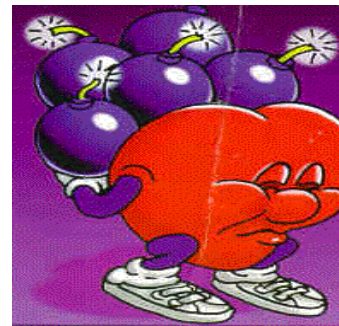
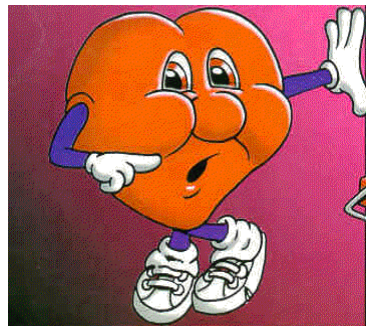


**Efeitos de Diferentes Doses de Atividade Física na aptidão Cardio-respiratória entre Mulheres Pós-menopausadas Sedentárias, com sobrepeso e Obesas com Pressão Arterial Elevada**

**Apresentado por Tatiana Goveia de Araujo  
na reunião da Unidade de Hipertensão  
do Hospital das Clínicas da Faculdade de Medicina  
da Universidade de São Paulo  
em 31 de Maio de 2007**

**Effects of Different Doses of  
Physical Activity on  
Cardiorespiratory Fitness Among  
Sedentary, Overweightt or Obese  
Postmenopausal Women With  
Elevated Blood Pressure  
A Randomized Controlled Trial**





# Effects of Different Doses of Physical Activity on Cardiorespiratory Fitness Among Sedentary, Overweight or Obese Postmenopausal Women With Elevated Blood Pressure

## A Randomized Controlled Trial

**Context** Low levels of cardiorespiratory fitness are associated with high risk of mortality, and improvements in fitness are associated with reduced mortality risk. However, a poor understanding of the physical activity–fitness dose response relation remains.

**Objective** To examine the effect of 50%, 100%, and 150% of the NIH Consensus Development Panel recommended physical activity dose on fitness in women.

**Design, Setting, and Participants** Randomized controlled trial of 464 sedentary, postmenopausal overweight or obese women whose body mass index ranged from 25.0 to 43.0 and whose systolic blood pressure ranged from 120.0 to 159.9 mm Hg. Enrollment took place between April 2001 and June 2005 in the Dallas, Tex, area.

**Intervention** Participants were randomly assigned to 1 of 4 groups: 102 to the non-exercise control group and 155 to the 4-kcal/kg, 104 to the 8-kcal/kg, and 103 to the 12-kcal/kg per week energy-expenditure groups for the 6-month intervention period. Target training intensity was the heart rate associated with 50% of each woman's peak  $\dot{V}O_2$ .

**Main Outcome Measure** The primary outcome was aerobic fitness assessed on a cycle ergometer and quantified as peak absolute oxygen consumption ( $\dot{V}O_{2abs}$ , L/min).

**Results** The mean (SD) baseline  $\dot{V}O_{2abs}$  values were 1.30 (0.25) L/min. The mean (SD) minutes of exercising per week were 72.2 (12.3) for the 4-kcal/kg, 135.8 (19.5) for the 8-kcal/kg, and 191.7 (33.7) for the 12-kcal/kg per week exercise groups. After adjustment for age, race/ethnicity, weight, and peak heart rate, the exercise groups increased their  $\dot{V}O_{2abs}$  compared with the control group by 4.2% in the 4-kcal/kg, 6.0% in the 8-kcal/kg, and 8.2% in the 12-kcal/kg per week groups ( $P < .001$  for each vs control;  $P$  for trend  $< .001$ ). There was no treatment  $\times$  subgroup interaction for age, body mass index, weight, baseline  $\dot{V}O_{2abs}$ , race/ethnicity, or baseline hormone therapy use. There were no significant changes in systolic or diastolic blood pressure values from baseline to 6 months in any of the exercise groups vs the control group.

**Conclusion** In this study, previously sedentary, overweight or obese postmenopausal women experienced a graded dose-response change in fitness across levels of exercise training.

**Trial Registration** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT00011193

JAMA. 2007;297:2081-2091

[www.jama.com](http://www.jama.com)

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Timothy S. Church, MD, MPH, PhD

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Conrad P. Earnest, PhD

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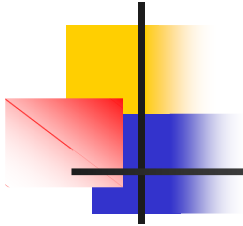
James S. Skinner, PhD

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Steven N. Blair, PED

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# Introdução



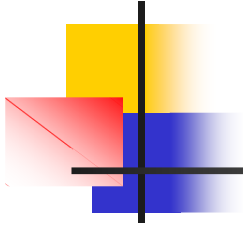
↓ Atividade física      ↑ Mortalidade  
Uma melhora nesse aspecto      → Diminui risco

- Estudos x dose-resposta ao exercício.

