whether or not an individual has altered glucose homeostasis.[10] Impaired fasting blood glucose between 100 and 125 mg/dl indicates that an individual is experiencing metabolic abnormalities that are characteristic of pre-diabetes, while fasting blood glucose above 126 mg/dl is indicative of T2D.[12]

In highly controlled research settings, moderate intensity exercise and moderate intensity exercise plus lifestyle intervention have shown significant positive impact on glucose homeostasis in overweight and obese older adults.[13,14] Behavioral lifestyle interventions, including programs combining low intensity exercise with dietary weight management, have shown promise for reducing the adverse effects of overweight and obesity on glucose homeostasis. The Diabetes Prevention Program demonstrated that a combined low-impact exercise and weight management intervention was efficacious in lowering fasting blood glucose concentrations in persons with pre-diabetes, with a more pronounced effect in older versus younger participants.[15,16] Further, other comprehensive behavioral lifestyle interventions conducted with older overweight and obese adults with and without OA have demonstrated marked improvements in body weight, glucose homeostasis, and systemic inflammation.[15-17] However, for the most part, existing behavioral lifestyle interventions for obese individuals with and without comorbid conditions like pre-diabetes and OA have been conducted in highly controlled settings and not under "real world" conditions. Further, the majority of studies have examined intervention effects in predominately Caucasian participants.[13-18]

Although obesity and T2D are more prevalent among older minority adults, few studies have examined whether low intensity exercise coupled with lifestyle changes that promote weight loss, implemented in a "real world" community-based setting, can improve glucose metabolism and systemic inflammation in this population. Therefore, the aim of this investigation was to examine the impact of an 8-week exercise only and 8-week exercise plus dietary weight management intervention on biomarkers of glucose metabolism and systemic inflammation among overweight and obese African American older adults with OA. We also examined if changes in these biomarkers were associated with changes in body weight and body composition. It was hypothesized that fasting blood glucose, fasting insulin, insulin sensitivity based on homeostatic model assessment of insulin resistance (HOMA-IR) calculation and systemic inflammation would improve in both intervention groups, but significantly more in the combined exercise plus dietary weight management group. Also hypothesized was that changes in these biomarkers would be associated with reduced body weight and body fat.

Materials and Methods

Study design and participants

The *Customary Fit & Strong! (FNS!) versus Fit & Strong! Plus (FNS!+)* study is a randomized controlled trial, sponsored by the National Institutes of Health, designed to examine the comparative effect of exercise only versus exercise plus dietary weight management through community-based behavioral lifestyle interventions on body weight, diet quality, and osteoarthritis symptomatology in overweight and obese older adults with OA. As part of this study (herein referred to as the 'parent study'), an ancillary study was conducted to explore the intervention's effects on glucose homeostasis and systemic inflammation.

The parent study was designed to enroll and randomize 400 participants. Participants were recruited from neighborhoods located in the southeastern, western and northeastern regions of Chicago. Recruitment methods for the parent study included in-person recruitment by research staff and advertisement postings at partnering Chicago Park Districts and nearby senior housing/centers. Persons were screened over the phone for eligibility.

Eligibility criteria for the parent study included: 1) lower extremity OA determined by self-reported pain in or around the hips, knees, ankles, feet, or lower back; 2) > 60 years old; 3) not currently participating in an exercise program and engaging in < 150 minutes of moderate to vigorous physical activity per week; 4) BMI 25 - 50 kg/m^2; 5) agreeable to randomization; 6) willing to attend class at scheduled times; and 7) to participate in measurement and intervention procedures.

Exclusion criteria for the parent study included: 1) severe cardiovascular disease; 2) active thrombophlebitis; 3) recent pulmonary embolus; 4) acute systemic illness; 5) poorly controlled diabetes; 6) diagnosis of rheumatoid arthritis; 7) other health conditions that may preclude exercise training; 8) < 60 years of age; 9) BMI < 25 kg/m^2 or > 50.0 kg/m^2; 10) currently participating in an organized exercise program; 11) uncomplicated hip or knee surgery in past 6 months or complicated surgery in the past year; 12) plans for hip or knee surgery within the next year; 13) steroid injections in the lower extremities in the past 3 months; and 14) a score of 3 or more on the 9-item Mini Mental Status Questionnaire.[19]

Participants found to be eligible for the parent study and agreeing to enrollment were then invited and screened to participate in the ancillary study. In addition to the parent study eligibility and exclusionary criteria, the ancillary study employed the following eligibility criteria: 1) self-described as African American; 2) agreeable to venous blood draw and whole body dual energy absorptiometry (DXA) scan at baseline and post-intervention; 3) willing to travel to UIC for two study visits; 4) self-reported body weight ≤ 450 pounds due to the weight limitations of the DXA scanner; 5) willing to fast for at least 8 hours prior to the blood draw; 6) willing to refrain from certain medications that could confound blood test results; and 7) cancer-free within the past five years.

