# Effects of whey protein and resistance exercise on body cell mass, muscle strength, and quality of life in women with HIV

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**Objective:** To determine the effects of whey protein, resistance exercise, and combined protein and exercise treatment on body cell mass (BCM), muscle strength, and quality of life (QOL) in HIV-infected women with reduced BCM.

**Design and setting:** Prospective, randomized, controlled trial at a university hospital in New York City.

**Methods:** A volunteer sample of 30 HIV-infected women were randomized to whey protein (PRO), progressive resistance exercise (PRE), or combined treatment (PRO–PRE) for 14 weeks after a 6-week control period. The main outcome measures were body weight, BCM, skeletal muscle, fat mass, muscle strength, and QOL.

**Results:** There were no significant changes in BCM, strength, or QOL during the control period. PRO patients gained 3.6 kg (P = 0.001), and 2.5 kg fat (P = 0.002) with no change in BCM (0.5 kg; P = 0.07) or skeletal muscle (0.6 kg; P = 0.12). The PRE group increased BCM (0.74 kg;P = 0.03) and skeletal muscle (1.2 kg; P < 0.001) and decreased fat (1.7 kg; P = 0.02). PRO–PRE increased BCM (0.61 kg; P = 0.01) without change in skeletal muscle (0.6 kg; P = 0.30). Strength increased for both exercise groups (range, 40.6–95.3%; P < 0.001). The QOL physical activity score improved for PRE (P = 0.02) and worsened for PRO (P = 0.01).

**Conclusions:** Resistance exercise significantly increased BCM, muscle mass, muscle strength, and QOL in HIV-infected women with reduced BCM. Whey protein had little effect on BCM accrual. Combined protein and exercise did not increase BCM in excess of gains achieved by exercise alone.

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#### Keywords: HIV women, body cell mass, whey protein, resistance exercise, quality of life, muscle strength

### Introduction

The unintentional loss of life-supporting body cell mass (BCM) is characteristic of several catabolic conditions including HIV infection [1,2]. Unlike the fat-free mass (FFM) which includes all body compartments other than fat, the BCM comprises intracellular, metabolically-active cells in organs and skeletal muscle [3], and is the clinical concern in wasting disease. BCM deple-

tion in HIV-infected people can occur with or without weight loss [4,5] and is associated with decreased survival time [6,7], impaired physical function [8] and poor quality of life (QOL) [9]. Modern drug therapies including protease inhibitors have decreased the incidence of severe body weight and BCM wasting, yet malnutrition is still observed. From a public health standpoint, low BCM may be viewed as a comorbid consequence of HIV illness with direct influence on

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patient productivity and public health care costs. Pharmacologic trials with testosterone [10–14], anabolic steroids [15], recombinant human growth hormone (rhGH) [16,17], and combined rhGH and insulin-like growth factor-1 [18,19] have resulted in variable changes in skeletal protein, physical function, and QOL. These regimens require physician supervision, have unpleasant or adverse side effects, and are costly, thereby hindering widespread use.

Whey protein and resistance exercise are natural nonpharmacologic approaches to restore BCM. Several studies propose increased dietary protein needs in states of injury and metabolic stress [20–22]. Nutritional guidelines for HIV disease support the intake of high quality protein [23] as found in whey, a protein source of high biological value [24]. Our unpublished pilot data of four HIV-malnourished men consuming ancillary whey protein (PRO) indicated that BCM could be enhanced by an average of 1 kg in 12 weeks.

A small number of trials have concluded that progressive resistance exercise (PRE) augments muscle strength [25–28], lean body mass (LBM) [27], and muscle mass [25] in HIV-infected patients. These studies were either uncontrolled, lacked power, used imprecise body composition techniques, or were primarily limited to men. There have been few nutritional studies of malnourished HIV-positive women, although the proportion of infected people who are women is rising [29].

We conducted this prospective, randomized, controlled experiment, utilizing high precision body composition methodology, to determine the effects of whey protein and resistance exercise on BCM in BCM-wasted, HIV-infected women. We hypothesized that singular treatment with whey protein or resistance exercise would increase BCM and that combined protein and exercise treatment would result in greater BCM gains than either treatment alone. We further examined the effects of treatment upon muscle strength and subjective physical, psychological, and social well-being, given that low BCM would probably curtail total function.

