

# Muscle-Strengthening Activity and Its Association With Insulin Sensitivity

YILING J. CHENG, MD, PHD  
EDWARD W. GREGG, PHD  
NATHALIE DE REKENEIRE, MD, MS  
DESMOND E. WILLIAMS, MD, PHD

GIUSEPPINA IMPERATORE, MD, PHD  
CARL J. CASPERSEN, PHD, MPH  
HENRY S. KAHN, MD

## RESEARCH DESIGN AND METHODS

### Study population and data sources

The NHANES, which is conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, is an ongoing representative survey designed to measure the health and nutrition status of the civilian noninstitutionalized U.S. population. NHANES 1999–2004 used a complex, multistage probability sample. Data were collected by household interviews and through standardized physical examinations conducted in mobile examination centers in different locations around the U.S. (5). Half of the participants were randomly assigned to the morning session of the mobile examination center and asked to fast from 8 to <24 h. In the 1999–2004 survey, the overall response rate was 82% for those in the interviewed survey and 77% for those in mobile examination center examination. Informed consent was obtained for all participants.

There were 5,554 participants, aged 20–79 years, who attended the morning examination and who had fasted at least 8 h. We excluded women who were pregnant ( $n = 318$ ), participants who had been diagnosed with diabetes ( $n = 430$ ), participants with fasting glucose  $\geq 7.0$  mmol/l ( $n = 180$ ), participants who had missing insulin or glucose measurement ( $n = 77$ ), and those who were missing a weight or height measurement ( $n = 45$ ). The remaining 4,504 participants were included in the analyses. Among this final sample, median values of cotinine (men: 0.24 ng/ml, women: 0.06 ng/ml,  $n = 41$ ), total kilocalories (kcal) of energy intake (men: 2,502 kcal/day, women: 1,754 kcal/day,  $n = 45$ ), and alcohol consumption (0 drinks/week,  $n = 136$ ) were used to impute missing values for these variables, all of which were used in the analysis.

### Measures of insulin sensitivity

Fasting plasma glucose and insulin concentrations were measured on participants who fasted from 8 to <24 h before the examination. All insulin and glucose assays were performed at the Diabetes Diagnostic Laboratory at the University of Missouri, Columbia, Missouri. Fasting

**OBJECTIVE**— Muscle-strengthening activities (MSAs) may increase insulin sensitivity, thereby reducing the risk of diabetes. The purpose of this study was to assess the relationship between MSAs and insulin sensitivity among American adults.

**RESEARCH DESIGN AND METHODS**— We analyzed data on 4,504 adults without diabetes, aged 20–79 years, who participated in the National Health and Nutrition Examination Survey 1999–2004 and had information on MSAs. Self-reported frequency (times/week) of MSAs was grouped as low (<1), moderate (1–2.9), or high ( $\geq 3$ ). Insulin sensitivity was measured by the fasting quantitative insulin sensitivity check index  $\times 100$  (QUICKI).

**RESULTS**— After adjustment for age, race/ethnicity, physical activity other than MSAs, BMI, smoking, alcohol consumption, and daily total caloric intake, the mean values for QUICKI by low, moderate, and high MSA were 33.6, 33.9, and 34.2, respectively ( $P$  for linear trend = 0.008) for men and 34.2, 34.6, 34.6, respectively ( $P$  for linear trend = 0.009) for women. Mean fasting insulin (picomols per liter) concentrations were 75.0, 68.9, and 65.9, respectively ( $P$  for linear trend = 0.017) for men and 66.9, 63.3, 61.2, respectively ( $P$  for linear trend = 0.007) for women. There were no significant differences across MSA groups for fasting glucose among men or women.

**CONCLUSIONS**— MSA is independently associated with higher insulin sensitivity among U.S. adults. Efforts to increase MSA may be a realistic, feasible, and effective method of reducing insulin resistance among the U.S. population.

*Diabetes Care* 30:2264–2270, 2007

Studies (1,2) have demonstrated the association of muscle-strengthening activities (MSAs) with improved insulin sensitivity and enhanced glycemic control among people with type 2 diabetes. These observations, along with the recognized benefits of MSA in terms of maintaining functional status and reducing the odds for other risk factors for chronic disease, have led several organizations to recommend MSAs at the level of two or three times per week (3,4).

Despite this general agreement about the value of strength training, experimental interventions have largely lasted only

3–6 months (3). Such interventions may not reflect the patterns of MSAs typically performed in the real world, and they may not reveal its natural impact on risk of diabetes or long-term outcomes, as would be available from a population-based, cross-sectional study in which participants report on their customary use of MSAs.

In these analyses, we examine whether MSAs and other lifestyle factors are independently associated with insulin sensitivity among U.S. adults by using the U.S. National Health and Nutrition Examination Survey (NHANES) 1999–2004.

From Diabetes Translation, Centers for Disease Control and Prevention, Atlanta, Georgia.

Address correspondence and reprint requests to Yiling J. Cheng, MD, PhD, Diabetes Translation, Centers for Disease Control and Prevention, 4770 Buford Hwy. NE, Mailstop K-10, Atlanta, GA 30341. E-mail: ycc1@cdc.gov.

Received for publication 22 February 2007 and accepted in revised form 14 June 2007.

Published ahead of print at <http://care.diabetesjournals.org> on 22 June 2007. DOI: 10.2337/dc07-0372.

**Abbreviations:** MSA, muscle-strengthening activity; NHANES, National Health and Nutrition Examination Survey; QUICKI, quantitative insulin sensitivity check index  $\times 100$ .

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

© 2007 by the American Diabetes Association.

The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

plasma glucose was measured enzymatically by the hexokinase method. Serum insulin was measured by radioimmunoassay with the double-antibody batch method. Details about these laboratory procedures and quality control have been previously published (6).

We measured insulin sensitivity using the quantitative insulin sensitivity check index (QUICKI) percent ( $100/[\log \text{fasting insulin } \{\text{uU/ml}\} + \log \text{glucose } \{\text{mg/dl}\}]$ ) or ( $100/[0.48 + \log \text{fasting insulin } \{\text{pmol/l}\} + \log \text{glucose } \{\text{mmol/l}\}]$ ) (7), which largely reflects hepatic insulin sensitivity and basal hepatic glucose production (8). The higher the QUICKI value the higher the predicted insulin sensitivity.