Both the parent and ancillary study procedures were reviewed and approved by the UIC Institutional Review Board. All participants signed an informed consent prior to participation in the parent and ancillary research studies.

Parent study interventions

The parent study is a randomized controlled trial with multiple participant assessments at baseline, post-intervention (8 weeks), and 6, 12, and 18 months follow-up. The parent study interventions are community-facility and group-based programs that last 8 weeks. Each class accommodates approximately 17 enrollees. Participants are randomized to participate in one of two interventions: *Customary FNS!* or *FNS!+*. Certified exercise instructors are trained to deliver the interventions. A comprehensive description of the parent study interventions has been published elsewhere.[20] A brief description of the lifestyle interventions follows.

Customary FNS! is an evidence-based physical activity/behavioral change lifestyle program that is recommended by the Centers for Disease Control and National Council on Aging for older adults with OA. This intervention addresses symptoms experienced by older adults with OA by improving muscle strength and bone integrity. The program strengthens participants' self-efficacy (SE) for exercise and exercise adherence while subsequently diminishing OA related symptoms. *Customary FNS!* is a group-based program that meets for 90 minutes, 3 times per week, for 8 weeks (24 sessions in total). The first 60 minutes focuses on multiple-component exercises including flexibility/balance (20 minutes), aerobics (20 minutes), and lower extremity strengthening using exercise bands and adjustable ankle weights (20 minutes). The remaining 30 minutes is dedicated to manual-based group discussion/health education with a focus on OA symptom management, during which participants are taught to manage pain and other OA related symptoms.

The *Fit & Strong! Plus* intervention puts equal emphasis on dietary weight management and exercise. It is a modified version of the *Customary FNS!* program in which there is an added component that addresses SE for dietary weight management behaviors adapted from the Diabetes Prevention Program Group Lifestyle Balance curriculum.[21] The *FNS!+* program condenses the exercise-related content of *Customary FNS!* and adds 16 topics that address dietary weight management behaviors to promote weight loss and weight loss maintenance. The program's goals are to increase healthy eating/diet quality, increase exercise and physical activity, decrease body weight by at least 5% at 6 months, and to maintain diet and PA changes over time. Participants are encouraged to increase consumption of fruits, vegetables, whole grains, low-fat dairy and lean protein while decreasing sugar-sweetened beverages and saturated fats. To boost SE for dietary weight management-related behaviors, participants are asked to keep detailed food diaries. The food diaries and periodic weigh-ins allow participants to track their progress.

Ancillary study measures and data collection

Participants attended data collection visits at the UIC Integrative Physiology Lab at baseline and within approximately 10 days after completing the 8-week intervention. To prepare for the research visits, participants were instructed to 1) refrain from consuming foods or beverages, except water, for at least 8 hours; 2) refrain from vigorous exercise for 24 hours; 3) refrain from dietary supplements; 4) refrain from certain medications including non-steroidal anti-inflammatory drugs, oral hypoglycemic agents and insulin; and 5) wear comfortable clothing free of excess metal for the DXA scan. Participants with a cold or flu or taking antibiotics in the past 7 days were scheduled at least one week after their course of antibiotics was completed or the cold/flu resolved. At each data collection visit, participants completed surveys, physical assessments, a venous blood draw and a whole body composition scan via DXA.

