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Cardiovascular Risk Factor Reduction in First Responders Resulting From an Individualized Lifestyle and Blood Test Program

A Randomized Controlled Trial

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Objective: We tested the hypothesis that a lifestyle program would improve risk factors linked to cardiovascular disease (CVD) in first responders. **Methods:** A 1-year cluster-randomized controlled clinical trial in 10 cities. Participants were 175 first responders, with increased waist circumference and/or low levels of large (α_1) high-density lipoprotein (HDL) particles. The intervention group received personalized online tools and access to telephonic coaching sessions. **Results:** At 1 year the intervention significantly reduced body weight ($P = 0.004$) and waist circumference ($P = 0.002$), increased α_1 HDL ($P = 0.01$), and decreased triglyceride ($P = 0.005$) and insulin concentrations ($P = 0.03$). Program adherence was associated with weight loss ($P = 0.0005$) and increases in α_1 HDL ($P = 0.03$). **Conclusions:** In first responders, a personalized lifestyle intervention significantly improved CVD risk factors in proportion to program adherence. Changes in large HDL particles were more sensitive indicators of lifestyle changes than HDL-cholesterol measurement. **Clinical Trial Registration Number:** ClinicalTrials.gov: NCT03322046

Keywords: coronary heart disease, diet, firefighters, high density lipoprotein-cholesterol, high density lipoprotein, lifestyle, police officers, risk modification

Learning Objectives

- Become familiar with the increased risk of cardiovascular disease (CVD) in first responders and the associated risk factors.
- Describe the design of the lifestyle program to address CVD risk factors in first responders and the evaluation methods used in the study.
- Summarize the impact of the study interventions on CVD risk factors, including the role of program adherence.

The high incidence of cardiovascular disease (CVD) in firefighters and law enforcement officers is well documented.[1–8] The mortality ratio for middle-aged firefighters is reported to be 73% greater ($P < 0.005$) compared with non-firefighters.[2] The Centers for Disease Control concluded that sudden cardiac death is a leading cause of death in both volunteer and career firefighters during emergency responses.[3] The odds of coronary heart disease (CHD) death are increased 5.6-fold and 6.4-fold during alarm response and fire suppression, respectively.[4] Similarly, law enforcement officers are at higher risk of sudden cardiac death during stressful duties compared with non-emergency duties.[5] Their risk of sudden cardiac death is 34 to 69 times higher during restraints and altercations, 32 to 51 times higher during pursuits, 20 to 23 times higher during physical training, and six to nine times higher during medical and rescue operations compared with routine non-emergency activities.[5] Most on-duty CHD fatalities in firefighters are in those with underlying CHD,[4] suggesting that improved medical screening and management could prevent many premature deaths. The elevated CVD-risk in firefighters and law enforcement officers could be considered a threat to national security given their importance as first responders to national emergencies.

A major cause of premature CVD in first responders is atherogenic dyslipidemia secondary to modifiable unhealthy lifestyle habits.[1] This type of dyslipidemia is characterized by impaired lipid metabolism including increased levels of small-dense low-density lipoprotein (LDL) particles and depressed levels of large high-density lipoprotein (HDL) particles.[9] Excess dietary intake of refined carbohydrates in the setting of insulin resistance exacerbates the atherogenic dyslipidemia.[10] As demonstrated by the Federal Firefighter Heart Disease Prevention Study, atherosclerosis in firefighters is associated with insulin resistance and reduced concentrations of large HDL particles, suggestive of impaired HDL metabolism.[1]

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Potential Conflicts of interest:

Rosalynn Gill: None to declare currently. Previously employed by Boston Heart Diagnostics at the time of the investigation.

H. Robert Superko: Medical consultant to Boston Heart Diagnostics.

Megan M. McCarthy: Employed by Heart Fit for Duty.

Kepra Jack: Employed by Heart Fit for Duty.

Briana Jones: Employed by Boston Heart Diagnostics at the time of the investigation.

Debanjali Ghosh: Employed by Boston Heart Diagnostics at the time of the investigation.

Steve Richards: None to declare.

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Paul T Williams: Statistical consultant to Boston Heart Diagnostics.

Michael Dansinger: Medical Director and VP Clinical Affairs, Boston Heart Diagnostics.

Superko, Gill, McCarthy, Jack, Jones, Ghosh, Richards, Gleason, Williams, and Dansinger have no relationships/conditions/circumstances that present potential conflict of interest.

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Various methods have been proposed for distinguishing HDL-subclasses.[11] Large HDL particles and other HDL subspecies may be measured in clinical practice using gradient gel electrophoresis technology.[12–20] This approach, based on gel electrophoresis and automated image analysis of immunoblots, provides precise measurements of the major subspecies of HDL enabling more accurate assessment of CVD risk and response to lifestyle treatment. Large HDL, known as "α_1 HDL" due to its electrophoretic mobility pattern, is much more strongly associated with CVD events, atherosclerosis, and HDL functionality than HDL-cholesterol.[12,16,21] Furthermore, changes in α_1 HDL levels are much more sensitive to weight loss and dietary effects than HDL cholesterol levels.[15,22,23]

Our objective was to determine if a life-style modification program could significantly improve the CVD risk in firefighters. We conducted a 1-year randomized controlled trial to assess the real-world clinical effectiveness of an evidence-based individualized lifestyle program designed to identify and treat atherogenic dyslipidemia, CVD risk factors, and abdominal obesity in first responders. The specific primary outcome measure was an increase of 5 mg/dL or more of α_1 HDL in the intervention population after 12 months on the lifestyle program as a surrogate measure for reduction of cardiovascular risk. Secondary outcome measures included, reduction of weight, reduction of percentage body fat, reduction of waist/hip circumference and measures of glycemic control, insulin resistance, lipids, and inflammation markers.