### Physical activity

History of physical activity was obtained by a questionnaire administered during the home interview. The MSA level was evaluated by asking, "Over the past 30 days, how often did you do any physical activities designed to strengthen your muscles such as lifting weights, push-ups, or sit-ups? Include all such activities even if you have mentioned them before."

The American Heart Association (3) has recommended that resistance exercise be done at least twice per week, and Sigal et al. (4) recommend that resistance training be performed three times a week. Accordingly, we divided self-reported MSA (times/week) into three groups: low (<1), moderate (1–2.9), and high ( $\geq 3$ ), whose associated medians were 0, 2, and 5 times/week, respectively.

Participants were also asked to report the frequency and duration of moderate and vigorous physical activity during the past month, allowing for 51 anticipated activities and other reported activities that were not anticipated (9). MSAs such as push-ups, sit-ups, weight lifting, and wrestling were excluded from the list for calculating physical activities other than MSAs (non-MSAs) levels. Non-MSAs estimated metabolic cost in metabolic equivalents (METs) were assigned according to a standardized coding system developed by Ainsworth et al. (10) and was defined as the ratio of work metabolic rate to standard resting metabolic rate. We assigned MET codes of 4.5 and 7.0 for moderate and vigorous activity, respectively. One MET is equivalent to the oxygen consumed during seated rest ( $\sim 3.5$  ml of oxygen  $\cdot$  kg $^{-1}$   $\cdot$  min $^{-1}$ ). Individuals who did not report any activity lasting at least 10 min were classified as sedentary. In those who reported any physical activ-

ity lasting at least 10 min, physical activity was categorized into two groups based on the median of the MET distribution: moderate (<14.4 MET  $\times$  h/week) and high ( $\geq 14.4$  MET  $\times$  h/week).

### Other variables

Exposure to tobacco smoke increases the concentration of nicotine in the blood, and nicotine is highly specific for such exposure. Cotinine is a major metabolite of nicotine. Using their serum cotinine concentrations (in ng/ml), we classified participants in four groups: nonsmoker (<14), light smoker (14–99), moderate smoker (100–199), and heavy smoker ( $\geq 200$ ) (11).

The data on daily intake obtained by interview were used to estimate total intake of energy, nutrients, and nonnutrient food and beverages that were consumed during the 24 h before the interview on any day of a week. Drinking levels were categorized by weekly drinks (nondrinker, <1; moderate drinker, 1–7; and heavy drinker,  $\geq 8$ ). A drink was defined as 12 ounces of beer, 4 ounces of wine, or 1.5 ounces of 80-proof distilled spirits (12). Daily intake of calories was divided into rounded tertiles with cut points of 2,000 and 3,000 for men and 1,500 and 2,000 for women.

Weight with minimal clothing (on a digital electronic scale) was measured. Standing height is measured with a fixed stadiometer with a vertical backboard and a moveable headboard. BMI was calculated as weight in kilograms divided by the square of height in meters and was used to measure obesity (three groups). Waist circumference was measured just above the uppermost lateral border of the ilium to provide sex-specific tertiles (cut points for men: 92.1 and 103.3 cm; for women: 83.8 and 96.8 cm). Because BMI is more widely used as an index for measurement of obesity and may affect subjects' MSA behavior more than waist circumference does, BMI was used in most of our multivariate analyses. Age (in years) was categorized as 20–39, 40–59, or 60–79 in multivariate analyses. Race/ethnicity was divided into three groups: non-Hispanic white, non-Hispanic black, and others.

### Statistical analysis

SAS (version 9.1; SAS Institute, Cary, NC) was used for data management. Statistical analyses were performed with SAS-Callable SUDAAN software (version 9.0.1; Research Triangle Institute, Re-

search Triangle Park, NC) to obtain point estimates and SEs applicable to the U.S. population. We applied fasting sample weights to the data that indicated the inverse of the probability of being sampled. Linear regression models were used as primary analyses. Adjustment was made for age, sex, race/ethnicity, non-MSA, smoking and alcohol consumption, and BMI groups in the multivariate regression model. There were no significant interactions between MSAs and the other covariates included in the multivariate analysis (all *P* values >0.05) except between MSAs and sex on QUICKI, fasting insulin, and fasting plasma glucose (all *P* values for interaction terms <0.001). In light of the interaction between MSAs and sex on dependent variables, as well as the major biological and lifestyle differences between men and women, most analyses were stratified by sex.

**RESULTS**— Of 4,504 study participants, aged 20–79 years, 84.7% performed MSAs less than three times per week, and 76.9% performed MSAs less than once a week. The latter prevalence (less than once a week) increased to 83.0% among subjects aged  $\geq 60$  years. The average age of subjects included in this analysis was 44 years, and 48.9% were men. Descriptive and other characteristics for the study sample are shown in Table 1 by MSA category. Participants who performed MSAs less than one time per week were older, more likely to be people without physical activities other than MSAs, and to be heavy smokers. Women who performed MSAs less than one time per week tended to have a higher BMI than other groups. Higher MSA was related to higher insulin sensitivity, lower fasting insulin, and lower fasting glucose.

After adjustment for age and race/ethnicity, MSA was positively related to higher insulin sensitivity (Table 2). Mean levels of QUICKI among subjects with lower, moderate, and high MSA were 33.5, 34.1, and 34.4, respectively (*P* for linear trend <0.001) and 34.0, 35.0, and 35.3, respectively, for women (*P* for linear trend <0.001). The association between higher MSA and lower QUICKI was influenced more by lower insulin levels than glucose levels. As expected, higher BMI was strongly related to lower insulin sensitivity and higher fasting insulin and fasting glucose concentrations. Moderate and heavy smokers tended to have higher insulin sensitivity than nonsmokers (*P* < 0.05). Being a moderate drinker was as-