Table 1

Demographic Characteristics of Participants

	Fit & Strong! Plus (*n* = 48)	*Customary Fit & Strong!* (*n* = 59)	All (*n* = 107[a])
Age, y, mean (*SD*)	66.3 (5.0)	67.8 (6.0)	67.1 (5.6)
60-64, *n* (%)	24 (50%)	26 (44%)	50 (47%)
65-69, *n* (%)	14 (29%)	15 (25%)	29 (27%)
70-79, *n* (%)	9 (19%)	16 (27%)	25 (23%)
≥80, *n* (%)	1 (2%)	2 (3%)	3 (3%)
Sex, *n* (%)			
Female	42 (88%)	50 (85%)	92 (86%)
Male	6 (12%)	9 (15%)	15 (14%)
Education, y, mean (*SD*)	14.3 (1.5)	13.9 (2.2)	14.1 (1.9)
Not HS graduate, *n* (%)	1 (2%)	7 (12%)	8 (%)
HS graduate/GED, *n* (%)	7 (15%)	7 (12%)	14 (13%)
Some college or tech school, *n* (%)	24 (50%)	25 (42%)	49 (46%)
College graduate, *n* (%)	16 (33%)	20 (34%)	36 (34%)
Employment, *n* (%)			
Full-time	4 (8%)	2 (3%)	6 (6%)
Part-time	7 (15%)	5 (8%)	12 (11%)
Retired/not employed	37 (77%)	52 (88%)	89 (83%)
Marital status, *n* (%)			
Married	12 (25%)	12 (20%)	24 (22%)
Divorced	17 (35%)	21 (36%)	38 (36%)
Widowed	8 (17%)	12 (20%)	20 (19%)
Separated	3 (6%)	4 (7%)	7 (7%)
Never married	6 (12%)	10 (17%)	16 (15%)
Member of unmarried couple	2 (4%)	0 (0%)	2 (2%)
Income, median	$25,000	$25,000	$25,000
Insurance,[b] *n* (%)			
Medicare Part A only	10 (21%)	3 (5%)	13 (12%)
Medicare Parts A & B	16 (33%)	31 (53%)	47 (44%)
Medicaid	7 (15%)	5 (8%)	12 (11%)
Medicare HMO	5 (10%)	7 (12%)	12 (11%)
Private/supplemental	21 (44%)	27 (46%)	48 (45%)
Chronic conditions,[c] mean (*SD*)	2.6 (1.3)	3.2 (2.0)	2.9 (1.8)
Diabetes, *n* (%)	12 (25%)	17 (29%)	29 (27%)
Hypertension, *n* (%)	38 (79%)	49 (83%)	87 (81%)
Heart disease, *n* (%)	6 (12%)	9 (15%)	15 (14%)
Lung disease, *n* (%)	3 (6%)	4 (7%)	7 (7%)
Thyroid, *n* (%)	1 (2%)	4 (7%)	5 (5%)

[a]*n* = 95 for income. Data from iterations 2-6 of parent study.

[b]Percentage of participants reporting each type of insurance; some participants reported more than one type of insurance.

[c]Number of self-reported conditions (of 17) currently affecting health.

Demographics and health history
At baseline, demographic information including age, income, marital status, employment, educational attainment and health insurance coverage was collected and a medical history questionnaire was administered to obtain self-reported disease status and current medication use.

Anthropometric measures
All research staff members were trained in adult anthropometric assessment using standard protocols and certified by a master trainer. Participants were instructed to remove shoes, jewelry, eyeglasses, hats, hair ornaments, heavy clothing and to empty their pockets prior to anthropometric assessments. Height was measured to the nearest 0.5 cm in duplicate using a stadiometer (seca, Chino, CA). Weight was measured in duplicate to the nearest 0.1 kg using a digital scale (Tanita BWB 800, Arlington Heights, IL). Body fat was measured via DXA (GE Healthcare iLunar DXA, USA). If a participant was too large to fit within the regions of interest, a DXA half-body scan was completed and whole-body parameters were extrapolated by the machine.

Laboratory assays
Fasting venous blood samples were collected at baseline and post-intervention from each participant by a phlebotomist. Samples were processed within 30 minutes for serum or plasma and stored at -80º C until analysis.

Glucose homeostasis
Fasting serum glucose was assessed via spectrophotometry and serum insulin via immunoassay at Quest Diagnostics (Wood Dale, IL). The homeostatic assessment - insulin resistance model equation [HOMA-IR = fasting insulin (mU/L) x fasting glucose (mmol/L)/22.5] was calculated from measured fasting serum insulin and serum glucose.[22]

Systemic inflammation
Serum high sensitivity interleukin-6 (IL6) and high sensitivity C-reactive protein (hs-CRP) was assessed to evaluate systemic inflammation. IL-6 was analyzed at UIC via ELISA (R&D systems, Minneapolis, MN). High sensitivity CRP was analyzed at Quest Diagnostics (Wood Dale, IL) via nephelometry.