METHODS

Design

Station houses (firefighters) and police headquarters (police officers) were identified in 10 cities in the suburban areas of Boston, Massachusetts and Phoenix, Arizona and these cities were randomized to 12 months in the intervention and control group via a computerized randomization program. The study was designed to detect a 5 mg/dL increase in α_1 HDL in the treatment group versus the control group with 80% statistical power and a significance level (alpha) of 0.05. The 12-month improvement in alpha1 should be at least 5 mg/dL greater in the treatment group than the control group (eg, 5 mg/dL vs 0 mg/dL). The standard deviation of that change is estimated to be 6.0 mg/dL for the combined group (about 8 mg/dL for the treatment group and 4 mg/dL for the control group). Sample size calculations indicate we need 46 participants to complete the trial (eg. 23 intervention, 23 control) to achieve 80% power to find a significant difference ($P < 0.05$) between intervention and control. Sample size calculator used for these calculations: http://stat.ubc.ca/~rollin/stats/ssize/n2.html

Once recruitment was completed, participating cities were paired (three city-pairs in Massachusetts and two city-pairs in Arizona) based on similar geographic location, city size, work conditions for first-responders, and numbers of eligible program participants. A computerized randomization program implemented by a statistician indicated which city within each pair was assigned to the intervention or control group.

Subjects and Protocol

Subjects were eligible for the study if they had low α_1 HDL (males: less than 20 mg/dL; females less than 30 mg/dL) or had waist circumferences more than or equal to 40 in. (more than 101.6 cm) in men or more than or equal to 35 in. (more than 88.9 cm) for women. In addition, they needed to be between 18 and 65 years old, have Internet access, and successfully complete a baseline food log. Exclusion criteria included use of insulin for diabetes, currently pregnant or plan to become pregnant over the next 12 months, more than 10 lb (4.5 kg) weight loss during the past 6 months, inability or unwillingness to follow the protocol, lack of availability, and moderate or severe chronic medical problems that would likely worsen or lead to acute illness or hospitalization during the next 12 months.

Recruitment began with an introductory 90-minute lecture 6 to 8 weeks prior to the intervention or through visits to fire stations or police departments with screening information. Interested participants then attended a 2-hour baseline screening clinic visit approximately 4-weeks prior to intervention that included fasting blood draws (post 8 hour fast), clinic measurements, and health questionnaires. The screening visit included training for the online entry of the food and exercise log (www.loseit.com, FitNow Inc., Boston, MA). The fasting blood draws and clinic measurements were repeated at the second (3 months) and third (6 months) and final (1 year) clinic visits. The intervention group was encouraged to report their diet and exercise daily whereas the control group was instructed to complete 3-day food diaries prior to their 3-, 6-, and 12-month intervals. The control group had access to the online food diary throughout the study if they chose to use it. Treatment and control participants all remained under the care of their usual health care provider during the study, and all participants were compensated for participating (up to $375 to offset time and travel). The study protocol was reviewed by Schulman IRB (Cincinnati, OH) and all subjects signed informed consent.

Clinical Measurements

Demographics (age, sex, race/ethnicity, education level), medical conditions, medications, family history, and adverse events during the study were obtained by self-report. Height and weight were measured without shoes. Percent body fat was estimated from bioimpedance (Omron Fat Loss Monitor HBF-306C, OMRON Healthcare, Inc., Lake Forest, IL), blood pressure and heart rate were measured via an automated instrument (Omron HEM-712C). Circumferences of the waist and hip were measured using a plastic tape over light clothing.

Laboratory Measurements

Laboratory assays of the blood draws were run at the time of collection for the intervention group, and deferred (frozen at −70 °C) until the conclusion of the study (1-year) for the control group in a College of American Pathologist (CAP) and Clinical Laboratory Improvement Amendments (CLIA) accredited laboratory (Boston Heart Diagnostics, Framingham, MA). They included total cholesterol (enzymatic colorimetric), triglycerides (enzymatic colorimetric), low-density lipoprotein (LDL)-cholesterol (direct, enzymatic colorimetric), HDL-cholesterol (enzymatic colorimetric), very-low-density lipoprotein (VLDL)-cholesterol (enzymatic colorimetric), apolipoprotein A-1 (apo A-1, immunoturbidimetric), small dense LDL (% of total LDL-cholesterol, Denka Seiken Co, LTD, Tokyo Japan), HDL-subclasses (PAGE system),[14] C-reactive protein (hsCRP, immunoturbidimetric), adiponectin (immunoassay—competitive principle), glycated hemoglobin (HbA1c, turbidimetric inhibition immunoassay), glycated serum protein (immunoassay—competitive principle), fasting insulin (immunoassay), fasting glucose (enzymatic), homeostatic model assessment for insulin resistance (HOMA-IR) was calculated as (HOMA-IR = [glucose × Insulin]/405), albumin (colorimetric principle), and glycated albumin. Sharing laboratory results with usual health care provider was at the discretion of each participant.