Table 1—Description of variables for sample population (n = 4,504) aged 20–79 years by sex and level of MSAs

| Variable                          | Men          |              |             |             | Women  |              |             |             | P      |
|-----------------------------------|--------------|--------------|-------------|-------------|--------|--------------|-------------|-------------|--------|
|                                   | n (%)        | <1*          | 1–2.9       | ≥3          | P      | <1           | 1–2.9       | ≥3          |        |
| Total                             | 2,275 (100)  | 1,739 (74.9) | 170 (8.5)   | 366 (16.7)  | —      | 1,816 (78.9) | 136 (7.2)   | 277 (13.9)  | —      |
| Age (years)                       | 2,275 (100)  | 44.0 ± 0.5   | 38.5 ± 1.2  | 39.0 ± 0.9  | <0.001 | 45.3 ± 0.5   | 41.0 ± 1.4  | 42.2 ± 1.0  | <0.001 |
| Age-group (years)                 |              |              |             |             |        |              |             |             |        |
| 20–39                             | 919 (46.5)   | 43.1 (1.6)   | 58.5 (4.8)  | 55.8 (3.1)  | <0.001 | 38.7 (1.6)   | 53.3 (5.6)  | 46.9 (3.4)  | 0.024  |
| 40–59                             | 745 (38.4)   | 40.1 (1.5)   | 34.7 (4.6)  | 32.5 (2.7)  |        | 41.6 (1.4)   | 34.3 (5.8)  | 36.8 (3.2)  |        |
| 60–79                             | 611 (15.1)   | 16.8 (0.9)   | 6.7 (1.4)   | 11.7 (1.7)  |        | 19.8 (1.0)   | 12.5 (3.1)  | 16.3 (2.4)  |        |
| Race/ethnicity                    |              |              |             |             |        |              |             |             |        |
| Non-Hispanic white                | 1,154 (72.5) | 72.7 (2.1)   | 75.5 (3.6)  | 70.0 (3.0)  | <0.001 | 71.7 (2.1)   | 78.6 (3.1)  | 81.4 (2.4)  | 0.025  |
| Non-Hispanic black                | 409 (9.9)    | 8.5 (1.0)    | 12.6 (2.0)  | 15.2 (2.1)  |        | 11.2 (1.2)   | 12.8 (2.4)  | 9.2 (1.9)   |        |
| Others                            | 712 (17.6)   | 18.8 (2.0)   | 11.9 (2.9)  | 14.8 (2.2)  |        | 17.1 (2.1)   | 8.6 (2.5)   | 9.5 (1.7)   |        |
| Non-MSA (MET × h/week)            |              |              |             |             |        |              |             |             |        |
| Sedentary                         | 942 (34.5)   | 41.7 (1.9)   | 11.6 (2.9)  | 13.6 (2.0)  | <0.001 | 42.5 (1.5)   | 13.9 (3.6)  | 13.8 (1.8)  | <0.001 |
| Moderate (0.1–14.3)               | 615 (30.1)   | 30.3 (1.5)   | 36.6 (4.0)  | 26.1 (2.9)  |        | 35.8 (1.7)   | 35.4 (3.3)  | 25.4 (2.4)  |        |
| High (≥14.4)                      | 718 (35.4)   | 28.0 (1.5)   | 51.8 (4.2)  | 60.4 (3.3)  |        | 21.7 (1.8)   | 50.8 (4.6)  | 60.8 (3.0)  |        |
| Body composition                  |              |              |             |             |        |              |             |             |        |
| Weight (kg)                       | 2,275 (100)  | 87.3 ± 0.6   | 84.6 ± 1.6  | 85.5 ± 1.1  | 0.107  | 75.1 ± 0.6   | 72.1 ± 1.8  | 68.2 ± 1.3  | <0.001 |
| Height (cm)                       | 2,275 (100)  | 176.5 ± 0.2  | 178.0 ± 0.6 | 177.3 ± 0.5 | 0.056  | 162.6 ± 0.2  | 165.2 ± 0.4 | 163.4 ± 0.4 | <0.001 |
| BMI (kg/m <sup>2</sup> )          | 2,275 (100)  | 27.9 ± 0.2   | 26.7 ± 0.4  | 27.2 ± 0.3  | 0.007  | 28.4 ± 0.2   | 26.3 ± 0.6  | 25.5 ± 0.4  | <0.001 |
| BMI group (kg/m <sup>2</sup> )    |              |              |             |             |        |              |             |             |        |
| Normal (<25)                      | 721 (32.0)   | 30.5 (1.3)   | 36.2 (4.2)  | 36.8 (2.7)  | 0.153  | 36.7 (1.7)   | 53.9 (4.7)  | 60.2 (3.3)  | <0.001 |
| Overweight (25–29.9)              | 954 (41.7)   | 41.8 (1.7)   | 44.7 (3.8)  | 39.7 (2.9)  |        | 29.8 (1.6)   | 24.9 (5.5)  | 23.1 (2.8)  |        |
| Obese (≥30)                       | 600 (26.2)   | 27.7 (1.3)   | 19.1 (4.1)  | 23.5 (2.8)  |        | 33.5 (1.3)   | 21.2 (4.1)  | 16.8 (2.6)  |        |
| Smoking status (cotinine, ng/ml)  |              |              |             |             |        |              |             |             |        |
| None (<14)                        | 1,534 (65.3) | 62.5 (1.9)   | 74.9 (3.3)  | 73.0 (2.7)  | <0.001 | 74.5 (1.4)   | 84.8 (2.9)  | 88.5 (2.3)  | <0.001 |
| Light (14–99)                     | 178 (7.0)    | 7.1 (0.7)    | 8.5 (2.4)   | 6.0 (1.4)   |        | 4.5 (0.5)    | 3.2 (1.5)   | 2.6 (1.3)   |        |
| Moderate (100–199)                | 185 (9.1)    | 9.7 (0.9)    | 5.8 (2.0)   | 7.9 (1.6)   |        | 9.2 (0.8)    | 7.7 (1.6)   | 4.6 (1.5)   |        |
| Heavy (≥200)                      | 378 (18.6)   | 20.7 (1.5)   | 10.8 (2.7)  | 13.1 (2.4)  |        | 11.8 (1.1)   | 4.4 (2.1)   | 4.2 (1.1)   |        |
| Alcohol consumption (drinks/week) |              |              |             |             |        |              |             |             |        |
| None (<1)                         | 1,533 (65.3) | 68.1 (1.6)   | 57.9 (4.1)  | 56.7 (3.3)  | <0.001 | 83.5 (1.2)   | 77.6 (4.3)  | 75.9 (2.5)  | 0.035  |
| Moderate (1–7)                    | 385 (17.6)   | 15.2 (1.4)   | 26.1 (3.9)  | 23.7 (2.8)  |        | 11.3 (0.9)   | 15.4 (3.0)  | 19.2 (2.2)  |        |
| Heavy (≥8)                        | 357 (17.1)   | 16.7 (1.0)   | 16.0 (3.2)  | 19.6 (2.7)  |        | 5.2 (0.9)    | 7.1 (2.5)   | 5.0 (1.5)   |        |
| Daily total caloric intake (kcal) | 2,275 (100)  | 2,689 ± 35   | 2,752 ± 100 | 2,678 ± 55  | 0.803  | 2,229 (100)  | 1,979 ± 70  | 1,930 ± 57  | 0.125  |
| QUICKI                            | 2,275 (100)  | 33.5 ± 0.1   | 34.2 ± 0.2  | 34.5 ± 0.2  | <0.001 | 34.0 ± 0.1   | 35.1 ± 0.2  | 35.4 ± 0.2  | <0.001 |
| Fasting insulin (pmol/l)          | 2,275 (100)  | 76.4 ± 2.5   | 64.4 ± 6.3  | 62.1 ± 3.1  | <0.001 | 69.0 ± 1.4   | 57.6 ± 2.6  | 52.3 ± 2.1  | <0.001 |
| Fasting glucose (mmol/l)          | 2,275 (100)  | 5.32 ± 0.02  | 5.22 ± 0.03 | 5.20 ± 0.02 | <0.001 | 5.21 ± 0.02  | 5.07 ± 0.04 | 5.08 ± 0.03 | <0.001 |