Data management and statistical analysis
Data was collected via paper-based questionnaire and entered into a Research Electronic Capture (RedCap) database. Prior to statistical analysis, data entry errors and the distribution of variables were assessed. Descriptive data is presented as means or geometric means and standard deviations (SD) or 95% confidence intervals (CI 95%) for the continuous normally and non-normally distributed variables and frequencies for the categorical variables. Because of their non-normal distribution, hs-CRP, IL6, glucose, insulin and HOMA-IR were log transformed. Differences by treatment group at baseline were assessed via t-test, chi-square test or a non-parametric equivalent. Between- and within-group changes from baseline to post-intervention, adjusted for BMI, were assessed using generalized estimating equations (GEE), a method that accounts for intra-individual correlation over time. Spearman rank correlations were used to examine the relationships between changes in body weight, body fat, inflammatory markers, fasting serum glucose, fasting serum insulin, HOMA-IR and class attendance. All analyses were conducted with SAS software (version 9.4, SAS Institute, Cary, NC).

Results

A total of 107 older overweight and obese African American adults with lower extremity OA were recruited from the parent study for the ancillary investigation. Forty-eight of the ancillary participants were randomized to the *Customary FNS!* (exercise-only) intervention and 59 participants were randomized to the *FNS!+* (exercise plus dietary weight management) intervention. A general description of the participant demographic and health characteristics are presented in Table 1. The mean age was 67.1 *(SD* = 5.6) years old, the majority of participants were female (86%), unemployed or retired (83%), and not married (78%). Eighty-one percent of participants reported having hypertension and twenty-seven percent reported having T2D at baseline. There was no difference in the frequency or number of comorbid chronic conditions between treatment groups. The groups were similar at baseline for sex, age, education, income, employment, marital status, and Medicaid enrollment.

Table 2

Customary Fit & Strong! and Fit & Strong! Plus Class Attendance

	Fit & Strong! Plus (*n* = 47)	*Customary Fit & Strong!* (*n* = 59)	All (*n* = 106[a])
Classes attended, %, mean (*SD*)	66.3% (27.1)	63.9% (32.3)	65.0% (30.0)
Range	4-100	0-100	0-100
Classes attended, *n*, mean (*SD*)[b]	15.8 (6.5)	15.1 (7.7)	15.4 (7.2)
Range	1-24	0-24	0-24
Attendance categories, *n* (%)			
< 25%	4 (9%)	12 (20%)	16 (15%)
25 - 50%	7 (15%)	4 (7%)	11 (10%)
50 - 75%	12 (26%)	12 (20%)	24 (23%)
≥ 75%	24 (51%)	31 (53%)	55 (52%)
Attended no classes, *n* (%)	0 (0%)	3 (5%)	3 (3%)

[a]Data from iterations 2-6 of parent study. Attendance was missing for one *Fit & Strong! Plus* participant.

[b]For most iterations, 24 classes were offered. In one iteration, two classes in the *Customary Fit & Strong!* group were skipped and could not be made up, and in another iteration one class was missed in the *Fit & Strong! Plus* group.

Table 3

Mean or Geometric Mean (95% CI) Clinical Values at Baseline and Post-intervention[a] by Treatment Group, Adjusted for Body Mass Index and Gender

	Fit & Strong! Plus			*Customary Fit & Strong!*			
	Baseline (n = 48)	Post-Intervention (n = 45)		Baseline (n = 59)	Post-Intervention (n = 56)		
	Mean (95% CI)	Mean (95% CI)	Change[b] (%)	Mean (95% CI)	Mean (95% CI)	Change[b] (%)	p[c]
Weight, kg	96.7 (89.7-103.6)	94.7 (87.8-101.6)	-2.0 (-2.0%)***	97.8 (92.2-103.4)	97.7 (92.0-103.3)	-0.1 (-0.1%)	<0.001
BMI, kg/m^2	34.0 (31.9-36.1)	33.2 (31.2-35.3)	-0.7 (-2.2%)***	34.1 (32.1-36.0)	34.0 (32.1-36.0)	0.0 (-0.1%)	<0.001
Body fat, %[d]	41.3 (39.8-42.9)	40.6 (38.9-42.3)	-0.7 (-1.8%)***	40.4 (39.1-41.8)	40.5 (39.2-41.9)	0.1 (0.2%)	0.02
hs-CRP, mg/L[e]	3.7 (2.4-5.6)	3.8 (2.6-5.7)	0.1 (3.5%)	3.4 (2.4-4.8)	3.2 (2.3-4.5)	-0.2 (-5.8%)	0.62
IL-6, pg/mL[e]	2.9 (2.4-3.6)	2.9 (2.3-3.7)	0.0 (-0.1%)	2.7 (2.3-3.2)	2.6 (2.2-3.1)	-0.1 (-3.5%)	0.77
Glucose, mg/dL[e]	106.2 (99.1-113.8)	101.1 (93.3-109.6)	-5.1 (-4.8%)	104.4 (98.7-110.4)	104.9 (98.2-112.0)	0.5 (0.5%)	0.18
Insulin µIU/mL[e]	11.1 (8.7-14.2)	10.1 (7.4-13.7)	-1.1 (-9.5%)	10.3 (8.0-13.3)	9.8 (7.8-12.4)	-0.5 (-4.7%)	0.69
HOMA-IR[e]	2.9 (2.2-3.8)	2.5 (1.8-3.5)	-0.4 (-14.1%)	2.7 (2.0-3.5)	2.5 (2.0-3.3)	-0.1 (-4.4%)	0.47