Intervention

The lifestyle intervention (Boston Heart Diagnostics, Framingham, MA) consisted of a personalized diet and exercise plan that was provided to the participants electronically via an online portal and reviewed during telephone coaching with registered dietitians and online tools for tracking diet, exercise, and weight. Recommended carbohydrate intakes ranged from 30% to 60% (median 45%), saturated fat intake from 5% to 10% with no more

than 7% for known CVD or LDL-cholesterol is equal to or more than 160 mg/dL, and total calorie intake set to facilitate healthy weight as determined by the waist to height ratio. Carbohydrate recommendations were based on the severity of metabolic syndrome with particular reference to small dense LDL[24] and α_1 HDL,[11–20] and promoted unrefined natural sources such as vegetables, legumes, fruits, low-fat dairy, and whole grains. The recommendation could be further modified based on HbA1c and fasting insulin and glucose concentrations. Dietary cholesterol was limited to 300 mg/d, or 200 mg/d for subjects with CVD, LDL more than or equal to 160 mg/dL or abnormally high cholesterol absorption. A 30% reduction in total energy intake was recommended to those requiring weight loss, where energy intake was estimated from the Mifflin-St. Jeor equation.[25] Macronutrient and calorie targets were translated into food servings and personalized 7-day menus that were consistent with the dietary approaches to stop hypertension (DASH) and Mediterranean diets. Participants' online food journals were reviewed by the coach as part of the lifestyle program. Twenty-minute one-on-one telephone coaching sessions occurred weekly for the first 2 months, then every other week for the remainder of the intervention. Participation was also promoted through gamification with the goal of making the intervention a fun, engaging, and compelling experience.

Statistical Analyses

Statistical analyses were performed using the JMP statistical package for the Macintosh (version 13, SAS institute, Cary, NC). Differences between intervention and control conditions were tested using expected mean squares analysis of variance where geographic areas were random effects nested within treatment condition (ie, two-factor random effect model). Mean differences between groups are presented ±standard error (ie, ±SE). The significance levels were entirely consistent with those obtained from residual maximum likelihood (REML) estimation. Least-squares regression analysis was used to test whether improvements in risk factors within the intervention group were significantly related to frequency of food journaling per week submitted to the online portal (a measure of adherence). The effects of dropouts were evaluated by comparing the baseline values of completers and dropouts by analysis of variance, by carrying forward the dropouts' last measurements, by assuming the dropouts had returned to their baseline values, and by multiple imputation (1000 imputations from multivariate normal regression with treatment, sex, age, BMI, and total cholesterol as independent variable and evaluated using the multilevel mixed effect linear regression option, STATA version 15, College Station, TX).

RESULTS

Baseline Characteristics of the Treatment and Control Conditions

The 96 treatment and 79 control subjects who began the study were well matched for age, sex, measures of adiposity, α_1 HDL (the primary outcome variable), and most other variables (Table 1). Thirty-six percent of the baseline sample (32.2% of treatment, 40% controls) had clinically low HDL-cholesterol (<40 mg/dL). However, there was a 4-fold range in α_1 HDL in subjects with clinically low HDL-cholesterol, and a 5.6-fold range in α_1 HDL for subjects with normal to high HDL-cholesterol. Cholesterol medication use at baseline was nearly twice as high in the treatment as in the control group (27.1% vs 15.2%), but its use remained relatively stable during the study, 28.2% versus 14.3% at 3 months, 32.0% versus 11.4% at 6 months, and 29.7% versus 14.5% at 12 months. Statins represented all of the cholesterol medication use in the control group, and 92.3% in treatment group.

TABLE 1. Baseline Characteristics of the Recruited Sample

	Mean (SD)		
	Treatment	**Control**	***P***
Sample size	96	79	
Male (%)	89.58	97.46	0.18
Age, yrs	43.02 (8.25)	41.77 (9.68)	0.59
BMI, kg/m^2	31.80 (5.01)	31.57 (4.48)	0.70
Bodyfat (%)	26.69 (6.66)	26.18 (6.64)	0.55
Waist circumference, cm	104.59 (12.75)	106.50 (12.87)	0.66
Hip circumference, cm	107.48 (10.52)	107.89 (10.90)	0.84
Systolic blood pressure, mmHg	128.03 (14.06)	129.49 (15.28)	0.79
Diastolic blood pressure, mmHg	85.99 (10.23)	84.32 (8.85)	0.54
Heart rate, bpm	71.09 (9.72)	66.97 (8.73)	0.05
Total cholesterol, mg/dL	197.09 (36.23)	202.17 (35.11)	0.59
Triglycerides, mg/dL	162.39 (105.92)	157.53 (100.67)	0.44
Log triglycerides	4.93 (0.56)	4.90 (0.54)	0.44
HDL-cholesterol, mg/dL	45.58 (12.13)	42.72 (10.37)	0.08
LDL-cholesterol, mg/dL	130.64 (30.55)	135.10 (31.87)	0.26
VLDL-cholesterol, mg/dL	21.26 (14.87)	24.80 (16.51)	0.60
Non-HDL-cholesterol, mg/dL	151.51 (37.15)	159.45 (35.37)	0.29
HDL/Triglyceride	0.41 (0.32)	0.38 (0.23)	0.57
Total cholesterol/HDL	4.60 (1.44)	5.03 (1.65)	0.67
VLDL-cholesterol/Triglycerides	0.13 (0.04)	0.16 (0.06)	0.15
Apo A1, mg/dL	143.83 (23.36)	138.88 (21.34)	0.11
Small dense LDL, mg/dL	40.72 (18.47)	44.47 (20.91)	0.43
HDL-map, mg/dL of Apo-A1			
α1	18.15 (8.37)	18.18 (7.87)	0.78
α2	60.30 (13.59)	57.83 (11.11)	0.13
α3	26.64 (5.50)	24.63 (4.26)	0.05
α4	16.07 (4.25)	16.82 (3.76)	0.75
preβ1	10.89 (4.42)	9.46 (2.99)	0.09
F Glucose, mg/dL	100.66 (21.54)	103.50 (9.19)	0.86
F Insulin, μU/mL	15.98 (16.87)	13.68 (8.15)	0.35
HOMA-IR	4.24 (5.03)	4.15 (2.05)	0.97
HbA1c (%)	5.48 (0.39)	5.64 (0.40)	0.15
CRP	2.25 (2.04)	2.05 (2.40)	0.86
Adiponectin	8.87 (4.19)	7.10 (3.07)	0.07
Glycated serum protein, μg/mL	217.49 (58.56)	212.05 (35.87)	0.79
Glycated albumin, %	11.39 (1.08)	11.27 (0.33)	0.90

