

also important to consider that the study population had a relatively high education level (only 7.5% of the participants had less than a high school education). Because limited education or literacy may be expected to attenuate the effects of an education program, their results may not be relevant for other countries that have a lower average education level<sup>5</sup> or for segments of the US population with less literacy.

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**Financial Disclosures:** None reported.

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**In Reply:** We agree with Dr Mariotto that many diverse factors contribute to hypertension and success in its management and that the evaluation of such potential confounders is an important step in the evaluation of clinical trials. The intervention used in the Federal Study of Adherence to Medications in the Elderly focused on adherence to medications that have known efficacy in the treatment of hypertension and hyperlipidemia. No data were collected on factors such as physical activity or diet, so we cannot present a comparison between the study groups or adjust for any differences.

Regarding the generalizability of our findings to other populations, the participant characteristics we described in Table 1 suggest the types of patients for whom our results are most directly applicable. We agree that data from clinical trial populations are most appropriately translated to clinical care populations when both are closely matched on relevant variables.

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**Financial Disclosures:** Dr Taylor reported receiving research grants and honoraria from Kos Pharmaceuticals, honoraria from Pfizer Pharmaceuticals, Wyeth Pharmaceuticals, and Merck KgA, and a consulting agreement with Alinea Pharmaceuticals. Drs Lee and Grace reported no financial disclosures.

## RESEARCH LETTER

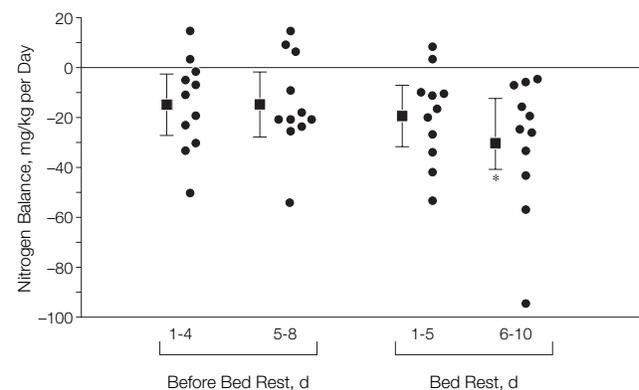
### Effect of 10 Days of Bed Rest on Skeletal Muscle in Healthy Older Adults

**To the Editor:** Older adults are more likely to be hospitalized and are at risk for functional decline during hospitalization. Bed rest may contribute to this functional compromise. We examined the effect of 10 days of bed rest in healthy older men and women on skeletal muscle protein synthesis, nitrogen balance, lean tissue mass, and lower extremity strength.

**Methods.** Twelve healthy older adults who were moderately active (mean [SD] age, 67 [5] years; 50% women) were recruited from advertisements and compensated for their participation. They remained in bed continuously for 10 days, except for toileting, and they consumed a eucaloric diet providing the recommended dietary allowance for protein (0.8 g/kg of protein per day). Measurements before and after bed rest included the fractional muscle protein synthesis rate over 24 hours, lean body mass by dual-energy x-ray absorptiometry (DEXA, Hologic Inc, Waltham, Mass), and unilateral knee extension strength (Cybex Strength Systems, Ronkonkoma, NY). Urinary nitrogen balance was determined before and during the bed rest period. Prophylactic measures were performed to prevent deep vein thrombosis, and ultrasound examination results were negative for all participants at the conclusion of the bed rest. One participant was excluded from all analyses due to insufficient protein intake; an additional participant was excluded from the DEXA analysis because a DEXA scan was not administered before bed rest, and another participant's fractional synthesis rate measurement was excluded because of a technical error.

Values for muscle protein synthesis, DEXA, and knee extension strength before and after bed rest were compared by paired *t* tests. Nitrogen balance data were analyzed with repeated measures analysis of variance and post hoc Tukey

**Figure.** Daily Nitrogen Balance (n=11)



Squares with error bars represent means and 95% confidence intervals for the time period.

\*Significantly different from days 1 through 4 and days 5 through 8 before bed rest (repeated measures analysis of variance with post hoc Tukey test,  $P=.02$ ).