Questões levantadas:

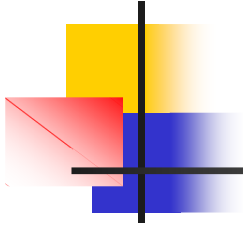
- Sedentários podem ter melhoras com 30 min de atividade física/ dia?
- Quanto maior a aptidão, maiores os ganhos?
- Quantidade de exercício X populações especiais.

# Introdução



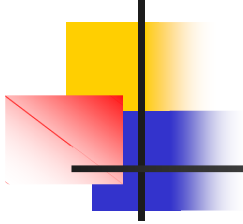
- Mais de 1 entre 3 mulheres Americanas estão na pós-menopausa.
- Mulheres pós-menopausa X Doença Coronariana.
- Cerca de 30% dessas mulheres reportam ser sedentárias e isso progride com a idade.

## Objetivo

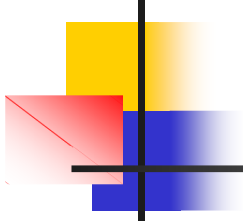


- Avaliar a dose-resposta ao exercício em mulheres na pós menopausa (DREW), sedentárias e hipertensas, em 50%, 100% e 150% da recomendação de atividade física do consenso do NIH.

## Participantes do Estudo



- 464 mulheres na pós menopausa.
- Idade entre 45 a 75 anos que eram sedentárias.
- Acima do peso ou obesas (IMC entre 25,0 e 43,0).
- PAS entre 120,0 a 159,9 mmHg.
- Randomizadas em 4 grupos.
- Critérios exclusão:  
Histórico de AVC, IAM ou de toda a condição médica séria que pudesse impedir o participante de aderir ao protocolo ou exercitar-se com segurança.



- Abril 2001 e junho 2005
- Estudo DREW.
- Verificar a dose-resposta em:

Grupo sem exercício

X

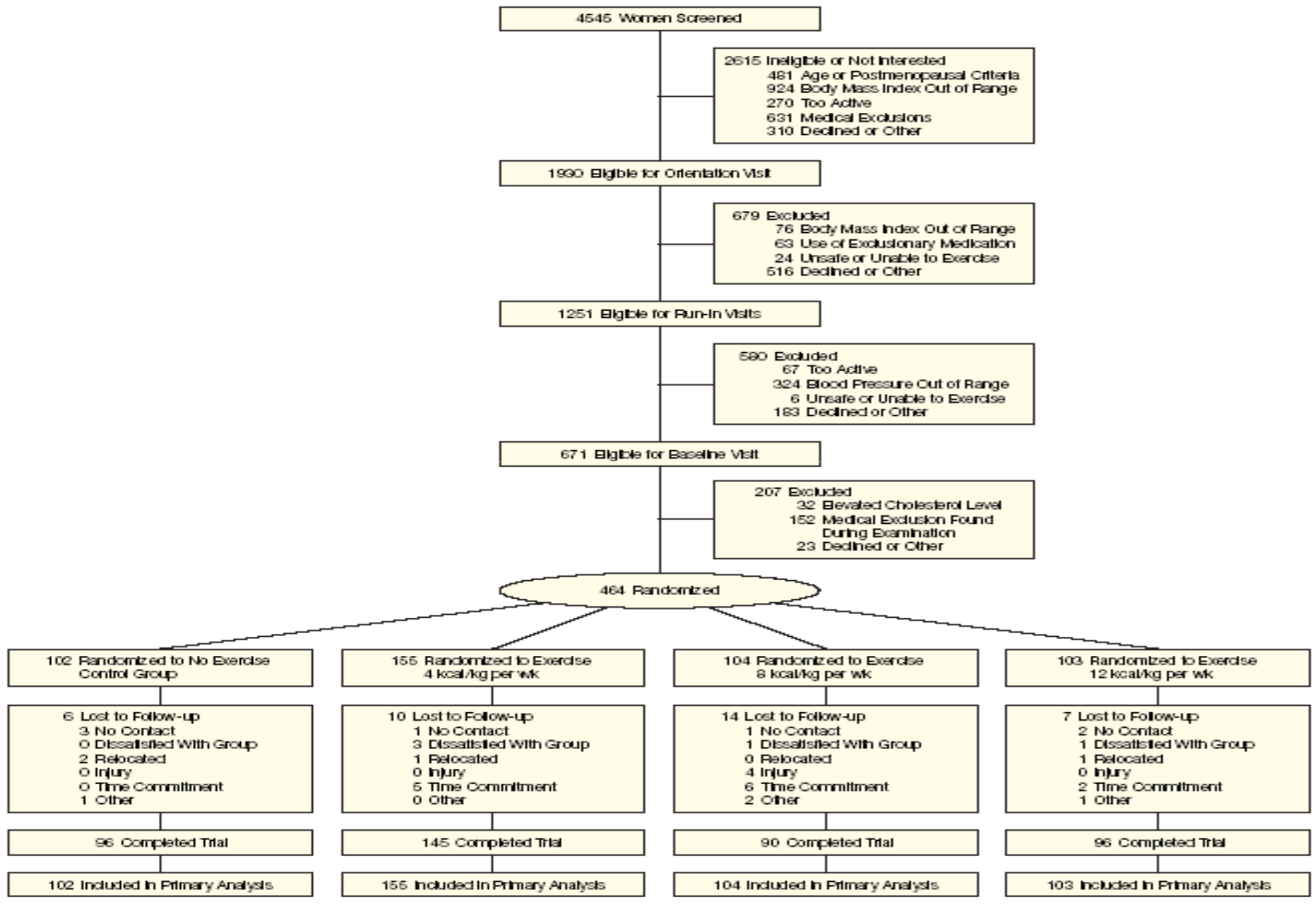
Exercício em três intensidades diferentes:

4kcal/kg (50%)

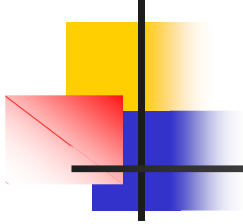
**8kcal/kg (100%) NIH**

12kcal/kg (150%)

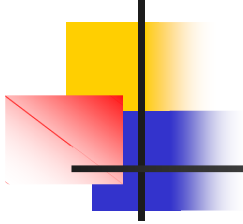
**Figure 1.** Participant Flow Diagram



# Método



- Ergoespirometria.
- Passômetro.
- Questionário – Dieta, histórico de tabagismo e medicamentos.
- PA – Pelo menos 4 medidas.
- Estudo Cego



- Aderência
- \$150 (\$75 cada) para completar o período de base.
- Poderiam ganhar outros \$350 caso garantissem a aderência.
- Para o grupo de controle, a aderência foi baseada no retorno mensalmente (preenchimento de questionários, etc).
- Para cada mês faltados, \$50 foram deduzidos do incentivo \$350 para os dois grupos.



# Resultados

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**Table 1.** Baseline Participant Characteristics\*

| Characteristics                                     | All<br>(N = 464) | Control<br>(n = 102) | Exercise Groups        |                        |                         |
|---|------------------|----------------------|------------------------|------------------------|-------------------------|
|   |                  |                      | 4 kcal/kg<br>(n = 155) | 8 kcal/kg<br>(n = 104) | 12 kcal/kg<br>(n = 103) |
| Age, mean (SD), y                                   | 57.3 (6.4)       | 57.2 (5.8)           | 57.7 (6.6)             | 57.3 (6.6)             | 56.6 (6.6)              |
| Education, mean (SD), y                             | 14.0 (2.1)       | 14.0 (2.0)           | 13.8 (2.0)             | 14.4 (2.0)             | 14.0 (2.3)              |
| Ethnicity/race, No (%)                              |                  |                      |                        |                        |                         |
| White   | 299 (64.5)       | 67 (65.7)            | 94 (60.6)              | 63 (60.6)              | 75 (72.8)               |
| African American                                    | 137 (29.5)       | 25 (24.5)            | 52 (33.6)              | 34 (32.7)              | 26 (25.3)               |
| Hispanic or other                                   | 28 (6.0)         | 10 (9.8)             | 9 (5.8)                | 7 (6.7)                | 2 (1.9)                 |
| Current cigarette smoking, No (%)                   | 25 (5.3)         | 5 (4.9)              | 9 (5.8)                | 4 (3.9)                | 7 (6.8)                 |
| Medication use, No. (%)                             |                  |                      |                        |                        |                         |
| Blood pressure                                      | 132 (28.6)       | 25 (24.8)            | 42 (27.1)              | 33 (32.0)              | 32 (31.1)               |
| Cholesterol   | 76 (16.5)        | 16 (15.8)            | 31 (20.0)              | 17 (16.5)              | 12 (11.7)               |
| Thyroid   | 71 (15.4)        | 16 (15.8)            | 19 (12.2)              | 16 (15.5)              | 20 (19.4)               |
| Antidepressant                                      | 84 (18.2)        | 18 (17.8)            | 29 (28.7)              | 18 (17.5)              | 19 (18.4)               |
| Current hormone therapy                             | 209 (45.0)       | 52 (51.0)            | 67 (43.2)              | 44 (42.3)              | 46 (44.6)               |
| Energy intake, mean (SD), kcal/d                    | 2238 (973)       | 2238 (961)           | 2184 (962)             | 2251 (966)             | 2306 (1019)             |