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.

As percent of total energy intake, the median prescribed intake in the intervention group was 29% for protein (minimum, 25th percentile, 75th percentile, maximum: 15%, 24.5%, 32%, 35%, respectively), 41% for carbohydrates (30%, 38%, 45.5%, 55%, respectively), 30% for total fat (30%, 30%, 30%, 35%, respectively), and 10% for saturated fat (7%, 10%, 10%, 10%, respectively). Daily dietary cholesterol intake was recommended to stay below 200 mg/d for 45.2% of the sample and below 300 mg/d for 54.8% of the sample.

Supplementary Figure 1, http://links.lww.com/JOM/A488 presents the number of subjects screened, randomized, and participated in the baseline, 3-, 6-, and 12-month visits. One-hundred thirteen of the 288 individuals screened did not meet eligibility criteria or declined to participate. The 1-year dropout rate was greater in the treatment than the control group (31.25% vs 11.39%, $P = 0.008$), presumably reflecting the greater demands placed upon the intervention group. Dropouts were significantly younger at baseline than completers (mean ± SE: 39.5 ± 1.5 vs 43.2 ± 0.8 years, $P = 0.03$) and had lower baseline total cholesterol concentrations (188.3 ± 5.6 vs 202.7 ± 3.0 mg/dL, $P = 0.03$). Differences between dropouts and completers showed no significant interaction with treatment status.

Treatment-Group Change from Baseline versus Control Change ± Standard Error (±SE)

Significant weight loss occurred in the treatment group throughout the intervention, however, one-quarter of the average weight lost by 6 months was regained between months 6 and 12 (Table 2). Reductions in percent body-fat and waist circumference were also significant in the treatment group relative to the control group at the end of 1 year. Triglyceride concentrations declined steadily throughout the year. Reductions in small dense LDL and increases in apo A-1 were significant after 6 months, at the point of greatest weight loss, but not after 12 months, when weight loss was partially regained. Total HDL-cholesterol did not significantly increase at any point on the trial.

Primary End Point

The HDL map measurements showed the intervention significantly increased α_1 HDL at 3-, 6-, and 12-months. Increases in α_2 HDL were significant at 3- and 6-months, but not after 12 months.

TABLE 2. Differences in the Risk Factor Changes Between the Treatment and Control Groups