# Materials and methods

#### Experimental design

The study was a prospective, randomized, 20-week trial comprised of a 6-week control period followed by a 14-week intervention conducted from October 1997 to May 1999, just following the availability of highly active anti-retroviral therapy (HAART) in 1996. Forty-three HIV-positive women, ranging in age from 28 to 66 years, were recruited via flyer, HIV support group, or personal contact to be randomized to one of

the following three groups: whey protein (PRO), progressive resistance exercise (PRE), or combined treatment (PRO-PRE). Extensive consultation with clinical AIDS investigators led us to conclude that with the addition of a randomized control group receiving no treatment, the study would likely fail to retain control subjects. Eligibility criteria for study entry included a confirmed HIV diagnosis and BCM  $\leq 90\%$ of race-sex-derived normal values by bioimpedance analysis (BIA) [30]. Exclusionary measures were resting blood pressure > 140/90 mmHg, pregnancy, ongoing exercise training or use of anabolic agents or protein supplements within 1 year of study entry, untreated comorbid disease, musculoskeletal complications that would interfere with strength testing, and patients unwilling to participate in testing or unable to commute to the exercise site three times per week. The nature, intent, and risks of the study were explained to each subject prior to obtaining written informed consent. The experiment was approved by the St. Luke's/ Roosevelt Hospital Center Institutional Review Board.

# Control period (weeks 0-6)

Subjects were their own controls by participating in a 6-week pre-treatment assessment. At weeks 0 and 6 of the control interval, body weight (BW), BCM by BIA, muscle strength by the one-repetition maximum method (1-RM) [31], and QOL by the Medical Outcomes Study (MOS) survey [32] were monitored to acquire control data and assure patient stability.

# Treatment period (weeks 6-20)

Following the control period, patients were individually randomized to PRO, PRE, or combined PRO– PRE intervention for 14 weeks. Sequential randomization was generated by two research assistants using a random number table. Group assignment was executed by the principal investigator and concealed until the time of treatment. The primary outcome measures were change in BW, BCM by total body potassium-40 counting (TBK), skeletal muscle (SM) and fat mass (FM) by magnetic resonance imaging (MRI), 1–RM muscle strength, and QOL. Secondary measures included FFM and FM by dual energy X-ray absorptiometry (DXA) and dietary assessment.

TBK was measured in a 4-pi whole body liquid scintillation apparatus by external counting of gamma rays produced from the natural decay of the 40 K radioisotope [33]. TBK values were then adjusted by a 42 K-derived correction equation to account for the reduction in photon absorption by overlying body fat [34]. Whole body MRI was performed using a 1.5T scanner (6X Horizon; General Electric, Milwaukee, Wisconsin, USA), with approximately 41 head to toe transverse images of 10 mm thickness collected at 50 mm intervals, as previously described [35]. Images were studied on a Sun Workstation (Silicon Graphics, Mountain View, California, USA) using Vect image analysis software (Martel Inc, Montreal, Canada). Body composition was also assessed by DXA (DPX; Lunar Radiation Corp, Madison, Wisconsin, USA; Version 3.6) which measures the attenuation of two energy sources as they are absorbed by body tissue of variable density [36].

1–RM muscle strength was measured for seven muscle groups of the chest, shoulder, back, arms, and legs. Subjects lifted weights in a progressive manner beginning at a low level and gradually reaching the maximal amount of weight that could be lifted one time by the target muscle group. All treatment groups received identical instruction, identical warm-up prior to 1– RM testing, and the identical level of encouragement.

The MOS survey has been previously validated for use in HIV-infected men and women [37–39], and includes eight health status scales containing physical, psychological, and social dimensions. Standardized scores were derived from the formula [(raw scoreminimum score)/score range]  $\times$  100 and ranged from 0–100 for all scales except mental health which ranged from 4–100. Measured values were compared with mean and median standard scores obtained from 1412 healthy women aged from 18 to above 65 years [32]. Patients were fully versed as to the personal nature of the survey, assured of total anonymity, and instructed to answer all questions honestly.

Food intake was estimated during in-depth face-to-face and telephone interviews conducted by a trained registered dietitian (M.L.) using a modification of the Burke method [40]. Total dietary energy, protein, carbohydrate, and fat content were calculated by nutrition analysis software (Food Processor Software; Esha Research, Salem, Oregon, USA; Version 6.22).