| Cardiovascular disease factors,<br>mean (SD), mg/dL |                  |                      |                        |                        |                         |
| Cholesterol   |                  |                      |                        |                        |                         |
| Low-density lipoprotein                             | 118.3 (26.3)     | 118.5 (26.5)         | 117.1 (26.9)           | 117.9 (25.2)           | 120.5 (26.3)            |
| High-density lipoprotein                            | 57.4 (14.6)      | 57.3 (15.3)          | 57.9 (14.6)            | 56.7 (15.0)            | 57.6 (13.7)             |
| Triglycerides                                       | 129.5 (63.4)     | 133.3 (67.8)         | 130.0 (59.1)           | 129.9 (58.5)           | 124.6 (70.0)            |
| Fasting glucose                                     | 95.0 (9.1)       | 96.3 (10.3)          | 94.4 (8.6)             | 94.5 (9.2)             | 95.1 (8.4)              |
| Blood pressure, mean (SD), mm Hg                    |                  |                      |                        |                        |                         |
| Systolic  | 139.8 (12.9)     | 141.8 (12.0)         | 139.1 (13.1)           | 140.0 (13.3)           | 138.3 (12.8)            |
| Diastolic   | 81.0 (8.4)       | 81.1 (7.8)           | 81.0 (9.0)             | 81.1 (8.2)             | 80.8 (8.6)              |
| Anthropometrics, mean (SD)                          |                  |                      |                        |                        |                         |
| Weight, kg  | 84.5 (11.9)      | 85.9 (12.4)          | 83.7 (11.3)            | 85.1 (12.8)            | 83.9 (11.2)             |
| Body mass index*                                    | 31.8 (3.8)       | 32.3 (3.9)           | 31.6 (3.8)             | 32.1 (4.1)             | 31.3 (3.6)              |
| Body fat, %   | 28.8 (4.8)       | 30.7 (5.4)           | 27.5 (4.0)             | 29.0 (4.8)             | 28.6 (4.8)              |
| Waist circumference, cm                             | 100.9 (11.7)     | 102.6 (11.9)         | 100.0 (11.1)           | 101.5 (12.4)           | 99.6 (11.7)             |
| Exercise test variables, mean (SD)                  |                  |                      |                        |                        |                         |
| Maximal heart rate, beats/min                       | 151.2 (16.4)     | 150.2 (16.4)         | 150.6 (17.1)           | 151.2 (15.3)           | 153.1 (16.6)            |
| Respiratory exchange ratio                          | 1.13 (0.07)      | 1.12 (0.06)          | 1.13 (0.08)            | 1.13 (0.07)            | 1.14 (0.07)             |
| Peak absolute $\dot{V}O_2$ , L/min                  | 1.30 (0.25)      | 1.33 (0.27)          | 1.29 (0.24)            | 1.26 (0.24)            | 1.33 (0.24)             |
| Peak relative $\dot{V}O_2$ , mL/kg<br>per minute    | 15.5 (2.8)       | 15.6 (2.9)           | 15.5 (2.9)             | 14.9 (2.4)             | 16.0 (2.9)              |
| Maximal power output, W                             | 94.7 (20.9)      | 96.1 (22.0)          | 93.8 (20.3)            | 91.4 (20.7)            | 98.0 (20.8)             |

Abbreviation:  $\dot{V}O_2$ , volume of oxygen consumed.

SI conversions: To convert low-density lipoprotein and high-density lipoprotein cholesterol to mmol/L, multiply by 0.0259; triglycerides to mmol/L, multiply by 0.0113; and fasting glucose to mmol/L, multiply by 0.0555.

\*Calculated as weight in kilograms divided by height in meters squared.