**Table.** Effects of 10 Days of Bed Rest in Older Adults

	No. of Participants (N = 12)*	Mean (95% Confidence Interval)			P Value
		Bed Rest		Change	
		Before	After		
Muscle fractional synthetic rate, % per h†	10	0.077 (0.059 to 0.095)	0.051 (0.035 to 0.067)	-0.027 (-0.007 to -0.047)	.02
% Change				-30.0 (-7.0 to -54.0)	
DEXA lean mass, kg‡	10				
Whole body		48.05 (40.61 to 55.49)	46.51 (39.57 to 53.45)	-1.50 (-0.62 to -2.48)	.004
% Change				-3.2 (-1.4 to -5.0)	
Lower Extremity		15.01 (12.41 to 17.61)	14.06 (11.85 to 16.27)	-0.95 (-0.42 to -1.48)	.003
% Change				-6.3 (-3.1 to -9.5)	
Isokinetic muscle strength, Nm per s§	11	120 (96 to 145)	101 (81 to 121)	-19 (-11 to -30)	.001
% Change				-15.6 (-8.0 to -23.1)	

Abbreviation: DEXA, dual-energy x-ray absorptiometry; Nm, Newton meter.

\*One participant was excluded from all analyses because of insufficient protein intake.

†Because of a technical error, the muscle fractional synthesis rate measurement was excluded for 1 participant.

‡One participant was excluded from the DEXA analysis because the scan before bed rest was not administered.

§Isokinetic knee extension at 60° per second.

test. A change in the mean (SD) fractional synthesis rate of 0.034% (0.019%) per hour (2-tailed  $\alpha = .05$ ) would result in a power of 99.9% with 12 participants. However, when power was calculated with the actual changes for each parameter and the number of participants assessed, the following values were obtained: fractional synthetic rate, 77%; whole body lean mass, 90%; leg lean mass, 94%; strength, 97%; and nitrogen balance, 70%. Analyses were performed with Excel 2004 (Microsoft Corp, Redmond, Wash) and SPSS version 12.0 (SPSS Inc, Chicago, Ill). The institutional review board at each site approved this study, and each participant signed a written informed consent.

**Results.** Comparing values after bed rest with before bed rest values, there was a significant decrease in muscle protein synthesis (-0.027% per hour; 95% confidence interval [CI], -0.007 to -0.047% per hour; % change, -30%; 95% CI, -7% to -54%;  $P = .02$ ), whole body lean mass (-1.50 kg; 95% CI, -0.62 to -2.48 kg;  $P = .004$ ), lower extremity lean mass (-0.95 kg; 95% CI, -0.42 to -1.48 kg;  $P = .003$ ), and strength (-19 Newton meters per second; 95% CI, -11 to -30 Newton meters per second; % change, -15.6%; 95% CI, -8.0% to -23.1%;  $P = .001$ ; TABLE). Total mean nitrogen balance remained negative throughout the study (including before bed rest) but was significantly lower during the last half of the bed rest period compared with before bed rest (-30 mg/kg per day; 95% CI, -7 to -32 mg/kg per day vs -15 mg/kg per day; 95% CI, -3 to -27 mg/kg per day;  $P = .02$ ; FIGURE). Total body fat did not change significantly (-0.07 kg; 95% CI, -0.67 to 0.53 kg; % change, -0.3%; 95% CI, -2.3 to 1.8). No differences between sexes were found.

**Comment.** In this group of healthy older adults, there was a large loss of skeletal muscle as a result of bed rest, particularly from the lower extremities. Participants experienced a greater lean tissue loss in 10 days than did young individuals after 28 days,<sup>1</sup> whereas the decline in protein synthesis and strength was similar to that of younger partici-

pants after 14 days.<sup>2</sup> Protein undernutrition is common in hospitalized older adults<sup>3</sup>; the participants in this study were in negative nitrogen balance even before bed rest despite being on a diet with the recommended dietary allowance for protein. Their nitrogen balance declined further during bed rest.

The results of this study cannot be directly extrapolated to chronically ill or frail elderly persons. However, the pronounced effect of bed rest alone on skeletal muscle mass and function suggests that this factor combined with the physiological stress and other deleterious factors associated with hospitalization<sup>4</sup> may result in a more substantial loss of muscle size and function for many older adults during hospitalization. Further studies are needed to characterize other key components (eg, nutritional compromise, inflammation) compromising muscle function, as well as interventions to prevent or ameliorate the functional decline that frequently occurs in this patient population.