#### **Protein supplementation treatment**

The two groups of patients assigned to PRO treatment received 1.0 g/kg per day of undenatured bovinederived whey protein powder (Optimune; Optim Nutrition, Salt Lake City, Utah, USA). Whey contains a variety of amino acids and immunoglobulins, which are activated with reconstitution of the protein powder. Patients received instructions on preparation of the protein powder, and care was taken to avoid concurrent consumption of acidic and hot foods that might disturb the undenatured state of the protein. Dietary consumption was otherwise ad libitum, provided that energy and protein consumption was maintained above the dietary recommendations set by the Committee on Dietary Allowances [41]. Adherence to the protein supplement was measured through weekly phone and/ or personal contact with the principal investigator.

# **Exercise training treatment**

PRE groups visited the study exercise room at St.-Luke's/ Roosevelt Hospital on alternate days, 3 days per week for 14 weeks. Patients performed progressive resistance training on a multi-gym apparatus (Tuff Stuff; Task Enterprises, Pomona, California, USA) for seven major muscle groups. Dumbbells were provided for supplementary exercises. Subjects performed three sets of 10 exercises at 8-10 repetitions per set as per American College of Sports Medicine guidelines [42]. For week 1, weight loads were set at 50% of the baseline 1-RM to acclimate patients to equipment and proper technique. Thereafter, weight loads were approximately 75% of 1-RM, with adjustments based on number of repetitions and corresponding percentages of 1-RM [43]. Weight loads were increased by at least 2.5 pounds when the patient accomplished 10 consecutive repetitions for a particular muscle group without undue fatigue. Repeat 1-RM testing was performed at weeks 13 and 20 to confirm strength increases. Subject supervision during exercise training and 1-RM testing was conducted by the same exercise physiologist.

#### Statistical analysis

Data obtained during the control period were compared using Student's t-test for paired comparisons. This was carried out to examine group similarity before patient assignment to the three study conditions. Within group pre- to post-treatment effects for dependent variables were analysed using paired Student's t-test. Between group comparisons for PRO, PRE, and PRO-PRE groups were attained by one-way analysis of variance. For 1-RM comparisons, statistical inference was determined from natural logarithmic transformation of raw data to normalize the distribution of the strength variable. This method creates a difference model for proportional change, with post-treatment values expressed as a percentage of the pre-test value. When a significant F-ratio was found in the overall analysis, post-hoc pair-wise comparisons were performed with the Fisher's least significant difference technique. Analyses represent data for study completers. No intention-to-treat analyses were performed due to patient withdrawals prior to post-testing.

Prior studies of PRE in HIV-infected-persons reported strength increases ranging from 30-60% depending on muscle group. Based on these results, to detect a 30% strength increase the experimental design was expected to offer 0.80 power of avoiding a type II error when employing a sample size of n = 11 for each of three groups. Recruitment of 43 subjects allowed for significance to be detected after accommodating drop-outs. There were no experimental data on repletion of BCM in HIV-infection from which to predict power. Data analysis was performed using SPSS for Windows (SPSS Inc, Chicago, Illinois, USA; Version 8.0). Data in text and figures are described as mean (SD) unless otherwise indicated. A two-tailed alpha level of P < 0.05 was required for significance.

## Results

#### Patient characteristics

Based on low BCM levels, 66 of 138 women screened were eligible for enrollment. Additional ineligibility criteria, particularly family constraints, disqualified 23 of those eligible. Of the 43 who completed the control period, six withdrew at the point of randomization (two dissatisfaction with group assignment, two family constraints, two unexplained non-compliance) and 37 were assigned to treatment groups (12 PRO, 12 PRE, 13 PRO-PRE). Seven women did not complete the intervention for non-compliance, six due to family constraints (two from each group) and one death (PRO-PRE group). Baseline characteristics of 30 study completers are presented in Table 1. Prior to treatment there were no demographic or clinical mean differences between groups for BW, age, CD4+ lymphocytes or HIV RNA (all P > 0.05). One patient in the PRO-PRE group complained of nausea when consuming the protein mixture but tolerated a half dose at 0.5 g/kg per day for the entire treatment period. QOL surveys were self-administered except for one subject with impaired vision and two illiterate participants who required assistance. There were no injuries resulting from resistance training or 1-RM testing. Adherence to protein treatment was 96% for PRO and 93% for PRO-PRE groups. Adherence to exercise training was 94% for PRE and 95% for PRO-PRE groups.