**Table 2.** Descriptive Training Data for Individuals Who Completed the Exercise Intervention\*

|   | Exercise Groups |              |              |
|---|-----------------|--------------|--------------|
|   | 4 kcal/kg       | 8 kcal/kg    | 12 kcal/kg   |
| Prescribed energy expenditure, kcal/wk† | 335 (45)        | 681 (102)    | 1006 (132)   |
| Time exercise, min/wk‡                  | 72.2 (12.3)     | 135.8 (19.5) | 191.7 (33.7) |
| Average METs per session‡               |                 |              |              |
| Cycle ergometer                         | 3.8 (0.4)       | 3.8 (0.3)    | 3.9 (0.4)    |
| Treadmill                               | 3.1 (0.6)       | 3.3 (0.6)    | 3.5 (0.8)    |
| Sessions/wk‡                            | 2.6 (0.3)       | 2.8 (0.4)    | 3.1 (0.5)    |
| 6-mo adherence, %                       |                 |              |              |
| All                                     | 94.6 (16.6)     | 89.0 (25.6)  | 93.3 (20.3)  |
| Completers                              | 98.0 (8.4)      | 97.8 (7.7)   | 97.4 (11.0)  |

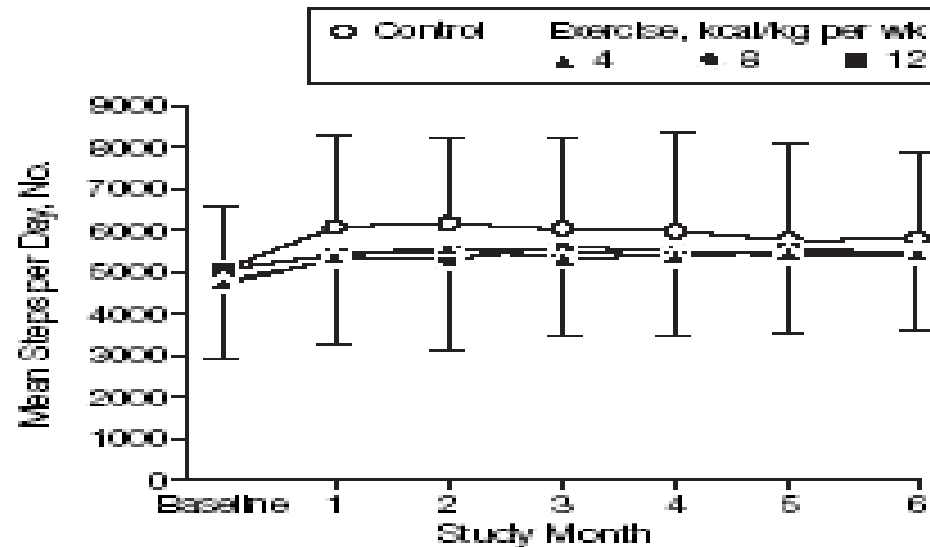
Abbreviation: METs, metabolic equivalents (1 MET = 3.5 mL O<sub>2</sub> uptake/kg per minute).

\*All data are presented as mean (SD).

†Data for all participants and based on baseline weight.

‡Data for all individuals who completed the intervention. Data are for exercise training period excluding the initial ramping period which represents 6 months of data for the 4-kcal/kg, 5 months for the 8-kcal/kg, group, and 4 months for the 12-kcal/kg week groups. Adherence was calculated for each individual by dividing the kilocalories expended during the 6-month exercise training by the kilocalories prescribed for the training period × 100%.

**Figure 2.** Mean Steps per Day During Study Months



**Participants With Complete Step Data**

|                          |     |     |     |     |     |     |     |
|--------------------------|-----|-----|-----|-----|-----|-----|-----|
| Control                  | 101 | 80  | 78  | 77  | 76  | 76  | 73  |
| Exercise, kcal/kg per wk |     |     |     |     |     |     |     |
| 4                        | 160 | 126 | 123 | 117 | 115 | 114 | 104 |
| 8                        | 104 | 85  | 84  | 79  | 78  | 77  | 72  |
| 12                       | 103 | 90  | 85  | 85  | 83  | 78  | 74  |

The mean steps calculations do not include steps accumulated during supervised exercise. The upper error bars indicate 95 % confidence intervals for the control group and the lower error bars for the 4-kcal/kg per week group. At baseline there were no differences in groups. All groups had a significant increase in steps from baseline to month 1 ( $P < .05$  for each). At months 1, 2, 3, and 4, the control group had a greater number of steps than 1 or more of the exercise groups ( $P < .05$  for each), but by months 5 and 6, there were no differences between any groups.