[a]From longitudinal GEE models adjusted for gender. At baseline, n = 106 for insulin and HOMA-IR. At follow-up, n = 100 for body fat, n = 98 for CRP, IL-6, glucose, insulin, HOMA-IR. Data from iterations 2-6 of parent study.

[b]Test for within-group difference in change from baseline to post-intervention visit:.

[c]Test for difference between groups in change from baseline to post-intervention visit.

[d]Adjusted for BMI and gender.

[e]Log-transformed to improve normality and adjusted for BMI. The values shown are geometric means adjusted for BMI and gender. BMI = body mass index; hs-CRP = high sensitivity C-reactive protein; IL-6 = interleukin-6; HOMA-IR = homeostatic assessment - insulin resistance model

*p < 0.05. ** p < 0.01. *** p < 0.001.

Table 4a

Spearman Correlations (r_s) between Change in Anthropometric and Clinical Variables in the Fit & Strong! Plus group (n = 45)

Change	BMI	Body fat	CRP	IL-6	Glucose	Insulin	HOMA-IR
Weight, kg	0.99[a]***	0.42[b]**	-0.17[c]	0.23[c]	0.29[c]	0.25[c]	0.29[c]
BMI, kg/m^2	1.0[a]	0.43[b]**	-0.15[c]	0.23[c]	0.30[c]	0.25[c]	0.30[c]
Body fat, %		1.0[b]	-0.10[d]	0.22[c]	0.23[d]	-0.08[d]	0.02[c]
hs-CRP, mg/L			1.0[c]	0.31[c]*	0.03[c]	-0.14[c]	-0.07[c]
IL-6, pg/mL				1.0[c]	0.14[c]	0.20[c]	0.28[c]
Glucose, mg/dL					1.0[c]	0.26[c]	0.58[c]***
Insulin, µIU/mL						1.0[c]	0.88[c]***
HOMA-IR							1.0[c]

Note. BMI = body mass index; hs-CRP = high sensitivity C-reactive protein; IL-6 = interleukin-6; HOMA-IR = homeostatic assessment - insulin resistance model

[a]$n = 45$

[b]$n = 44$

[c]$n = 43$

[d]$n = 42$

*$p < 0.05$. **$p < 0.01$. *** $p < 0.001$.

Table 4b

Spearman Correlations (r_s) between Change in Anthropometric and Clinical Variables in the Fit & Strong! Group (n = 56)

Change	BMI	Body fat	CRP	IL-6	Glucose	Insulin	HOMA-IR
Weight, kg	1.0[a]***	-0.15[a]	- 0.35[b]**	0.07[b]	-0.19[b]	0.00[b]	-0.08[b]
BMI, kg/m^2	1.0[a]	-0.13[a]	- 0.35[b]**	0.05[b]	-0.20[b]	0.00[b]	-0.09[b]
Body fat, %							
hs-CRP, mg/L			1.0[b]	0.22[b]	0.06[b]	-0.02[b]	0.00[b]
IL-6, pg/mL				1.0[b]	0.21[b]	0.09[b]	0.17[b]
Glucose, mg/dL					1.0[b]	0.37[b]**	0.62[b]***
Insulin, µIU/mL						1.0[b]	0.92[b]***
HOMA-IR							1.0[b]

Note. BMI = body mass index; hs-CRP= high sensitivity C-reactive protein; IL-6 = interleuki HOMA-IR = homeostatic assessment - insulin resistance model

[a]$n = 56$

[b]$n = 55$

* $p < 0.05$. ** $p < 0.01$. *** $p < 0.001$.