#### Control period (weeks 0–6)

Patients were clinically stable throughout the control period with no significant mean differences observed

 Table 1. Baseline characteristics of study completers<sup>a</sup>.

for BW, BCM by BIA, 1–RM muscle strength, or QOL sub-scales (all P > 0.05).

#### Treatment period (weeks 6–20)

Body weight and body composition

Table 2 shows the mean (SD) change in BW, and body composition for the three groups over the 14-week treatment period. A significant BW gain [3.6 (2.3) kg] was noted only for the PRO group (P = 0.001), and resulted in significant differences in BW between PRO and PRE groups (P = 0.007) (Fig. 1a). BCM significantly increased for both exercise groups [PRE = 0.74](0.90) kg; P = 0.03 and PRO-PRE = 0.61 (0.64) kg; P = 0.01 with a smaller increase for PRO women [0.50 (0.77) kg; P = 0.07] (Fig. 1b), and no difference between groups. The PRE group significantly increased SM by 1.2 (0.69) kg (P < 0.001), with no change in SM observed for the protein-supplemented groups, and no difference between the three groups (Fig. 1c). FM, measured by MRI significantly increased [2.5 (1.8) kg, P = 0.002] and decreased [1.7 (1.8) kg,P = 0.02] for PRO and PRE, respectively, with no change for the PRO-PRE group (P = 0.43) (Fig. 1d). Group differences for MRI-derived FM were significant between PRO and PRE groups (P < 0.001) and PRE and PRO-PRE (P = 0.02).

All groups comparably increased FFM (Table 2) [PRO = 1.4 (1.4) kg; P = 0.01; PRE = 1.6 (2.4) kg; P = 0.06; PRO-PRE = 1.4 (2.0) kg; P = 0.05]. The changes in DXA-derived FM for the three groups were distinct and agreed closely with FM analyses by MRI (Table 2). A significant FM gain of 2.1 (1.4) kg for the PRO group (P = 0.001) contrasted a 1.8 (2.4) kg FM loss for the PRE group (P = 0.05), and resulted in significant between group differences for PRO versus PRE (P = 0.003). There was no change in FM observed for the PRO-PRE treatment group (P = 0.94).

	Group <sup>b,c</sup>		
	PRO	PRE	PRO-PRE
Height (cm)	160.5 (6.9)	159.3 (4.0)	160.5 (8.9)
Weight (kg)	55.6 (6.9)	59.0 (5.9)	54.6 (9.0)
Body mass index (kg/m <sup>2</sup> )	23.4 (2.0)	24.8 (2.5)	23.0 (2.3)
Age (years)	38.2 (8.6)	41.0 (10.2)	43.4 (10.6)
Age range (years)	28-55	31-50	29-66
Race			
White	n = 1	n = 1	n = 0
Black	n = 7	n = 8	n = 7
Hispanic	n = 2	n = 1	n = 3
CD4+ lymphocytes (cells $\times$ 10 <sup>6</sup> /l)	215.3 (295.0)	248.8 (176.3)	335.1 (295.0)
Viral load (copies/ml)	93 847.7 (158 609.8)	44 449.7 (88 724.7)	100 343.7 (230 928.6)

<sup>a</sup>Data are mean (SD) unless otherwise indicated. <sup>b</sup>PRO indicates protein supplementation; PRE indicates progressive resistance exercise; PRO– PRE indicates combined treatment. <sup>c</sup>No significant between group differences for body weight, age, CD4+ lymphocytes, or HIV RNA by analysis of variance (all P > 0.05).