**Table 3.** Primary and Secondary Outcome Measures After Intervention\*

| Characteristics                            | Exercise Groups      |                        |                        |                         | P Value† |
|--|----------------------|------------------------|------------------------|-------------------------|----------|
|  | Control<br>(n = 102) | 4 kcal/kg<br>(n = 155) | 8 kcal/kg<br>(n = 104) | 12 kcal/kg<br>(n = 103) |          |
| <b>Fitness variables</b>                   |                      |                        |                        |                         |          |
| Peak absolute $\dot{V}O_2$ , L/min         | 1.28 (0.01)          | 1.33 (0.01)            | 1.35 (0.01)            | 1.39 (0.01)             | <.001‡ ← |
| Peak relative $\dot{V}O_2$ , mL/kg per min | 15.5 (0.13)          | 16.2 (0.11)            | 16.4 (0.13)            | 16.8 (0.13)             | <.001§ ← |
| Maximal power output, W                    | 93.4 (0.9)           | 99.6 (0.7)             | 101.2 (0.9)            | 105.4 (0.9)             | <.001‡ ← |
| <b>Anthropometrics</b>                     |                      |                        |                        |                         |          |
| Weight, kg                                 | 83.7 (0.3)           | 83.3 (0.3)             | 82.9 (0.3)             | 83.3 (0.3)              | .39      |
| Body fat, %                                | 29.8 (0.5)           | 28.1 (0.4)             | 28.3 (0.5)             | 28.6 (0.5)              | .08      |
| Waist circumference, cm                    | 101.2 (0.7)          | 98.1 (0.5)             | 98.6 (0.7)             | 98.2 (0.7)              | .002   ← |
| <b>Cardiovascular disease risk factors</b> |                      |                        |                        |                         |          |
| Cholesterol                                |                      |                        |                        |                         |          |
| LDL  | 122.3 (2.0)          | 121.3 (1.6)            | 119.3 (2.0)            | 120.2 (2.0)             | .71      |
| HDL  | 57.2 (0.7)           | 57.2 (0.6)             | 57.1 (0.7)             | 56.0 (0.7)              | .56      |
| Triglycerides                              | 135.2 (6.1)          | 122.7 (4.9)            | 126.0 (6.0)            | 132.9 (6.1)             | .35      |
| Fasting glucose                            | 95.8 (0.7)           | 94.0 (0.6)             | 93.6 (0.7)             | 93.4 (0.7)              | .05      |

Abbreviations: HDL, high-density lipoprotein; LDL, low-density lipoprotein;  $\dot{V}O_2$ , volume of oxygen consumed.

SI conversions: To convert LDL and HDL to mmol/L, multiply by 0.0259; triglycerides to mmol/L, multiply by 0.0113; fasting glucose to mmol/L, multiply by 0.0555.

\*Values are expressed as fitted mean (SE) and all are adjusted for baseline value, age, and ethnicity/race with the fitness variables also adjusted for baseline weight and maximum heart rate during exercise testing at baseline and follow-up.

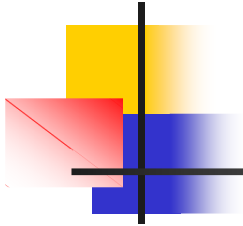
†P values for difference between groups, determined by analysis of variance. For a given outcome measure when the analysis of variance (last column) was statistically significant ( $P < .05$ ), all pairwise comparisons among groups were tested for statistical significance using Tukey studentized range test. Pairwise comparisons that were significantly different from one another are indicated in the following footnotes.

‡All pairwise comparisons significant except 4-kcal/kg vs 8-kcal/kg per week groups.

§All pairwise comparisons were statistically significant except 4-kcal/kg vs 8-kcal/kg per week groups and 8-kcal/kg vs 12-kcal/kg per week groups.

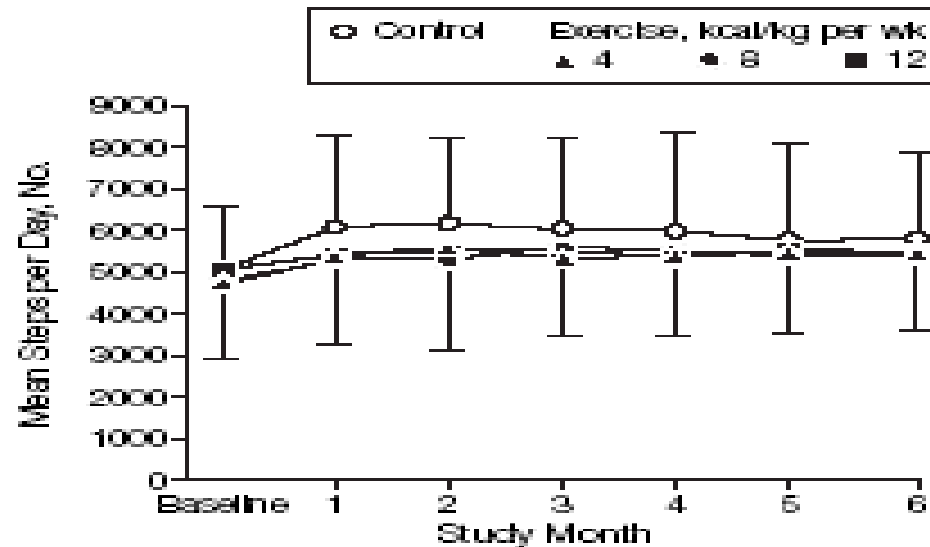
||All exercise groups were statistically significant vs control, but no significant differences existed between any exercise groups.