Data are means ± SE, % (SE), or n (%). \*Times/week

Table 2—Age-race/ethnicity adjusted means (95% CI) of the QUICKI, fasting insulin, and fasting glucose, by sex

| Variable                          | QUICKI           | P      | Fasting insulin (pmol/l) | P      | Fasting glucose (mmol/l) | P      |
|-----------------------------------|------------------|--------|--------------------------|--------|--------------------------|--------|
| <b>Men</b>                        |                  |        |                          |        |                          |        |
| MSA (times/week)                  |                  |        |                          |        |                          |        |
| Low (<1)                          | 33.5 (33.3–33.7) | Ref.   | 76.4 (71.3–81.6)         | Ref.   | 5.41 (5.37–5.46)         | Ref.   |
| Moderate (1–2.9)                  | 34.1 (33.7–34.6) | 0.007  | 64.2 (52.0–76.4)         | 0.010  | 5.39 (5.32–5.47)         | 0.608  |
| High (≥3)                         | 34.4 (33.9–34.8) | 0.001  | 62.1 (55.8–68.4)         | 0.001  | 5.33 (5.27–5.40)         | 0.022  |
| Non-MSA (MET × h/week)            |                  |        |                          |        |                          |        |
| Sedentary                         | 33.6 (33.4–33.8) | Ref.   | 75.4 (66.7–84.1)         | Ref.   | 5.45 (5.40–5.50)         | Ref.   |
| Moderate (0.1–14.3)               | 33.5 (33.2–33.8) | 0.613  | 75.7 (69.5–82.0)         | 0.935  | 5.41 (5.36–5.47)         | 0.270  |
| High (≥14.4)                      | 34.0 (33.6–34.3) | 0.124  | 68.3 (62.3–74.4)         | 0.169  | 5.34 (5.29–5.39)         | 0.003  |
| BMI (kg/m <sup>2</sup> )          |                  |        |                          |        |                          |        |
| Normal (<25)                      | 35.6 (35.4–35.9) | Ref.   | 44.8 (43.2–46.3)         | Ref.   | 5.28 (5.23–5.33)         | Ref.   |
| Overweight (25–29.9)              | 33.7 (33.5–33.9) | <0.001 | 66.3 (62.7–70.0)         | <0.001 | 5.41 (5.37–5.45)         | <0.001 |
| Obese (≥30)                       | 31.3 (31.0–31.6) | <0.001 | 118.1 (103.1–133.1)      | <0.001 | 5.53 (5.47–5.58)         | <0.001 |
| Smoking status (cotinine, ng/ml)  |                  |        |                          |        |                          |        |
| None (<14)                        | 33.5 (33.2–33.7) | Ref.   | 75.2 (70.5–80.0)         | Ref.   | 5.41 (5.37–5.46)         | Ref.   |
| Light (14–99)                     | 33.4 (32.9–33.9) | 0.777  | 83.6 (67.0–100.1)        | 0.304  | 5.43 (5.33–5.52)         | 0.785  |
| Moderate (100–199)                | 34.1 (33.7–34.6) | 0.012  | 63.7 (57.5–69.8)         | 0.005  | 5.33 (5.25–5.40)         | 0.028  |
| Heavy (≥200)                      | 34.4 (34.0–34.8) | <0.001 | 65.8 (54.4–77.2)         | 0.038  | 5.37 (5.30–5.44)         | 0.242  |
| Alcohol consumption (drinks/week) |                  |        |                          |        |                          |        |
| None (<1)                         | 33.4 (33.2–33.7) | Ref.   | 78.5 (71.2–85.7)         | Ref.   | 5.40 (5.36–5.45)         | Ref.   |
| Moderate (1–7)                    | 34.2 (33.9–34.6) | 0.001  | 63.1 (59.1–67.0)         | 0.001  | 5.36 (5.29–5.42)         | 0.220  |
| Heavy (≥8)                        | 34.2 (33.8–34.6) | 0.002  | 62.7 (57.3–68.1)         | 0.001  | 5.42 (5.36–5.48)         | 0.617  |
| Daily total caloric intake (kcal) |                  |        |                          |        |                          |        |
| Low tertile (<2,000)              | 33.9 (33.6–34.3) | Ref.   | 69.2 (60.4–77.9)         | Ref.   | 5.40 (5.33–5.45)         | Ref.   |
| Middle tertile (2,000–2,999)      | 33.7 (33.3–34.0) | 0.249  | 73.7 (66.1–81.3)         | 0.173  | 5.40 (5.34–5.45)         | 0.913  |
| High tertile (≥3,000)             | 33.5 (33.3–33.8) | 0.065  | 75.3 (69.1–81.4)         | 0.294  | 5.40 (5.35–5.46)         | 0.836  |
| <b>Women</b>                      |                  |        |                          |        |                          |        |
| MSA (times/week)                  |                  |        |                          |        |                          |        |
| Low (<1)                          | 34.0 (33.8–34.2) | Ref.   | 68.9 (65.9–71.8)         | Ref.   | 5.21 (5.17–5.25)         | Ref.   |
| Moderate (1–2.9)                  | 35.0 (34.6–35.5) | <0.001 | 57.9 (52.9–62.8)         | <0.001 | 5.12 (5.04–5.20)         | 0.048  |
| High (≥3)                         | 35.3 (34.8–35.7) | <0.001 | 53.1 (48.9–57.3)         | <0.001 | 5.10 (5.03–5.16)         | 0.002  |
| Non-MSA (MET × h/week)            |                  |        |                          |        |                          |        |
| Sedentary                         | 33.9 (33.6–34.2) | Ref.   | 70.5 (66.8–74.3)         | Ref.   | 5.23 (5.17–5.28)         | Ref.   |
| Moderate (0.1–14.3)               | 34.2 (33.9–34.6) | 0.126  | 66.4 (61.5–71.4)         | 0.176  | 5.18 (5.12–5.24)         | 0.102  |
| High (≥14.4)                      | 34.7 (34.4–35.0) | <0.001 | 59.5 (56.4–62.6)         | <0.001 | 5.14 (5.10–5.19)         | 0.013  |
| BMI (kg/m <sup>2</sup> )          |                  |        |                          |        |                          |        |
| Normal (<25)                      | 36.1 (35.9–36.4) | Ref.   | 44.1 (42.0–46.1)         | Ref.   | 5.03 (4.99–5.07)         | Ref.   |
| Overweight (25–29.9)              | 34.0 (33.8–34.2) | <0.001 | 64.3 (61.3–67.4)         | <0.001 | 5.21 (5.16–5.27)         | <0.001 |
| Obese (≥30)                       | 32.0 (31.8–32.2) | <0.001 | 97.0 (92.7–101.4)        | <0.001 | 5.36 (5.32–5.41)         | <0.001 |
| Smoking status (cotinine, ng/ml)  |                  |        |                          |        |                          |        |
| None (<14)                        | 34.2 (34.0–34.5) | Ref.   | 65.8 (62.9–68.7)         | Ref.   | 5.19 (5.15–5.22)         | Ref.   |
| Light (14–99)                     | 33.6 (32.9–34.4) | 0.126  | 74.8 (64.0–85.6)         | 0.126  | 5.19 (5.06–5.32)         | 0.945  |
| Moderate (100–199)                | 34.1 (33.5–34.8) | 0.705  | 69.9 (59.7–80.0)         | 0.422  | 5.20 (5.10–5.30)         | 0.697  |
| Heavy (≥200)                      | 34.8 (34.3–35.3) | 0.039  | 59.7 (54.7–64.7)         | 0.053  | 5.16 (5.07–5.26)         | 0.653  |
| Alcohol consumption (drinks/week) |                  |        |                          |        |                          |        |
| None (<1)                         | 34.1 (33.8–34.3) | Ref.   | 68.3 (65.4–71.2)         | Ref.   | 5.19 (5.15–5.23)         | Ref.   |
| Moderate (1–7)                    | 35.3 (34.7–35.9) | <0.001 | 54.3 (49.3–59.4)         | <0.001 | 5.13 (5.08–5.19)         | 0.072  |
| Heavy (≥8)                        | 34.9 (34.3–35.6) | 0.015  | 55.7 (51.2–60.1)         | <0.001 | 5.20 (5.08–5.33)         | 0.854  |
| Daily total caloric intake (kcal) |                  |        |                          |        |                          |        |
| Low tertile (<1,500)              | 34.3 (34.0–34.6) | Ref.   | 64.7 (60.5–69.0)         | Ref.   | 5.20 (5.15–5.26)         | Ref.   |
| Middle tertile (1,500–1,999)      | 34.3 (34.0–34.6) | 0.954  | 65.2 (62.3–68.2)         | 0.845  | 5.17 (5.11–5.23)         | 0.351  |
| High tertile (≥2,000)             | 34.2 (33.9–34.5) | 0.712  | 67.3 (63.6–71.1)         | 0.317  | 5.18 (5.13–5.24)         | 0.519  |