	Treatment versus Control Difference ± SE			Significance		
	Δ3 months	Δ6 months	Δ12 months	Δ3 months	Δ6 months	Δ12 months
Sample size (treatment/control)	87/71	81/72	66/70			
ΔBMI, kg/m^2	−0.94 ± 0.23	−1.59 ± 0.33	−0.96 ± 0.41	0.004	0.002	0.05
ΔWeight, kg	−3.79 ± 0.85	−5.11 ± 1.02	−3.92 ± 0.93	0.003	0.001	0.004
ΔBodyfat (%)	−0.96 ± 0.44	−2.54 ± 1.26	−1.51 ± 0.63	0.06	0.09	0.05
ΔWaist circumference, cm	−0.89 ± 2.45	−2.24 ± 1.70	−4.08 ± 0.88	0.73	0.23	0.002
ΔHip circumference, cm	−1.07 ± 2.43	−2.84 ± 1.67	−2.36 ± 1.18	0.67	0.13	0.08
ΔSystolic blood pressure, mmHg	−1.96 ± 2.10	−2.64 ± 2.33	−0.14 ± 2.05	0.38	0.29	0.95
ΔDiastolic blood pressure, mmHg	−2.16 ± 1.60	−1.02 ± 2.77	−2.31 ± 1.74	0.21	0.73	0.23
ΔHeart rate, bpm	−3.61 ± 3.16	−3.50 ± 2.29	−2.72 ± 2.43	0.29	0.17	0.30
ΔTotal cholesterol, mg/dL	1.99 ± 4.80	−6.53 ± 5.69	−3.92 ± 5.08	0.69	0.29	0.47
ΔTriglycerides, mg/dL	−21.24 ± 9.24	−43.13 ± 8.17	−57.76 ± 14.57	0.04	0.0001	0.005
ΔLog triglycerides, mg/dL	−0.10 ± 0.07	−0.21 ± 0.05	−0.29 ± 0.08	0.19	0.001	0.007
ΔHDL-cholesterol, mg/dL	0.94 ± 1.18	1.63 ± 1.36	0.92 ± 1.21	0.45	0.27	0.47
ΔLDL-cholesterol, mg/dL	0.17 ± 4.77	−4.42 ± 4.70	−1.98 ± 3.71	0.97	0.38	0.61
ΔVLDL-cholesterol (mg/dL)	0.83 ± 4.36	−3.84 ± 4.18	−3.08 ± 4.48	0.85	0.39	0.52
ΔLog VLDL-cholesterol, mg/dL	0.05 ± 0.23	−0.14 ± 0.18	−0.16 ± 0.24	0.69	0.48	0.61
ΔVLDL/Triglyceride	0.03 ± 0.04	0.02 ± 0.03	0.04 ± 0.03	0.46	0.51	0.29
ΔTotal cholesterol/HDL	0.10 ± 0.13	−0.35 ± 0.15	0.18 ± 0.17	0.45	0.05	0.31
ΔHDL/Triglyceride	0.04 ± 0.04	0.07 ± 0.04	0.10 ± 0.04	0.36	0.17	0.03
ΔApo A1, mg/dL	4.16 ± 3.83	6.18 ± 2.61	−0.04 ± 2.88	0.31	0.04	0.99
ΔSmall dense LDL, mg/dL	−2.85 ± 2.09	−5.83 ± 2.40	−0.44 ± 2.60	0.21	0.04	0.87
ΔHDL-map, mg/dL of Apo-A1						
α1	5.66 ± 0.93	7.97 ± 1.18	3.36 ± 0.98	0.0003	0.0002	0.01
α2	4.18 ± 1.05	5.90 ± 1.24	−0.40 ± 1.79	0.002	0.0008	0.83
α3	−2.50 ± 1.42	−1.82 ± 0.99	−3.46 ± 0.92	0.13	0.11	0.007
α4	0.31 ± 1.13	1.20 ± 1.18	0.56 ± 1.54	0.79	0.34	0.73
preα1	0.16 ± 0.35	−0.25 ± 0.23	0.57 ± 0.22	0.67	0.32	0.04
preα2	0.14 ± 0.59	−0.73 ± 0.28	0.62 ± 0.27	0.82	0.03	0.06
preα3	−0.14 ± 0.23	−0.43 ± 0.14	0.08 ± 0.21	0.58	0.02	0.71
preα4	0.04 ± 0.17	−0.05 ± 0.11	0.43 ± 0.16	0.84	0.68	0.03
preβ1	−2.95 ± 1.57	−5.35 ± 0.88	−0.93 ± 0.37	0.11	0.0005	0.03
preβ2	−0.76 ± 0.17	−0.68 ± 0.23	−0.92 ± 0.27	0.002	0.02	0.01
ΔCRP	−0.05 ± 0.48	0.32 ± 0.32	−0.13 ± 0.48	0.93	0.34	0.79
ΔAdiponectin	−0.23 ± 0.34	0.27 ± 0.39	−0.19 ± 0.31	0.52	0.52	0.55
ΔF glucose, mg/dL			3.20 ± 10.71			0.77
ΔF Insulin, μU/mL	−6.24 ± 2.53	−5.74 ± 2.64	−7.69 ± 2.86	0.04	0.07	0.03
ΔHOMA-IR			−1.51 ± 3.56			0.67
ΔHbA1c (%)	−0.10 ± 0.03	−0.11 ± 0.03	0.03 ± 0.03	0.005	0.02	0.37
ΔGlycated serum protein, μg/mL	−9.66 ± 9.37	7.20 ± 10.22	−1.69 ± 7.89	0.34	0.51	0.84
ΔGlycated albumin (%)						
ΔBeta-sitosterol absolute, mg/L	0.21 ± 0.19	0.29 ± 0.25	0.73 ± 0.17	0.31	0.28	0.005
ΔBeta-sitosterol absorption*	8.29 ± 6.11	16.41 ± 9.32	36.99 ± 6.47	0.22	0.13	0.0008
ΔCampesterol absolute, mg/L	0.09 ± 0.30	0.21 ± 0.28	0.64 ± 0.26	0.76	0.48	0.04
ΔCampesterol absorption*	1.53 ± 10.87	13.90 ± 10.23	35.09 ± 10.99	0.89	0.22	0.02
ΔCholesterol balance score	−0.02 ± 0.05	0.01 ± 0.13	−0.27 ± 0.05	0.77	0.94	0.0004
ΔCholestanol absolute, mg/L	−0.78 ± 0.11	−0.31 ± 0.18	−0.36 ± 0.14	0.0002	0.12	0.04
ΔCholestanol absorption*	−40.04 ± 5.74	−11.68 ± 10.30	−15.17 ± 8.37	0.0002	0.30	0.12
ΔDesmosterol absolute, mg/L	−0.16 ± 0.11	−0.05 ± 0.14	0.01 ± 0.05	0.17	0.71	0.84
ΔDesmosterol absorption*	−9.12 ± 3.86	1.43 ± 7.35	3.37 ± 2.15	0.03	0.85	0.15
ΔLathosterol absolute, mg/L	0.21 ± 0.17	0.40 ± 0.21	−0.28 ± 0.22	0.24	0.10	0.24
ΔLathosterol synthesis*	8.06 ± 6.12	26.35 ± 9.17	−9.20 ± 6.95	0.22	0.02	0.22

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very-low-density lipoprotein.
*μmol × 100/mmol of total cholesterol.