## Resultados



- Nenhum dos grupos com exercício, teve uma diferença significativa na PAS, quando comparado ao grupo sem exercício.
- Não houve diferença na PAD
- Embora não tenha havido uma diferença significativa de PA entre os grupos, verificou –se uma redução no grupo controle (54.9% vs 43.1%,  $P=.05$ ) e no 12-kcal/kg (48.5 vs 36.9%,  $P=.01$ ).

**Figure 2.** Mean Steps per Day During Study Months



**Participants With Complete Step Data**

|                          |     |     |     |     |     |     |     |
|--------------------------|-----|-----|-----|-----|-----|-----|-----|
| Control                  | 101 | 80  | 78  | 77  | 76  | 76  | 73  |
| Exercise, kcal/kg per wk |     |     |     |     |     |     |     |
| 4                        | 160 | 126 | 123 | 117 | 115 | 114 | 104 |
| 8                        | 104 | 85  | 84  | 79  | 78  | 77  | 72  |
| 12                       | 103 | 90  | 85  | 85  | 83  | 78  | 74  |

The mean steps calculations do not include steps accumulated during supervised exercise. The upper error bars indicate 95 % confidence intervals for the control group and the lower error bars for the 4-kcal/kg per week group. At baseline there were no differences in groups. All groups had a significant increase in steps from baseline to month 1 ( $P < .05$  for each). At months 1, 2, 3, and 4, the control group had a greater number of steps than 1 or more of the exercise groups ( $P < .05$  for each), but by months 5 and 6, there were no differences between any groups.

**Table 4.** Change in Blood Pressure Variables and Blood Pressure Medication Use\*

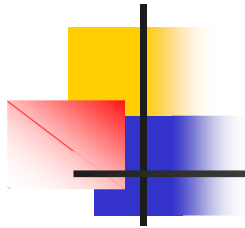
| Characteristics  | Control<br>(n = 102) | Weekly Energy Expenditure |                        |                         | P<br>Value† |
|--|----------------------|---------------------------|------------------------|-------------------------|-------------|
|  |                      | 4 kcal/kg<br>(n = 155)    | 8 kcal/kg<br>(n = 104) | 12 kcal/kg<br>(n = 103) |             |
| Change in blood pressure,<br>mean (SE), mm Hg                      |                      |                           |                        |                         |             |
| Systolic   | -1.7 (1.1)           | 0.8 (0.9)                 | -1.0 (1.1)             | -3.3 (1.1)‡             | .03 ←       |
| Diastolic  | -0.5 (0.6)           | 0.9 (0.5)                 | 0.1 (0.6)              | -0.4 (0.6)              | .29 ←       |
| Systolic blood pressure ≥140 mm Hg,<br>No. (%)‡                    |                      |                           |                        |                         |             |
| Baseline   | 56 (54.9)            | 74 (47.7)                 | 53 (51.0)              | 50 (48.5)               | .70         |
| Follow-up  | 44 (43.1)            | 74 (47.7)                 | 44 (42.3)              | 38 (36.9)               | .39         |
| P value  | .05                  | >.99                      | .09                    | .01                     |             |
| Changes in blood pressure medication<br>use during study, No. (%)§ |                      |                           |                        |                         |             |
| No change  | 83 (94.3)            | 125 (94.0)                | 75 (88.3)              | 78 (87.6)               | .07 ←       |
| Started  | 2 (2.3)              | 5 (3.8)                   | 8 (9.4)                | 3 (3.4)                 |             |
| Discontinued   | 3 (3.4)              | 3 (2.3)                   | 2 (2.3)                | 8 (9.0)                 |             |

\*Values are expressed as fitted mean (SE) adjusted for baseline value, age, ethnicity/race, and change in weight, blood pressure medication use at baseline and follow-up. P values are for group differences assessed by  $\chi^2$  tests and column P values are for within group differences assessed by the McNemar test. Row P values are for differences between groups, determined by analysis of variance. For a given outcome measure when the analysis of variance (last column) was statistically significant ( $P < .05$ ), all pairwise comparisons among groups were tested for statistical significance using Tukey studentized range test. The pairwise comparison that was significantly different is indicated in the following footnotes.