Ref., reference group.

sociated with higher insulin sensitivity. After adjustment for MSA, age, and race/ethnicity, the means for QUICKI accord-

ing to non-MSA levels of activity (sedentary, moderate, or high) were 33.7, 33.5, and 33.8, respectively, for men (*P* for linear

trend = 0.236) and 34.06, 34.27, and 34.49, respectively, for women (*P* for linear trend = 0.091).



Table 3—Multivariate adjusted means (95% CI) for QUICKI, fasting insulin, and fasting glucose, by sex\*

| Variable          | QUICKI           | P     | Fasting insulin (pmol/l) | P     | Fasting glucose (mmol/l) | P     |
|-------------------|------------------|-------|--------------------------|-------|--------------------------|-------|
| Men               |                  |       |                          |       |                          |       |
| MSA (times/week)  |                  |       |                          |       |                          |       |
| Low (<1)          | 33.6 (33.3–33.8) | Ref.  | 75.0 (70.4–79.7)         | Ref.  | 5.41 (5.36–5.45)         | Ref.  |
| Moderate (1–2.9)  | 33.9 (33.5–34.4) | 0.091 | 68.9 (54.5–83.3)         | 0.294 | 5.42 (5.34–5.49)         | 0.789 |
| High ( $\geq 3$ ) | 34.2 (33.8–34.6) | 0.003 | 65.9 (59.9–71.9)         | 0.007 | 5.36 (5.31–5.42)         | 0.163 |
| Women             |                  |       |                          |       |                          |       |
| MSA (times/week)  |                  |       |                          |       |                          |       |
| Low (<1)          | 34.2 (34.0–34.4) | Ref.  | 66.9 (64.3–69.6)         | Ref.  | 5.19 (5.15–5.23)         | Ref.  |
| Moderate (1–2.9)  | 34.6 (34.2–35.1) | 0.025 | 63.3 (58.2–68.5)         | 0.103 | 5.16 (5.08–5.24)         | 0.386 |
| High ( $\geq 3$ ) | 34.6 (34.3–35.0) | 0.021 | 61.2 (57.5–65.0)         | 0.007 | 5.15 (5.08–5.23)         | 0.366 |

\*Logistic regression adjusted for non-MSA, age-group, race/ethnicity, BMI group, smoking status, alcohol consumption, and daily total caloric intake. Ref., reference group.