Table 5

Spearman Correlations between Attendance (%) and Change in Anthropometric and Clinical Variables from Baseline to Post-intervention in the Customary Fit & Strong! and Fit & Strong! Plus Arms

	Fit & Strong! Plus		*Customary Fit & Strong!*	
Change	$n = 44$		$n = 56$	
	r_s	p	r_s	p
Weight (kg)	-0.54	<.001	0.06	0.66
BMI (kg/m2)	-0.53	<.001	0.08	0.57
Body fat (%)	-0.35[a]	0.02	-0.14	0.29
hs-CRP mg/L	-0.01[b]	0.97	-0.12[c]	0.38
IL-6 pg/mL	-0.03[b]	0.86	-0.11[c]	0.42
Glucose mg/dL	-0.25[b]	0.11	-0.07[c]	0.62
Insulin µIU/mL	-0.06[b]	0.73	-0.64[c]	0.64
HOMA-IR	-0.11[b]	0.50	-0.13[c]	0.35

Note. BMI = body mass index; hs-CRP = high sensitivity C-reactive protein; IL-6 = interleukin-6; HOMA-IR = homeostatic assessment - insulin resistance model

[a] $n = 43$;

[b] $n = 42$;

[c] $n = 55$

Class attendance for the *Customary FNS!* and *FNS!+* interventions are presented in Table 2. The mean attendance rate in the *Customary FNS!* group was 63.9% (~15 of 24) of classes while attendance for the *FNS!+* intervention was 66.3% (~16 of 24) of classes. Just over half of the participants attended 75% (18 of 24) of the classes.

The baseline and 8-week post-intervention anthropometrics, body composition and laboratory values are presented in Table 3 by treatment group. At baseline, the participants were obese [*FNS!+*: 34.0 kg/m^2 (95% CI: 31.9 - 36.1 kg/m^2); *Customary FNS!*: 34.1 kg/m^2 (95% CI: 32.1 - 36.0 kg/m^2)]. The baseline fasting serum glucose was only slightly impaired in both study arms [*FNS!+*: 106.2 mg/dl (95% CI: 99.1-113.8 mg/dl); *Customary FNS!*: 104.4 mg/dl (95% CI: 98.7-110.4 mg/dl)]. Both groups had modest systemic inflammation with mean hs-CRP > 3.0 mg/L indicating high cardiovascular risk.[15]

At the end of the 8-week interventions, there were no statistically significant within- or between-groups changes for fasting serum glucose, serum insulin, HOMA-IR or the systemic inflammatory markers hs-CRP and IL-6. However, a clinically meaningful decline in fasting serum glucose (-5.1 mg/dl), fasting serum insulin (-1.1 µIU/mL) and HOMA-IR (-0.4 units) was observed in the *FNS!+* group only. Weight, BMI, waist circumference, and percent body fat decreased significantly in the *FNS!+* group whereas these measures remained relatively unchanged in the *Customary FNS!* group.

Spearman correlations examining the association between the change scores (post-intervention minus baseline) and the anthropometric and clinical variables are presented in Tables 4a and 4b. Table 4a details the results for the *FNS!+* group and Table 4b details the results for the *Customary FNS!* group. When assessing the *FNS!+* group only, change in body weight was significantly correlated with change in percent body fat ($r_s = 0.36$, $p < 0.05$). Changes in the anthropometric measures were not correlated with changes in the markers of glucose metabolism or systemic inflammation. When examining the *Customary FNS!* only, the results were somewhat unexpected. Change in body weight was significantly negatively correlated with hs-CRP ($r_s = -0.35$, $p < 0.01$) suggesting that as weight decreased, hs-CRP increased. However, change in percent body fat was correlated with greater change in CRP and fasting glucose.

In the *FNS!+* group, higher attendance was correlated with greater reductions in body weight, BMI, waist circumference, percent body fat, and fasting serum glucose (Table 5). There was no association between class attendance and changes in the anthropometric and laboratory variables in the *Customary FNS!* group.

Discussion

We found that participation in an 8-week community-based exercise only (*Customary FNS!*) or 8-week exercise plus dietary weight management (*FNS!+*) intervention program, delivered under "real world" conditions, did not produce significant reductions in fasting serum glucose, fasting serum insulin, IL-6 or hs-CRP among overweight and obese older African American adults with OA. Improvements in insulin sensitivity based on HOMA-IR were also not observed for either intervention group. Despite no significant intervention effects on these parameters, participants in the exercise plus dietary weight management group (*FNS!+*) experienced clinically important reductions in fasting serum glucose and fasting serum insulin and improved insulin sensitivity based on HOMA-IR post-intervention.