	Group <sup>b</sup>		
	PRO	PRE	PRO-PRE
Body weight (kg)			
Baseline	55.6 (6.9)	59.0 (5.9)	54.6 (8.9)
Week 20	59.2 (7.5)	58.8 (5.6)	55.9 (9.2)
Change from baseline	3.6 (2.3) <sup>c</sup>	-0.1(2.0)	1.3 (3.8)
<i>P</i> value	0.001	0.86	0.31
Body cell mass by TBK (kg)			
Baseline	15.0 (1.7)	15.2 (1.1)	14.2 (2.4)
Week 20	15.5 (1.7)	15.9 (1.4)	14.8 (2.0)
Change from baseline	0.50 (0.77)	0.74 (0.90)	0.61 (0.64)
Pvalue	0.07	0.03	0.01
Skeletal muscle by MRI (kg)			
Baseline	18.2 (2.3)	18.5 (2.1)	17.5 (3.6)
Week 20	18.8 (1.6)	19.7 (1.9)	18.1 (3.2)
Change from baseline	0.6 (1.1)	1.2 (.69)	0.6 (1.6)
Pvalue	0.12	< 0.001	0.30
Fat mass by MRI (kg)			
Baseline	15.3 (6.0)	18.4 (5.1)	15.8 (4.4)
Week 20	17.8 (6.4)	16.7 (4.7)	16.4 (3.7)
Change from baseline	2.5 (1.8) <sup>d</sup>	-1.7 (1.8) <sup>e</sup>	0.7 (2.6)
Pvalue	0.002	0.02	0.43
Fat-free mass by DXA (kg)			
Baseline	40.5 (3.4)	40.2 (2.7)	38.8 (6.3)
Week 20	42.0 (3.2)	41.9 (2.5)	40.2 (6.1)
Change from baseline	1.4 (1.4)	1.6 (2.4)	1.4 (2.0)
<i>P</i> value	0.01	0.06	0.05
Fat mass by DXA (kg)			
Baseline	15.1 (5.9)	18.7 (5.4)	15.8 (5.0)
Week 20	17.2 (6.0)	17.0 (5.3)	15.7 (4.1)
Change from baseline	2.1 (1.4) <sup>f</sup>	-1.8(2.4)	-0.1(3.7)
Pvalue	0.001	0.05	0.94

Table 2.	Body weight and	body com	position <sup>a</sup> .
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<sup>a</sup>Data are mean (SD) by paired t-test. TBK, total body potassium counting; MRI, magnetic resonance imaging; DXA, dual energy X-ray absorptiometry. <sup>b</sup>PRO denotes protein supplementation; PRE denotes progressive resistance exercise; PRO–PRE denotes combined treatment. <sup>c</sup>Significantly different versus PRE group by analysis of variance (ANOVA), P = 0.007. <sup>d</sup>Significantly different versus PRE group by ANOVA, P < 0.001. <sup>e</sup>Significantly different versus PRO–PRE group by ANOVA, P = 0.02. <sup>f</sup>Significantly different versus PRE group by ANOVA, P = 0.003.

#### 1-Repetition maximum muscle strength

Maximum dynamic muscle strength for the exercise groups (PRE and PRO-PRE) significantly increased for all seven muscle groups trained (range of increase 40.6–95.3%, all P < 0.001) (Table 3). The range of increased strength for the PRO group was of a lesser magnitude at 6.6–16.9% (P = 0.01-0.12).

#### Quality of life

For the total study sample, half of the mean baseline scores for physical, psychological, and social MOS health status sub-scales were limited to a median percentile score of 25% as compared to standard control data (Table 4). Following treatment, the physical activity score significantly increased for the PRE group (P = 0.02), but significantly declined for PRO subjects (P = 0.01) with significant differences noted between PRO and PRE (P < 0.001) and PRO and PRO–PRE (P = 0.03) groups. Significant improvements in general health perceptions (P = 0.03) and vitality (P = 0.007) were also observed for PRE women.

Significant effects for the PRO-PRE group were restricted to social functioning (P = 0.04) with a ceiling effect noted for the response to the physical activity portion of the survey. Inspection of raw data revealed that six of 10 PRO-PRE subjects answered toward the upper end of the physical activity scale at baseline, leaving only a small margin to show improvement.

#### **Dietary analysis**

Volitional energy and protein consumption at baseline was similar for all three groups (P > 0.05) and in compliance with American Dietetic Association adult requirements [41]. The PRO group significantly increased energy intake (supplemental whey protein plus *ad libitum* food intake) by 42% during treatment (week 13 calculation) (data not shown). Mid-study total protein consumption (supplemental protein plus *ad libitum* food intake) increased from baseline by 85% for PRO and by 36% for PRO–PRE women (data not shown).



**Fig. 1.** Change in body weight, body cell mass by potassium-40 counting and skeletal muscle and fat by magnetic resonance imaging. Data are mean (SD). PRO, protein supplementation; PRE, progressive resistance exercise; PRO–PRE denotes combined treatment. Significant change from baseline by paired t-test, \*P < 0.05; \*\*P < 0.01; †P < 0.001. Significant change from PRE group by analysis of variance, ‡P = 0.007. Significant change from PRC group, P < 0.001. Significant change from PRE, P = 0.02.