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Drs Wolfe and Ferrando were affiliated with the University of Texas Medical Branch, Galveston, at the time of the study.

**Author Contributions:** Dr Kortebein had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Conception and design:** Ferrando, Wolfe, Evans.

**Acquisition of data:** Kortebein, Ferrando, Lombeida, Evans.

**Analysis and interpretation of data:** Kortebein, Ferrando, Lombeida, Wolfe, Evans.

**Drafting of the manuscript:** Kortebein.

**Critical revision of the manuscript for important intellectual content:** Kortebein, Ferrando, Lombeida, Wolfe, Evans.

**Statistical analysis:** Kortebein, Ferrando, Wolfe, Evans.

**Obtaining funding:** Ferrando, Wolfe, Evans.

*Administrative, technical, or material support:* Kortebein, Ferrando, Lombeida, Evans.  
*Supervision:* Ferrando, Wolfe, Evans.

**Financial Disclosures:** None reported.

**Funding/Support:** The work for this research letter was funded by grant PO1AG023591 from the National Institute on Aging (Evans). The studies were conducted in the General Clinical Research Center at the University of Arkansas for Medical Sciences and the University of Texas Medical Branch at Galveston, and funded by grant MO1 RR14288 (University of Arkansas Medical Sciences), and MO1 RR 00073 (University of Texas Medical Branch) from the National Center for Research Resources.

**Role of the Sponsor:** These organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

**Acknowledgment:** We thank Douglas Paddon-Jones, PhD, Ola Ronsen, MD, PhD, and T. Brock Symons, PhD, of the University of Texas Medical Branch, Galveston, for their significant contributions toward the completion of this study, including data collection and analysis, as well as review of the manuscript. These individuals received compensation.

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## CORRECTIONS

**Incorrect Wording:** In the Medical News & Perspectives story entitled "Trials Probe New Agents for Kidney Cancer" published in the July 12, 2006, issue of *JAMA* (2006;296:155-157), sunitinib was misidentified as a second-line treatment for

advanced renal cell carcinoma. On page 155, column 2, the first full sentence should be "The results led to sunitinib's approval by the US Food and Drug Administration in January for advanced renal cell carcinoma."

**Mislabeled Column Headings in Table 7:** In the Original Contribution entitled "Insurance Coverage, Medical Care Use, and Short-term Health Changes Following an Unintentional Injury or the Onset of a Chronic Condition" published in the March 14, 2007, issue of *JAMA* (2007;297:1073-1084), in Table 7, the column headings for columns 3 and 5 should be "Adjusted Difference, % (if Insured)." The dagger footnote should be "Underlying odds ratios (Table 4) for medical care use/health outcome category significantly different from insured,  $P < .05$ ."

**Incorrect References Cited:** In the Original Contribution entitled "Trends in Emergency Medicaid Expenditures for Recent and Undocumented Immigrants" published in the March 14, 2007, issue of *JAMA* (2007;297:1085-1092), 3 sentences cited incorrect references. On page 1090, within the Comment section, the second full sentence "In California, for example, a study in 2000 concluded that elimination of public funding for the prenatal care of undocumented immigrants would prove far more costly to taxpayers by substantially increasing low-birth weight, prematurity, and postnatal costs.<sup>33</sup>" should cite reference 32. The third sentence "Only 8 states have taken advantage of a 2002 "unborn child" option under the State Children's Health Insurance Program, which applies federal matching dollars to prenatal care coverage for undocumented women, while 5 additional states provide state funding for prenatal care regardless of immigration status.<sup>7,30</sup>" should cite reference 44 instead of 30. The fifth sentence "Immigrants, and particularly Hispanic immigrants, account for a disproportionate number of workplace injuries and fatalities in the United States.<sup>35</sup>" should cite "US Department of Labor. Occupational Safety and Health Administration's efforts to protect immigrant workers, statement of John L. Henshaw, Assistant Secretary of Labor for Occupational Safety and Health before the Subcommittee on Employment, Safety and Training Committee on Health, Education, Labor and Pensions, United States Senate, February 27, 2002. [http://www.osha.gov/pls/oshaweb/owadisp.show\\_document?p\\_table=TESTIMONIES&p\\_id=286](http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=TESTIMONIES&p_id=286). Accessed November 2, 2006," which is not listed among the article's references.