The impact of exercise and exercise plus dietary weight management on glucose homeostasis in overweight and obese older adults with and without OA has been somewhat mixed. In the ADAPT and IDEA trials, which tested the separate and combined effects of exercise and dietary weight management in overweight and older obese adults with OA on body weight, systemic inflammation and mobility, glucose homeostasis-related outcomes have not been reported.[18-23] However, in other behavioral lifestyle interventions designed for overweight and obese older adults, including the NEW trial, dietary weight management alone or combined with exercise significantly improved fasting glucose, fasting insulin and HOMA-IR compared to exercise alone. Compared to the NEW trial, our ac-

tive intervention phase was significantly shorter (8 weeks vs. 6 months), implemented in the community rather than a university setting and less intensive in regard to the exercise, diet, and participant dietary self-monitoring aspects of the program.[24] Thus, it would be interesting to reexamine the impact of our interventions on glucose homeostasis markers if we were to extend the active intervention phase to 6 months, making the duration of exposure comparable to other behavioral lifestyle interventions.

Similar to our findings, the multi-site LIFE-P trial, an 8-week exercise program implemented 3 days weekly for 60 minutes followed by a maintenance intervention, demonstrated no significant effect on fasting blood glucose, fasting insulin or HOMA-IR at 6, 12 or 18 months follow-up compared to participation in a healthy aging program (attention control).[25] Like our study, there was minimal weight loss and fat loss at follow-up. These authors suggested that the metabolic benefit of exercise may be less pronounced in the absence of body weight and composition changes. Further, these authors suggested that medication use may have masked the benefits of the exercise intervention. In a sub-group analysis, persons in the exercise group not taking cardiometabolic-related medications demonstrated significant metabolic improvement compared to those not taking medications in the attention control group. Examining the impact of medication use on our study outcomes is currently underway.

Several studies by Kirwan and colleagues have demonstrated the beneficial effects of moderate to high intensity exercise training alone or in the backdrop of a dietary intervention on fasting blood glucose and fasting insulin in previously sedentary healthy and pre-diabetic/T2D overweight and obese older adults.[13-14,26-29] These studies were conducted in very controlled clinical settings by exercise physiologists and registered dietitians. Typically, participants were asked to exercise under supervision for 8 – 16 weeks, five times weekly for 60 minutes to achieve a predetermined target maximal heart rate (60 – 80%). In some of these studies, exercise was combined with dietary recommendations from a registered dietitian, or in one case, all meals, beverages, and snacks were provided.[13, 28] Clearly our program was not implemented under this level of rigor and was instead conducted under "real world" conditions in the community by a trained certified fitness instructor.[20] Nonetheless, it appears that the important component associated with improvement in glucose homeostasis in the studies conducted by Kirwan and colleagues was not reductions in body fat, per se, but instead improvement in cardiorespiratory fitness (VO_2 max).[13,28] In the *Customary FNS!* and *FNS!+* programs, the exercises were relatively low impact and scaled to an individual's ability level by the instructor. Although we did not measure cardiorespiratory fitness, it is likely that the intensity (i.e., low impact and no significant increase in intensity throughout the trial), dose and duration (i.e., 3 times weekly for 60 minutes over 8 weeks) of the *Customary FNS!* and *FNS!+* exercise programs was not sufficient to produce significant improvements in cardiorespiratory fitness, and subsequently glucose homeostasis.

A recent study suggests that exercise-induced improvements in glucose homeostasis vary by pre-diabetes subtypes including those with impaired fasting blood glucose, those with impaired glucose tolerance as determined by an oral glucose tolerance test and in those with a combined phenotype. Malin and Kirwan (2012) indicated in those with both impaired fasting glucose and glucose tolerance, exercise may be less effective for normalizing glucose metabolism related measures compared to persons with either impaired fasting glucose or impaired glucose tolerance alone due to more significant insulin resistance.[14,29] Unfortunately, we used relatively crude measures of glucose metabolism including fasting serum glucose, fasting insulin, and HOMA-IR. Our study also included persons with normoglycemia and T2D. Thus, given our relatively small sample size and crude measures of glucose metabolism, we were unable to examine the interventions effects on healthy, diabetic and pre-diabetes sub-groups.

The *Customary FNS!* and *FNS!+* programs had no effects on systemic inflammation. Nicklas and colleagues conducted a study evaluating the impact of exercise alone, or combined with dietary weight management on systemic inflammation, in overweight and obese older adults with OA.[30] Diet alone, or combined with exercise, was associated with significant declines in CRP and IL-6 compared to the exercise only and control groups. Change in body weight was significantly associated with change in systemic inflammation. Similarly, in the IDEA trial, participants randomized to the exercise plus dietary weight management group demonstrated significant reductions in IL-6 compared to the exercise only group.[17] This suggests that weight loss is needed to facilitate reductions in systemic inflammation.[31] However, in another study conducted with relatively healthy overweight and obese older adults, participation in a 12-month walking program was associated with lower IL-6 with no change in body weight or body fat compared to a control group.[32] In our trial, body weight change was minimal and was not correlated with changes in hs-CRP or IL-6 in either treatment group.