# Discussion

This study demonstrated that exercise treatment with progressive resistance provides an overall health benefit for BCM-wasted, HIV-infected women, including significant gains in BCM, SM, dynamic muscle strength, and subjective physical, psychological, and social QOL. For PRO patients, non-significant increases in BCM and SM coincided with minor gains in 1–RM strength ranging from 1.7 to 5.4 lbs in weight lifted (Table 3), and little change in QOL sub-scales (Table 4). In fact, post-treatment, the QOL physical activity score significantly decreased for PRO women (P = 0.01) indicating worse physical function. Although BCM significantly increased for both exercise groups, a notable finding of this study is that ancillary whey protein coupled with resistance exercise offered no benefit for recovery of BCM for the PRO–PRE group compared to resistance exercise alone (Fig. 1b).

We also found that SM significantly increased for PRE patients (P < 0.001) (Fig. 1c), but not for the combined treatment group (P = 0.30). As the nature of the increase in BCM is uncertain, we would postulate that the increase in BCM for the PRO–PRE women could be partly attributable to gains in cell mass other than SM, i.e., visceral parenchyma [3]. The similar improvements in DXA-derived FFM for the three treatment groups may reflect change in any lean tissue component, including extracellular body water, and does not imply an increase in the functional body tissues of the BCM. This point should be considered when evaluating treatment effects of HIV-related anabolic trials that use DXA and other two-compartment body composition models.

A relevant issue concerns the characteristic loss of FM that often results from progressive resistance exercise [44-48]. For PRE subjects, post-training FM declined by 1.7 kg with BW unchanged (Fig. 1a, 1d). In contrast, the PRO group experienced significant gains in BW and FM, whereas PRO-PRE women maintained baseline FM levels with a small 1.3 kg increase in BW. The variations in BW change likely reflect the increase in total caloric consumption (data not shown). In addition, the energy expended during training may partly explain the disparity in body weight changes between the PRO-PRE and PRO groups. Our patients were malnourished as defined by low BCM but were not underweight on average (Table 1). For HIV patients and others who experience classical wasting disorders that may be defined by BW, BCM, and FM loss, the additive effect of combined PRO and PRE treatment may sustain energy dense FM stores while promoting increases in body protein and physical function. Of note, HIV-wasting with weight loss correlates with decreased food consumption [49], thus these data reflect the importance of maintaining caloric intake, and suggest that in the present trial, the effects of supplemental protein on body composition may not be different than effects of ancillary carbohydrate or fat.

Significant increases in muscle strength have been reported for resistance-trained HIV-positive men [25–28]. In accord, this is the first trial to demonstrate that HIV-positive women with depleted BCM show

	Group <sup>b</sup>		
	PRO	PRE	PRO-PRE
Bench press			
Baseline	33.6 (9.7)	33.1 (14.2)	28.6 (10.4)
Week 20	39.0 (13.3)	57.3 (19.5)	52.3 (15.8)
Percentage increase	13.5	76.9	86.7
<i>P</i> value	0.02	$< 0.001^{d}$	< 0.001 <sup>c</sup>
Seated back row			
Baseline	46.5 (8.9)	45.3 (12.5)	49 (12.6)
Week 20	50.5 (11.9)	81.5 (13.0)	74.3 (15.0)
Percentage increase	7.1	85.6	51.1
<i>P</i> value	0.12	< 0.001 <sup>c,f</sup>	$< 0.001^{d}$
Shoulder press			
Baseline	24.4 (9.7)	23.5 (6.1)	21.1 (6.3)
Week 20	27.5 (8.9)	44.5 (14.3)	39.3 (9.9)
Percentage increase	15.9	84.4	88.4
<i>P</i> value	0.02	< 0.001 <sup>c</sup>	< 0.001 <sup>c</sup>
Biceps curl			
Baseline	24.1 (7.7)	22.6 (6.1)	24.0 (5.1)
Week 20	27.8 (7.1)	36.0 (6.4)	35.3 (7.6)
Percentage increase	16.9	61.4	46.8
<i>P</i> value	0.01	< 0.001 <sup>c</sup>	$< 0.001^{e}$
Triceps extension			
Baseline	31.8 (4.4)	29.6 (4.6)	30.6 (5.1)
Week 20	33.5 (4.1)	50.0 (7.6)	43.8 (5.6)
Percentage increase	6.6	68.7	43.2
<i>P</i> value	0.02	< 0.001 <sup>c,t</sup>	< 0.001 <sup>c</sup>
Leg extension			
Baseline	46.8 (13.3)	44.4 (8.9)	49.5 (11.3)
Week 20	51.8 (10.0)	90.5 (16.1)	81.0 (20.6)
Percentage increase	12.6	95.3	63.3
<i>P</i> value	0.03	< 0.001 <sup>c,r</sup>	$< 0.001^{\circ}$
Leg curl			
Baseline	27.0 (8.3)	26.5 (6.5)	31.6 (12.3)
Week 20	30.8 (8.4)	46.3 (8.1)	44.0 (16.2)
Percentage increase	15.9	77.4	40.6
Pvalue	0.09	< 0.001 <sup>c,i</sup>	< 0.001°