To more fully evaluate the relationship of MSA with insulin sensitivity, fasting insulin, and fasting glucose, we calculated multivariate-adjusted means (Table 3). After adjustment for age, leisure-time non-MSAs, race/ethnicity, BMI, smoking status, alcohol consumption, and daily total caloric intake, MSA levels were positively associated with insulin sensitivity in both men and women. Higher MSA was also associated with lower fasting insulin. The statistically significant contrasts were mainly found between the highest and lowest MSA groups but not between referent and mid-categories. The *P* values of the linear trend test of QUICKI and fasting insulin by MSA were 0.008 and 0.017, respectively, among men and 0.009 and 0.007, respectively, among women. There was no evidence of a significant association between MSA and fasting glucose. BMI was strongly and negatively associated with QUICKI and positively associated with fasting insulin and fasting glucose. In men, age and daily total caloric intake were significantly and negatively associated with insulin sensitivity. The association of smoking with insulin sensitivity was still present in men in this multivariate model.

In additional multivariate analyses, we adjusted for waist circumference expressed as sex-specific tertiles along with non-MSA, age-group, race/ethnicity, smoking status, alcohol consumption, and daily total caloric intake. The resulting adjusted means of QUICKI for low, moderate, and high MSA groups were 33.6 (referent), 33.8 (*P* value = 0.317), and 34.0 (*P* value = 0.059) (*P* for linear trend = 0.128), respectively, among men and 34.2 (referent), 34.7 (*P* value = 0.004), and 34.7 (*P* value = 0.013) (*P* for

linear trend = 0.002), respectively, among women.

**CONCLUSIONS**—MSAs have important implications for health. Resistance training, which is the most effective method for developing musculoskeletal strength (13), is correlated with an individual's physical function (14) and is particularly appropriate among older adults with low cardiorespiratory function (15,16). Given the safety and acceptability of MSAs, it is disappointing that we have confirmed a low prevalence of MSA with our nationally representative sample of nondiabetic U.S. adults aged 20–79 years (17). We found that MSAs were associated with higher insulin sensitivity as evaluated by QUICKI and lower fasting insulin among U.S. adults in the age range we analyzed. Moreover, this association was independent of non-MSAs and actually stronger in magnitude than the association between non-MSAs and insulin sensitivity.

Most of the previously reported studies of MSAs and insulin sensitivity were performed among selected subpopulations evaluated after a few months of structured training (18,19). In these studies, the benefits of MSA plateau during subsequent months, particularly if the exercise training program did not contain adequate variation (20). In contrast, our population-based study provides a perspective on the role of habitual resistance exercise in natural settings.

There have been reports that suggest potential physiologic mechanisms by which MSAs are related to high insulin sensitivity (3). In an early report, Miller et al. (18) showed that the increased muscle mass resulting from strength training was responsible for the attenuated insulin re-

sponse to a standard 100-g oral glucose challenge in men. Others, however, have suggested that the effect of training is not caused solely by an increase in muscle mass and is likely also influenced by effects on peak aerobic and maximal working capacity (e.g.,  $VO_{2max}$ ) (21). In a population of older men, 9 weeks of high-intensity resistance training of the legs followed by 9 weeks of aerobic training on a cycle ergometer resulted in changes in both the  $VO_{2max}$  and the size of the capillary-fiber interface that were similar to those obtained from 18 weeks of aerobic training on the ergometer. In another study, the number of capillaries per length of fiber perimeter was increased after both resistance and aerobic training in men aged 65–74 years, paralleling the changes in  $VO_{2max}$ , and there was a significant positive correlation between the change in capillary supply and  $VO_{2max}$  (22). In brief, the mechanisms behind the effect of strength training seem similar to those seen with aerobic training, even though MSAs mainly recruit type II muscle (fast-twitch fibers), especially type IIb fibers, that are less sensitive to insulin than type I muscle (slow-twitch fibers) (23).

Other studies, however, have demonstrated that without altering  $VO_{2max}$ , resistance training improves insulin sensitivity in patients with diabetes (24) and can reduce risk factors for cardiovascular disease (25). After 6 weeks of one-legged resistance training performed three times per week, 10 men with diabetes and 7 men without diabetes had produced (independent of increased muscle mass) increased protein content of GLUT4, insulin receptor, protein kinase B- $\alpha/\beta$ , glycogen synthase, and glycogen synthase total activity (26).

In our study, the relation of MSAs and QUICKI among men was attenuated after adjusting for tertiles of waist circumference but did not change significantly after adjustment for BMI. This finding supports previous research (27) that waist circumference may account for >40% of the variance in insulin action. Hence, we propose that MSAs may be a potentially beneficial health behavior for which the relationship with insulin sensitivity may be reflected through reductions in waist circumference. We also propose that identifying the precise mechanism of MSA's influence on insulin sensitivity is worthy of further exploration.

Structured aerobic training has been related to the treatment and prevention of insulin resistance (28). We found initially that non-MSA was associated with higher insulin sensitivity and with lower concentrations of fasting insulin and fasting glucose, especially among women (Table 2). For both sexes, however, these statistical associations disappeared following adjustment for MSA levels. In this study, non-MSA is not equal to aerobic physical activity. The lack of an association may also be related to the use of absolute MET values for categorizing activity into moderate or vigorous activity.

Findings on the relationship between smoking and insulin sensitivity and diabetes are controversial (29,30). Our results showed that the relation of smoking to insulin sensitivity tends to be J shaped (Table 2). However, it is possible that smoking may damage not only pulmonary cells but also pancreatic cells (31), which will give the incorrect estimation of insulin sensitivity by using QUICKI.

Overweight and obesity, as measured by BMI, were negatively related to insulin sensitivity, a relationship that has been well defined by many studies (32). Weight loss reduces the lipid content of skeletal muscle in morbidly obese individuals, which may contribute to the improvement of insulin action (33). Our study supports the notion that physical activity and body weight are independently related to insulin sensitivity (34). Regarding consumption of alcohol, as did a study among women aged 64 years (35), we found that moderate drinking was related to higher insulin sensitivity and lower concentrations of insulin. In addition, our cross-sectional study found a statistically significant association in men between lower intake of energy and higher insulin sensitivity (after adjusting for other variables,  $P = 0.024$ ); this asso-

ciation was attenuated among women. These findings were consistent with those of Weiss et al. (36), who found that caloric restriction improved glucose tolerance and insulin action among nonobese, healthy men and women aged 50–60 years in a 12-month randomized trial. In contrast, Joseph et al. (37) found that 4 weeks of energy restriction did not improve insulin sensitivity among women aged ~63 years.