Although we reported excellent retention rates (91%), only half of the participants attended 75% or more of the classes. As with the Nicklas and Messier studies referenced above, our participants had lower body OA which could have impacted their adherence and exercise intensity.[17,30-31] Because the *Customary FNS!* and *FNS!+* programs were designed for individuals with OA, many of the exercises involve the use of a chair or standing in place, which can also impede exercise intensity. Another factor may be the duration of our intervention pro-

grams. In a recent article, Woods and colleagues suggested that intervention duration could be an important factor. In several behavioral intervention studies that had an active intervention phase 6 months or longer, significant reductions in systemic inflammatory markers were observed.[31] Another important factor to consider is the differential use of anti-inflammatory medications in the *Customary FNS!* and *FNS!*+ groups, although the use of statins and non-steroidal anti-inflammatory drugs did not alter the effects of exercise training on inflammatory markers in another study of overweight and obese older adults.[32]

In our study, the exercise plus dietary weight management group lost significantly more body weight and body fat compared to the exercise only group. This outcome translated to an approximately 2% change in body weight and a 2% change in body fat percentage. This level of body weight change is quite modest compared to other, more intensive and longer duration behavioral lifestyle interventions for overweight and obese older adults with and without OA. In previous studies, a 5–7% reduction in weight was accompanied by improvements in glucose homeostasis and systemic inflammation.[13-14,34-35] Thus, the magnitude of weight loss achieved in our exercise plus dietary weight management group was likely not sufficient to obtain metabolic and inflammatory benefit. Most lifestyle behavior intervention programs are a minimum of 16 weeks in length. Lifestyle changes, including exercise/physical activity and dietary changes involve the adoption of new positive health behaviors, and research suggests that lifestyle habits can take anywhere from 66 to 254 days to form.[33,36] Thus, the short duration of our intervention may not have allowed for the time needed to develop and adopt positive lifestyle behaviors.[33]

We found that greater adherence to the exercise plus dietary weight management intervention, as measured by class attendance, was associated with greater changes in body weight, body fat and fasting glucose. In the exercise only group, greater class attendance was not associated with changes in body weight or any of the biomarkers of interest. Our finding is consistent with findings from Mason et al. (2011) that participation and adherence to a 12-month exercise only program was not associated with significant weight loss or improvement of markers related to glucose metabolism. This observation was even more pronounced in the older women accrued to this study arm.[24]

Strengths of this study include accrual of an African American older adult sample, a randomized comparative effectiveness trial design, implementation in a "real world" community based setting, high retention (91%), use of DXA to examine body composition and inclusion of more than one marker of systemic inflammation. However, this study is not without limitations. First, we used relatively crude markers of glucose metabolism. Measuring oral glucose tolerance and or insulin sensitivity via euglycemic hyperinsulinemic clamp would have provided a more precise and comprehensive assessment of metabolic health. Second, as briefly mentioned above, the relatively small sample size precluded us from examining metabolic health subtypes (e.g., normoglycemic, impaired fasting glucose and T2D) or differences in effects between men and women. Third, this study did not control for actual food intake, and dietary recommendations in the *FNS!*+ arm were provided in a group setting by a non-nutrition professional. It is possible that diet quality and macronutrient composition differences amongst the participants enhanced or masked the interventions effects on glucose metabolism and systemic inflammation.[37-40] Diet is being examined in an ongoing analysis. Fourth, we did not examine medication use in the context of this analysis. It is possible that medication use is differential across treatment arms which could have confounded the results. Lastly, the short duration of our interventions may have hindered our ability to observe statistically significant changes to systemic inflammation and glucose metabolism. Given the potential exercise limitations of persons with OA, a longer duration versus more intense intervention period should be considered.

In conclusion, our findings indicate that the *Customary FNS!* and *FNS!*+ behavioral lifestyle intervention programs did not produce significant effects on glucose metabolism or systemic inflammation in overweight and obese African American older adults with OA. However, participants in the *FNS!*+ intervention lost significantly more body weight and body fat, albeit modest, compared to the *Customary FNS!* participants. Reduction in fasting serum glucose and fasting serum insulin and improved insulin sensitivity as assessed by HOMA-IR were observed in the *FNS!*+ group following the 8-week program, indicating that this intervention has clinical relevancy.

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