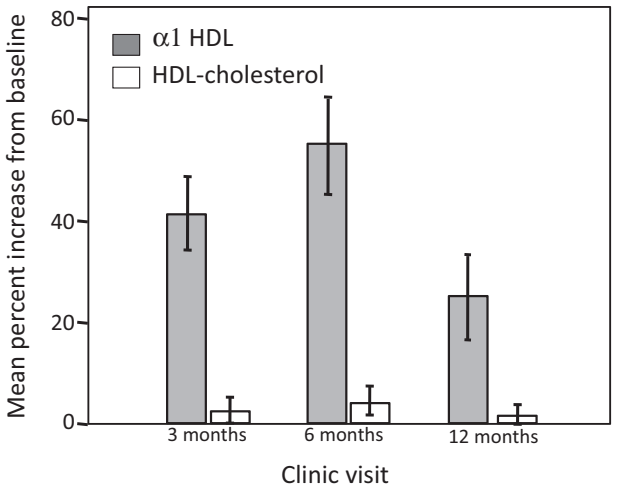

FIGURE 1. Net percent increase in α_1 HDL and HDL-cholesterol after 3 months (visit 2), 6 months (visit 3), and 12 months of intervention (visit 4). Brackets represent ±1 standard error. HDL, high-density lipoprotein.

Significant reductions in pre-β_1 HDL were achieved after 6 months. Figure 1 shows the net percent increase in α_1 HDL was substantially greater than that observed for HDL-cholesterol at 3 months ($41.50 \pm 7.46\%$ vs $2.61 \pm 2.52\%$, $P = 0.0006$ and $P = 0.33$, respectively), 6 months ($55.0 \pm 9.64\%$ vs $4.41 \pm 2.69\%$, $P = 0.0008$ and $P = 0.14$, respectively) and 12 months ($24.82 \pm 8.39\%$ vs $1.25 \pm 2.81\%$, $P = 0.02$ and $P = 0.67$, respectively).

Plasma HbA1c concentrations declined significantly during the periods of active weight loss but not after weight regain. Fasting insulin concentrations were reduced at all three follow-up visits, with significance achieved at 3 and 12 months.

Relationship to Compliance in the Treatment group

Table 3 presents the regression slopes between the risk factor change from baseline and the average number of food records entered per week through 3-, 6-, and 12-months (a measure of participation) within the intervention group (Table 3). Greater participation was significantly associated with greater reductions in total weight, BMI, and % body fat, at all time points, and with reductions in waist circumference at 6 and 12 months. Greater participation was also significantly related to increases in α_1 HDL at all time points and to reduced concentrations of α_4 HDL at 6 and 12 months. Participation levels were more strongly related to the average net percent increase in α_1 HDL than HDL-cholesterol. Figure 2 represents the quartiles of

TABLE 3. Regression Slope (±SE) of the Risk Factor Change in the Treatment Group (Dependent Variable) vs. Cumulative Number of Food Records Entered per Week (Independent Variable, a Measure of Compliance)