This is the first large study to examine how insulin sensitivity is associated with levels of MSAs as they are performed among the U.S. public. While our study had good data quality, was well designed, and was intensively controlled and evaluated, it still had a few limitations. With the data available, we were able to perform only a cross-sectional analysis of the population, which limits our understanding of the cause-and-effect relationship between the variables we evaluated. In addition, we lacked direct measurements of peripheral insulin sensitivity. We thus relied on QUICKI, which is derived from fasting glucose and insulin concentrations and reflects primarily hepatic insulin sensitivity and basal hepatic glucose production (7,8). Hepatic insulin resistance, however, correlates strongly with peripheral (muscle) insulin resistance (38). Although the NHANES computerized interview used the multipass method, the reliability and validity of self-reported physical activity and daily total caloric intake in NHANES have not been reported. The physical activity questionnaire covered the previous month, and the nutrition questionnaire only covered the previous 24 h. The information provided by these questionnaires, therefore, might not represent the participants' routine lifestyle over a longer time interval. We lacked information on the intensity and duration of MSAs. The intensity with which the general population exercises may be lower than that prescribed in trials of muscular training, and therefore our analysis might underestimate the relationship between MSAs and insulin sensitivity. The use of medications such as insulin, metformin, or thiazolidinediones might modify the associations between MSAs and body composition or insulin sensitivity, but our analytical sample is unlikely to include participants using these drugs because we excluded people with diabetes. In an extra analysis, adjusting for estrogen and progesterin use among nonpregnant, nonbreastfeeding women, the average QUICKI values were 34.1,

34.5, and 34.6 ( $P$  for linear trend = 0.007), the average fasting insulin (in pmol/l) were 67.2, 63.5, and 61.6 ( $P$  for linear trend = 0.008), and the average fasting glucose (in mmol/l) were 5.20, 5.17, and 5.16 ( $P$  for linear trend = 0.521) among women with low, moderate, and high MSA, respectively. Regardless, most studies of MSAs and insulin sensitivity have been based on small clinical trials and involved small samples of people with diabetes. We have not found any such studies on general populations without diabetes.

In summary, this cross-sectional study found that MSAs are related to higher insulin sensitivity among U.S. adults in a manner that is independent of age, race/ethnicity, non-MSA, BMI, smoking, alcohol consumption, and total energy intake. MSAs may be a realistic and effective way to prevent diabetes and cardiovascular disease.

**Acknowledgments**—Centers for Disease Control and Prevention disclaimer: The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

## References

1. Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ: Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA* 286:1218–1227, 2001
2. Dunstan DW, Daly RM, Owen N, Jolley D, De Courten M, Shaw J, Zimmet P: High-intensity resistance training improves glycemic control in older patients with type 2 diabetes. *Diabetes Care* 25: 1729–1736, 2002
3. Braith RW, Stewart KJ: Resistance exercise training: its role in the prevention of cardiovascular disease. *Circulation* 113: 2642–2650, 2006
4. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C: Physical activity/exercise and type 2 diabetes. *Diabetes Care* 27: 2518–2539, 2004
5. Centers for Disease Control and Prevention: *NHANES 2003–2004 Data Documentation: MEC In-Person Dietary Interviewer's Procedures Manual*. Centers for Disease Control and Prevention, Atlanta, GA, 2007. Available from [http://www.cdc.gov/nchs/data/nhanes/nhanes\\_03\\_04/DIETARY-MEC.pdf](http://www.cdc.gov/nchs/data/nhanes/nhanes_03_04/DIETARY-MEC.pdf). Accessed 10 July 2007
6. Centers for Disease Control and Prevention: *NHANES 1999–2000 Data Release: Revised April 2005: Laboratory 10AM–*