Table 3.	Maximum	dynamic	muscle	strength <sup>a</sup> .
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<sup>a</sup>Strength was assessed by the 1-repetition maximum method; Data are mean (SD) of original metric data in lbs; Statistical outcome is based on natural logarithmic-transformed data by paired t-test. <sup>b</sup>PRO denotes protein supplementation; PRE denotes progressive resistance exercise; PRO–PRE denotes combined treatment. <sup>c</sup>Significantly different versus PRO group by analysis of variance (ANOVA), P < 0.001. <sup>d</sup>Significantly different versus PRO group by ANOVA, P < 0.01. <sup>e</sup>Significantly different versus PRO group by ANOVA, P < 0.05.

marked increases in dynamic muscle strength for all muscle groups trained (P < 0.001) (Table 3), with the proportion of strength gains implying low initial strength [42]. Only two studies have reported body composition changes resulting from progressive resistance training in HIV disease. Roubenoff et al. [27] observed a DXA-derived 1.8 kg mean increase in mineral-free LBM for a predominantly male HIV cohort (20 men, five women) following 8 weeks of PRE. When combining the women from PRE and PRO-PRE groups, our findings in 20 women trained for 14 weeks were lower versus the men for accretion of absolute LBM by DXA (data not shown) (+1.2 kg women, +1.8 kg men), but near identical when comparing relative change (+3.1% women, +3.3% men). Bhasin et al. [25] compared the effects of resistance exercise, testosterone, and combined exercise-testosterone treatment on body composition and muscle strength in testosterone-deficient, moderately wasted, HIV-infected men. The data demonstrated that 16week treatment with resistance exercise resulted in significant increases in thigh muscle mass, FFM, and muscle strength. These gains were equivalent to that of the testosterone and combined testosterone–exercise regimens, thus questioning the necessity of anabolic hormone therapies to improve muscle size and function in malnourished persons with HIV.

We considered the effects of PRO and PRE treatment on subjective health status and demonstrated the importance of validated QOL surveys in clinical trials. At baseline, patient ratings for most MOS dimensions were quite low with a median percentile score of 25% in comparison with standardized values for 1412 female