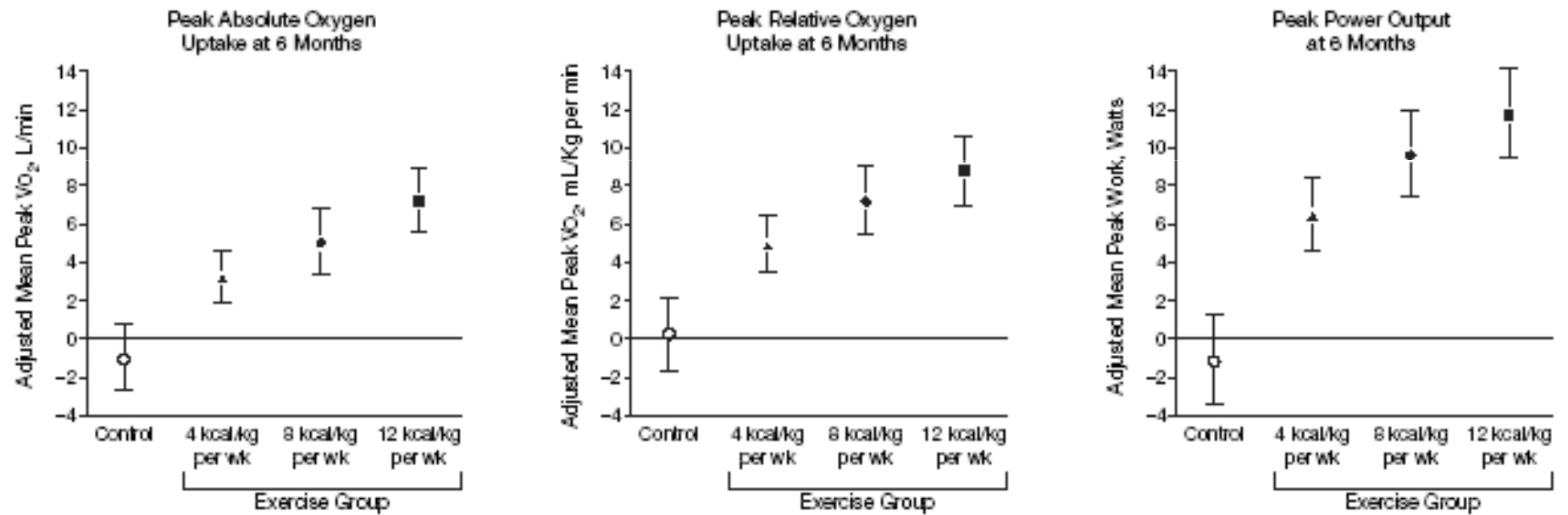
‡12 kcal/kg vs 4-kcal/kg per week,  $P = .02$ .

‡Column P values are for group differences assessed by  $\chi^2$  tests and row P values are for within-group differences assessed by the McNemar test.

§The number of participants were 88 in the 4-kcal/kg, 133 in the 8-kcal/kg, and 85 in the 12-kcal/kg per week groups and 89 in the control group. P value is for differences assessed by Fisher exact test.

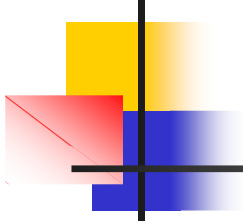


**Figure 3.** Percent Change in Fitness Data for Each Study Group



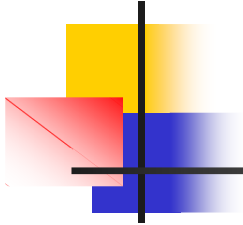
The data represent the least-squares means adjusted for age, ethnicity/race, weight, and peak heart rate. The *P* values for pairwise comparisons of control with 4-kcal/kg, 8-kcal/kg, and 12-kcal/kg per week groups are *P* < .001 for each variable. *P* for linear trend across groups < .001 for each outcome. Error bars indicate 95% confidence intervals.

## Comentários



- Quanto maior a dose, maior a resposta.
- Somente 4kcal/kg apresentam melhores resultados do os indivíduos sem exercício.
- 72 horas minutos de atividade física moderada, pelo menos 3x por semana em mulheres sedentárias na pós menopausa têm um efeito significativo no condicionamento físico.
- Não houve alteração de peso.
- Houve redução na circunferência da cintura, o que implica em uma importante redução no risco de resistência a insulina, diabetes, síndrome metabólica e mortalidade.

## Conclusão



- Mulheres sedentárias, acima do peso ou obesa tiveram uma mudança na aptidão através de níveis do treinamento do exercício.
- O efeito do treinamento foi similar através dos subgrupos baseados na idade, peso, aptidão da linha de base e etnia.