- Glucose, Insulin, and C-Peptide*. Centers for Disease Control and Prevention, Atlanta, GA, 2007. Available from [http://www.cdc.gov/nchs/data/nhanes/frequency/lab10am\\_doc.pdf](http://www.cdc.gov/nchs/data/nhanes/frequency/lab10am_doc.pdf). Accessed 10 July 2007
- Katz A, Nambi SS, Mather K, Baron AD, Follmann DA, Sullivan G, Quon MJ: Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. *J Clin Endocrinol Metab* 85:2402–2410, 2000
  - Turner RC, Holman RR, Matthews D, Hockaday TD, Peto J: Insulin deficiency and insulin resistance interaction in diabetes: estimation of their relative contribution by feedback analysis from basal plasma insulin and glucose concentrations. *Metabolism* 28:1086–1096, 1979
  - Centers for Disease Control and Prevention: *NHANES 1999–2000 Data Documentation: Physical Activity Individual Activities File*. Centers for Disease Control and Prevention, Atlanta, GA, 2007. Available from [http://www.cdc.gov/nchs/data/nhanes/frequency/paqlaf\\_doc.pdf](http://www.cdc.gov/nchs/data/nhanes/frequency/paqlaf_doc.pdf). Accessed 10 July 2007
  - Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS: Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc* 32 (Suppl. 9):S498–S504, 2000
  - Wei W, Kim Y, Boudreau N: Association of smoking with serum and dietary levels of antioxidants in adults: NHANES III, 1988–1994. *Am J Public Health* 91:258–264, 2001
  - Lichtenstein AH, Appel LJ, Brands M, Carnethon M, Daniels S, Franch HA, Franklin B, Kris-Etherton P, Harris WS, Howard B, Karanja N, Lefevre M, Rudel L, Sacks F, Van HL, Winston M, Wylie-Rosett J: Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation* 114:82–96, 2006
  - Kraemer WJ, Adams K, Cafarelli E, Dudley GA, Dooly C, Feigenbaum MS, Fleck SJ, Franklin B, Fry AC, Hoffman JR, Newton RU, Potteiger J, Stone MH, Ratamess NA, Triplett-McBride T: American College of Sports Medicine position stand: progression models in resistance training for healthy adults. *Med Sci Sports Exerc* 34:364–380, 2002
  - Ferrucci L, Penninx BW, Volpato S, Harris TB, Bandeen-Roche K, Balfour J, Leveille SG, Fried LP, Md JM: Change in muscle strength explains accelerated decline of physical function in older women with high interleukin-6 serum levels. *J Am Geriatr Soc* 50:1947–1954, 2002
  - Gastaneda C, Layne JE, Munoz-Orians L, Gordon PL, Walsmith J, Foldvari M, Roubenoff R, Tucker KL, Nelson ME: A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes. *Diabetes Care* 25:2335–2341, 2002
  - Eves ND, Plotnikoff RC: Resistance training and type 2 diabetes: considerations for implementation at the population level. *Diabetes Care* 29:1933–1941, 2006
  - Kruger J, Carlson S, Kohl HI: Trends in strength training—United States, 1998–2004. *MMWR Morb Morta Wkly Rep* 55:669–772, 2006
  - Miller WJ, Sherman WM, Ivy JL: Effect of strength training on glucose tolerance and post-glucose insulin response. *Med Sci Sports Exerc* 16:539–543, 1984
  - Balducci S, Leonetti F, Di Mario U, Falucca F: Is a long-term aerobic plus resistance training program feasible for and effective on metabolic profiles in type 2 diabetic patients? *Diabetes Care* 27:841–842, 2004
  - Marx JO, Ratamess NA, Nindl BC, Gotshalk LA, Volek JS, Dohi K, Bush JA, Gomez AL, Mazzetti SA, Fleck SJ, Hakkinen K, Newton RU, Kraemer WJ: Low-volume circuit versus high-volume periodized resistance training in women. *Med Sci Sports Exerc* 33:635–643, 2001
  - Hikida RS, Staron RS, Hagerman FC, Walsh S, Kaiser E, Shell S, Hervey S: Effects of high-intensity resistance training on untrained older men. II. Muscle fiber characteristics and nucleo-cytoplasmic relationships. *J Gerontol A Biol Sci Med Sci* 55:B347–B354, 2000
  - Hepple RT, Mackinnon SL, Goodman JM, Thomas SG, Plyley MJ: Resistance and aerobic training in older men: effects on VO<sub>2</sub>peak and the capillary supply to skeletal muscle. *J Appl Physiol* 82:1305–1310, 1997
  - Garg A, Stray-Gundersen J, Parsons D, Bertocci LA: Skeletal muscle morphology and exercise response in congenital generalized lipodystrophy. *Diabetes Care* 23:1545–1550, 2000
  - Ishii T, Yamakita T, Sato T, Tanaka S, Fujii S: Resistance training improves insulin sensitivity in NIDDM subjects without altering maximal oxygen uptake. *Diabetes Care* 21:1353–1355, 1998
  - Hurley BF, Hagberg JM, Goldberg AP, Seals DR, Ehsani AA, Brennan RE, Holloszy JO: Resistive training can reduce coronary risk factors without altering VO<sub>2</sub>max or percent body fat. *Med Sci Sports Exerc* 20:150–154, 1988
  - Holtén MK, Zacho M, Gaster M, Juel C, Wojtaszewski JF, Dela F: Strength training increases insulin-mediated glucose uptake, GLUT4 content, and insulin signaling in skeletal muscle in patients with type 2 diabetes. *Diabetes* 53:294–305, 2004
  - Kohrt WM, Kirwan JP, Staten MA, Bourey RE, King DS, Holloszy JO: Insulin resistance in aging is related to abdominal obesity. *Diabetes* 42:273–281, 1993
  - Sato Y, Nagasaki M, Nakai N, Fushimi T: Physical exercise improves glucose metabolism in lifestyle-related diseases. *Exp Biol Med (Maywood)* 228:1208–1212, 2003
  - Anan F, Takahashi N, Shinohara T, Nakagawa M, Masaki T, Katsuragi I, Tanaka K, Kakuma T, Yonemochi H, Eshima N, Saikawa T, Yoshimatsu H: Smoking is associated with insulin resistance and cardiovascular autonomic dysfunction in type 2 diabetic patients. *Eur J Clin Invest* 36:459–465, 2006
  - Masulli M, Riccardi G, Galasso R, Vaccaro O: Relationship between smoking habits and the features of the metabolic syndrome in a non-diabetic population. *Nutr Metab Cardiovasc Dis* 16:364–370, 2006
  - Ostgren CJ, Lindblad U, Ranstam J, Melander A, Rastam L: Associations between smoking and beta-cell function in a non-hypertensive and non-diabetic population: Skaraborg Hypertension and Diabetes Project. *Diabet Med* 17:445–450, 2000
  - Kahn SE, Hull RL, Utzschneider KM: Mechanisms linking obesity to insulin resistance and type 2 diabetes. *Nature* 444:840–846, 2006
  - Berggren JR, Hulver MW, Dohm GL, Houmard JA: Weight loss and exercise: implications for muscle lipid metabolism and insulin action. *Med Sci Sports Exerc* 36:1191–1195, 2004
  - Berggren JR, Hulver MW, Houmard JA: Fat as an endocrine organ: influence of exercise. *J Appl Physiol* 99:757–764, 2005
  - Englund OL, Brohall G, Behre CJ, Schmidt C, Fagerberg B: Alcohol consumption in relation to metabolic regulation, inflammation, and adiponectin in 64-year-old Caucasian women: a population-based study with a focus on impaired glucose regulation. *Diabetes Care* 29:908–913, 2006
  - Weiss EP, Racette SB, Villareal DT, Fontana L, Steger-May K, Schechtman KB, Klein S, Holloszy JO: Improvements in glucose tolerance and insulin action induced by increasing energy expenditure or decreasing energy intake: a randomized controlled trial. *Am J Clin Nutr* 84:1033–1042, 2006
  - Joseph LJ, Trappe TA, Farrell PA, Campbell WW, Yarasheski KE, Lambert CP, Evans WJ: Short-term moderate weight loss and resistance training do not affect insulin-stimulated glucose disposal in postmenopausal women. *Diabetes Care* 24:1863–1869, 2001
  - Abdul-Ghani MA, Tripathy D, DeFronzo RA: Contributions of  $\beta$ -cell dysfunction and insulin resistance to the pathogenesis of impaired glucose tolerance and impaired fasting glucose. *Diabetes Care* 29:1130–1139, 2006