#### Table 4. Quality of life<sup>a</sup>

	Group <sup>b</sup>		
—	PRO	PRE	PRO-PRE
Physical activity limitations due to health			
Standardized mean $= 81.5 (24.6)$			
25th percentile = $65.0$			
Baseline	65.0 (32.2)	62.5 (22.0)	75.0 (25.1)
20 Week	56.0 (29.7)	82.0 (21.4)	83.0 (18.9)
<i>P</i> value	0.01	$0.02^{\circ}$	0.15 <sup>u</sup>
Role activity limitations due to physical health			
Standardized mean = $77.8(36.2)$			
25th percentile = 50.0	45 0 (42 0)	50.0 (40.0)	
Baseline	45.0 (43.8)	50.0 (40.8)	65.0 (45.9)
Week 20	52.5 (46.3)	82.5 (33.4)	92.5 (12.1)
P value	0.43	0.06	0.13
Stor deading and more 72 ( (24.2)			
Standardized mean = $73.6(24.3)$			
25 m percentile = $52.0$	(1, 2, (20, 2))	$(4 \Gamma (17 C))$	FO ( (22, 4)
Moole 20	61.3(20.2)	04.5 (17.0) 72.1 (12.6)	59.0 (25.4)
Rualua	0.25	/2.1 (13.6)	0.28
Conoral health percentions	0.23	0.27	0.20
Standardized mean $= 70.6(21.5)$			
25th porcontilo = 57.0			
2501 percentrie – 57.0 Basolino	46 2 (22 3)	53 8 (23 8)	47 4 (24 5)
W/ook 20	53 8 (28 6)	67 3 (22.1)	56 0 (25 0)
Pyalue	0.05	0.03	0.06
Vitality	0.05	0.05	0.00
Standardized mean $= 58.4(21.5)$			
25th percentile = 45.0			
Baseline	54.0 (29.2)	52.0 (22.5)	54.0 (13.3)
Week 20	56.0 (31.8)	65.0 (20.9)	64.5 (21.0)
Pvalue	0.68	0.007	0.14
Social limitations due to physical/emotional problems			
Standardized mean = $81.5(23.7)$			
25th percentile = $62.5$			
Baseline	67.7 (29.0)	73.9 (24.6)	54.0 (30.0)
Week 20	66.4 (30.5)	87.6 (16.7)	77.7 (21.9)
<i>P</i> value	0.79	0.06	0.04
Role activity limitations due to emotional problems			
Standardized mean = $79.5(34.4)$			
25th percentile = $66.7$			
Baseline	49.9 (45.2)	73.1 (41.0)	49.9 (45.2)
Week 20	60.0 (51.6)	83.3 (36.1)	76.7 (35.3)
<i>P</i> value	0.34	0.62	0.07
Mental health			
Standardized mean = $73.3$ (18.7)			
25th percentile = $64.0$			
Baseline	60.0 (27.5)	71.6 (18.1)	57.6 (21.3)
Week 20	66.4 (27.5)	76.0 (12.6)	71.2 (24.1)
P value	0.12	0.53	0.05

<sup>a</sup>Data are mean (SD) by paired t-test; Possible range of values is 4–100 for mental health and 0–100 for all other sub-scales; Standardized mean and 25th percentile data taken from reference [32]; Higher scores denote improved health status. <sup>b</sup>PRO denotes protein supplementation; PRE denotes progressive resistance exercise; PRO–PRE denotes combined treatment. <sup>c</sup>Significantly different versus PRO group by analysis of variance (ANOVA), P < 0.001. <sup>d</sup>Significantly different versus PRO group by ANOVA, P < 0.05.

controls (Table 4). This attests to the severity of HIV and the limitations of these BCM-wasted women relative to eight subjective health status variables. Following treatment, the PRE women experienced favorable increases for all sub-scales with physical activity scores bypassing the mean standardized score for healthy women. For the PRO-PRE group, an elevated baseline score for the physical activity subscale left only a small margin to show improvement. This resulted in a ceiling effect that blunted the mean physical activity response, disallowed an association between BCM and physical activity, and depicts a shortcoming of survey data. All MOS domains, however, moved toward improved health status for PRO– PRE women.

It is noteworthy that objective measures of BCM and 1-RM increased for PRO women yet their subjective

response to QOL was a significant drop in physical activity ratings. Although the 1–RM increases were small and probably not clinically relevant (Table 3), these paradoxical responses offered an opportunity for further interpretation of biologic change versus overall function that might have otherwise been overlooked.

Pharmacologic studies designed to combat HIV-related wasting have not substantiated that any one treatment i.e., testosterone [10-14], anabolic steroids [15], rhGH [16,17] surpasses the universal benefits observed in the present trial. We successfully improved the health status of HIV-positive women of varied ages (28 to 66 years) without undue side effects, and without pharmacologic agents. Although the study concluded with data for only 30 of 43 eligible women, most withdrawals were due to the family constraints of single parenting. Treatment adherence was quite good, with only seven women discontinuing participation during the treatment period, including one death. Drop-outs were random between groups and presented no bias to our results.

In conclusion, the recent advent of HAART has successfully reduced death rates and disease complications in HIV illness, yet protein wasting, decreased physical function, and diminished QOL continue to affect patients. For BCM-wasted HIV-positive women, treatment with whey protein promoted weight and fat gain with little effect on physical function and QOL, whereas resistance training increased BCM, SM, muscle strength, and QOL leading to total functional improvement. Contrary to our hypothesis, the coupling of whey protein and resistance exercise did not promote BCM accretion in excess of that achieved by resistance exercise alone. The full potential of resistance exercise to restore BCM in HIV populations cannot be addressed in a short-term 14-week interval. Ongoing PRE therapy may provide further gains in BCM and surpass the muscle-building capabilities of anabolic pharmaceuticals, a point for further study.

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