	Slope ± SE			Significance		
	Δ3 months	Δ6 months	Δ12 months	Δ3 months	Δ6 months	Δ12 months
Sample size (treatment/control)	87	81	66			
ΔBMI (kg/m^2)	−0.26 ± 0.07	−0.30 ± 0.09	−0.37 ± 0.10	0.0008	0.0009	0.0005
ΔWeight (kg)	−0.75 ± 0.21	−0.95 ± 0.27	−1.16 ± 0.32	0.0004	0.0007	0.0005
ΔBodyfat (%)	−0.42 ± 0.15	−0.52 ± 0.20	−0.79 ± 0.21	0.005	0.01	0.0005
ΔWaist circumference (cm)	−0.49 ± 0.28	−0.94 ± 0.29	−1.03 ± 0.31	0.09	0.002	0.001
ΔHip circumference (cm)	−0.28 ± 0.31	−0.24 ± 0.32	−0.53 ± 0.32	0.37	0.45	0.10
ΔSystolic blood pressure (mmHg)	−1.01 ± 0.50	−1.28 ± 0.67	−0.26 ± 0.74	0.05	0.06	0.73
ΔDiastolic blood pressure (mmHg)	−0.35 ± 0.41	−0.72 ± 0.52	−0.73 ± 0.57	0.39	0.17	0.20
ΔHeart rate (bpm)	−0.74 ± 0.48	−1.26 ± 0.44	−1.08 ± 0.58	0.13	0.006	0.07
ΔTotal cholesterol (mg/dL)	0.02 ± 1.21	−0.85 ± 1.37	−2.34 ± 1.59	0.99	0.54	0.15
ΔTriglycerides (mg/dL)	−4.53 ± 3.27	−13.54 ± 4.78	−6.44 ± 4.98	0.17	0.006	0.20
ΔLog triglycerides (mg/dL)	−0.01 ± 0.02	−0.07 ± 0.02	−0.03 ± 0.03	0.53	0.004	0.21
ΔHDL-cholesterol (mg/dL)	0.46 ± 0.38	0.88 ± 0.40	0.48 ± 0.38	0.23	0.03	0.21
ΔLDL-cholesterol (mg/dL)	−0.33 ± 1.04	0.29 ± 1.14	−1.94 ± 1.47	0.75	0.80	0.19
ΔVLDL-cholesterol (mg/dL)	−0.15 ± 0.50	−2.13 ± 0.73	−0.99 ± 0.81	0.77	0.005	0.22
ΔLog VLDL-cholesterol (mg/dL)	0.00 ± 0.02	−0.08 ± 0.03	−0.06 ± 0.03	0.93	0.003	0.09
ΔVLDL/Triglyceride	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.91	0.47	0.31
ΔTotal cholesterol/HDL	−0.06 ± 0.04	−0.12 ± 0.04	−0.10 ± 0.05	0.10	0.004	0.07
ΔHDL/Triglyceride	0.00 ± 0.01	0.03 ± 0.01	0.01 ± 0.01	0.85	0.01	0.43
ΔApo A1 (mg/dL)	0.53 ± 0.89	0.27 ± 1.05	−0.13 ± 0.93	0.55	0.80	0.89
ΔSmall dense LDL (mg/dL)	−0.71 ± 0.60	−1.00 ± 0.63	−1.57 ± 0.88	0.24	0.11	0.08
ΔHDL-map (mg/dL of Apo-A1)						
α1	0.67 ± 0.31	0.92 ± 0.34	0.70 ± 0.30	0.03	0.009	0.03
α2	0.45 ± 0.48	0.69 ± 0.59	0.67 ± 0.52	0.36	0.25	0.20
α3	−0.33 ± 0.25	−0.59 ± 0.26	−0.44 ± 0.31	0.19	0.02	0.17
α4	−0.15 ± 0.23	−0.51 ± 0.25	−0.66 ± 0.27	0.53	0.05	0.02
preβ1	−0.20 ± 0.21	−0.30 ± 0.18	−0.13 ± 0.24	0.33	0.09	0.58
ΔCRP	−0.03 ± 0.08	−0.07 ± 0.09	−0.09 ± 0.09	0.69	0.44	0.32
ΔAdiponectin	0.04 ± 0.07	0.12 ± 0.08	0.22 ± 0.08	0.52	0.12	0.01
ΔFasting Glucose (mg/dL)	−0.50 ± 0.47	−0.92 ± 0.57	−0.88 ± 0.81	0.29	0.11	0.28
ΔFasting Insulin (μU/mL)	−1.18 ± 0.58	−1.27 ± 0.70	−0.47 ± 0.91	0.05	0.08	0.60
ΔHOMA-IR	−0.46 ± 0.28	−0.37 ± 0.21	−0.16 ± 0.27	0.10	0.08	0.55
ΔHbA1c (%)	−0.01 ± 0.01	−0.04 ± 0.01	−0.03 ± 0.01	0.28	0.002	0.09
ΔGlycated serum protein (μg/mL)	0.27 ± 1.43	1.92 ± 1.99	1.56 ± 2.62	0.85	0.34	0.55

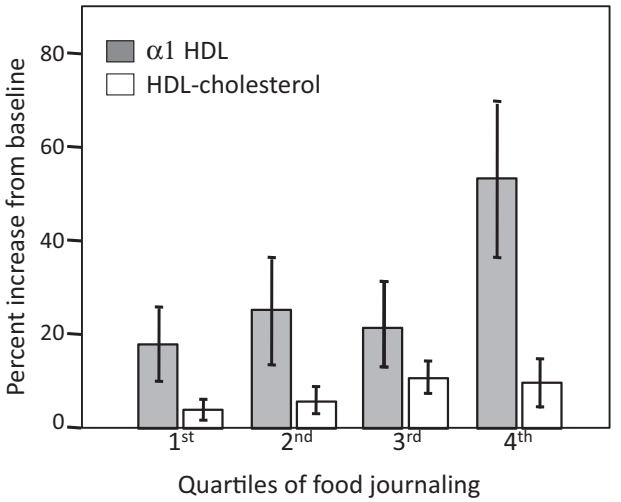

FIGURE 2. Mean percent increase in α_1 HDL and HDL-cholesterol in the treatment group after 12 months (visit 4) by quartiles of participation (average food journal entries per week). Brackets represent ±1 standard error. HDL, high-density lipoprotein.

food journals were 1st quartile (less than 1.22 food journal entries per week), 2nd quartile (1.23 to 3.02 food journal entries per week), 3rd quartile (3.03 to 5.66 food journal entries per week), and 4th (more than 5.66 food journal entries per week).

Adjustment for Baseline Differences and Dropouts

One-year differences in $\Delta\alpha_1$ HDL, Δbody weight, Δwaist circumference, Δtriglycerides, and the ΔHDL-triglyceride ratio all remained significant when adjusted for baseline age and total cholesterol, and when dropout values were imputed by carry-forward of the last measurement ($P = 0.02$, $P = 0.01$, $P = 0.02$, $P = 0.01$, $P = 0.03$, respectively), and when assumed to return to their baseline value ($P = 0.02$, $P = 0.006$, $P = 0.007$, $P = 0.0004$, $P = 0.02$, respectively, analyses not displayed) (Supplementary Table 1, http://links.lww.com/JOM/A489). Multiple imputation of dropout data showed significant 1-year treatment versus control group differences were retained for $\Delta\alpha_1$ HDL (mean difference ± SE: 3.68 ± 1.43 mg/dL, $P = 0.01$), Δwaist circumference (−3.78 ± 1.28 cm. $P = 0.003$), Δtriglycerides (−54.80 ± 19.29 mg/dL, $P = 0.005$), and Δtriglycerides/HDL (−1.61 ± 0.71, $P = 0.02$), became marginal for Δweight (−3.12 ± 1.64 kg, $P = 0.06$), and nonsignificant for Δ%bodyfat (−1.28 ± 0.97%, $P = 0.18$).

DISCUSSION

In first responders, we showed that a personalized lifestyle intervention significantly improved CVD risk factors at 1 year (Table 2, Fig. 1). Abdominal obesity, metabolic syndrome, atherogenic dyslipidemia, premature CVD, and sudden cardiac death are commonplace in this population,[1–6,26–28] so there is an urgent need to implement effective programs for the prevention and treatment of these conditions. Our program produced statistically significant improvements in the a priori outcomes (body weight and α_1 HDL), and the degree of improvement in these outcomes reflected the degree of program adherence (Fig. 2). One-year reductions in triglyceride/HDL-cholesterol ratio, and α3 HDL, preβ_1 HDL, and fasting insulin concentration were also significantly greater in the treatment than the control groups, further suggestive of decreased CVD risk due to the intervention.

When designing the study, we chose to focus on improvements in α_1 HDL as a clinically meaningful a priori outcome measure. Improvements in α_1 HDL are very sensitive to weight loss,[20] and are more accurate reflections of cardiovascular risk status than HDL cholesterol.[16,18,19] The HDL subclass defined as HDL2b or α_1 HDL has been associated with cardiovascular risk.[11] For example, in a 29-year follow-up of Gofman Livermore cohort, low HDL2 mass was significantly lower in men who developed premature CHD.[29] Truncal obesity has been correlated negatively with plasma HDL2b suggesting that lifestyle modification may be beneficial in regard to HDL2b levels.[30] Previous investigations have demonstrated that lifestyle changes can enhance the HDL subclass distribution. Williams et al[31] have demonstrated in a 1-year randomized trial that fat weight loss induced either by increased exercise, or reduced dietary caloric consumption can increase large HDL (HDL2) 4 to 5 mg/dL (7.7% to 9.6%). The combination of both exercise and dieting was shown to significantly increase large HDL (HDL2-mass).[32]

In our study, HDL cholesterol levels did not change significantly, and were not correlated with weight loss or dietary adherence. In contrast, changes in α_1 HDL levels mirrored changes in weight and dietary adherence (Table 2). The mg/dL net increases in α_1 HDL were over 3-fold greater than those observed for HDL-cholesterol at 3 months (5.66 vs 0.94 mg/dL), 6 months (7.97 vs 1.63 mg/dL), and 12 months (3.36 vs 0.92 mg/dL). Plasma triglyceride concentrations, a well-established CVD risk factor,[33] decreased significantly more in treatment than controls subjects, which may have contributed to the increases in α_1 HDL and decreases in pre-β_1 HDL. These results add to a growing body of evidence suggesting that favorable changes in HDL characteristics (such as particle size, subpopulation distribution, and/or functionality) cannot be reliably measured by changes in HDL cholesterol alone.[10–12,16,18,19,34,35]

Adherence typically limits the effectiveness of lifestyle programs. In our study, the tailored nutrition and exercise prescription may have assisted with initial engagement rates, repeated coaching sessions may have reinforced and extended the personalization and structure, and logging of food and exercise may have assisted with accountability and feedback. In both metropolitan areas tested, our program achieved clinically meaningful improvements as a result of sufficient participation rates and engagement. These findings suggest the program can potentially achieve similar results in a variety of other metropolitan areas, and could help build momentum toward a clinically effective program for first responders throughout the United States.

Our study has important limitations. Although our study was randomized and included a control group, it was modest in size and duration. Our study was designed to test the feasibility and effectiveness of a personalized intensive lifestyle program in the field, but the relative contribution of each individual component was not determined. Our program achieved moderate adherence to lifestyle recommendations, but adherence levels waned over time as is typical of such programs. Although changes in α_1 HDL levels were a sensitive measure of lifestyle change and program adherence, the availability of such measurements and medical insurance reimbursements currently vary throughout the United States.

CONCLUSIONS

In conclusion, an intensive 1-year lifestyle program was effective for reducing CVD risk factors including atherogenic dyslipidemia and metabolic syndrome features in firefighters and police officers in two metropolitan areas. Personalization, coaching, and food logging were used to facilitate program adherence, which predicted the degree of weight loss and blood test improvements. Measures of α_1 HDL were more sensitive to weight loss and program adherence than measures of HDL cholesterol. Together these findings may inform efforts to reduce cardiovascular disease on a national level in first responders and other high-risk populations.

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