What dose of exercise reduces insulin resistance in children, and application to NAFLD

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No conflicts of interest to disclose

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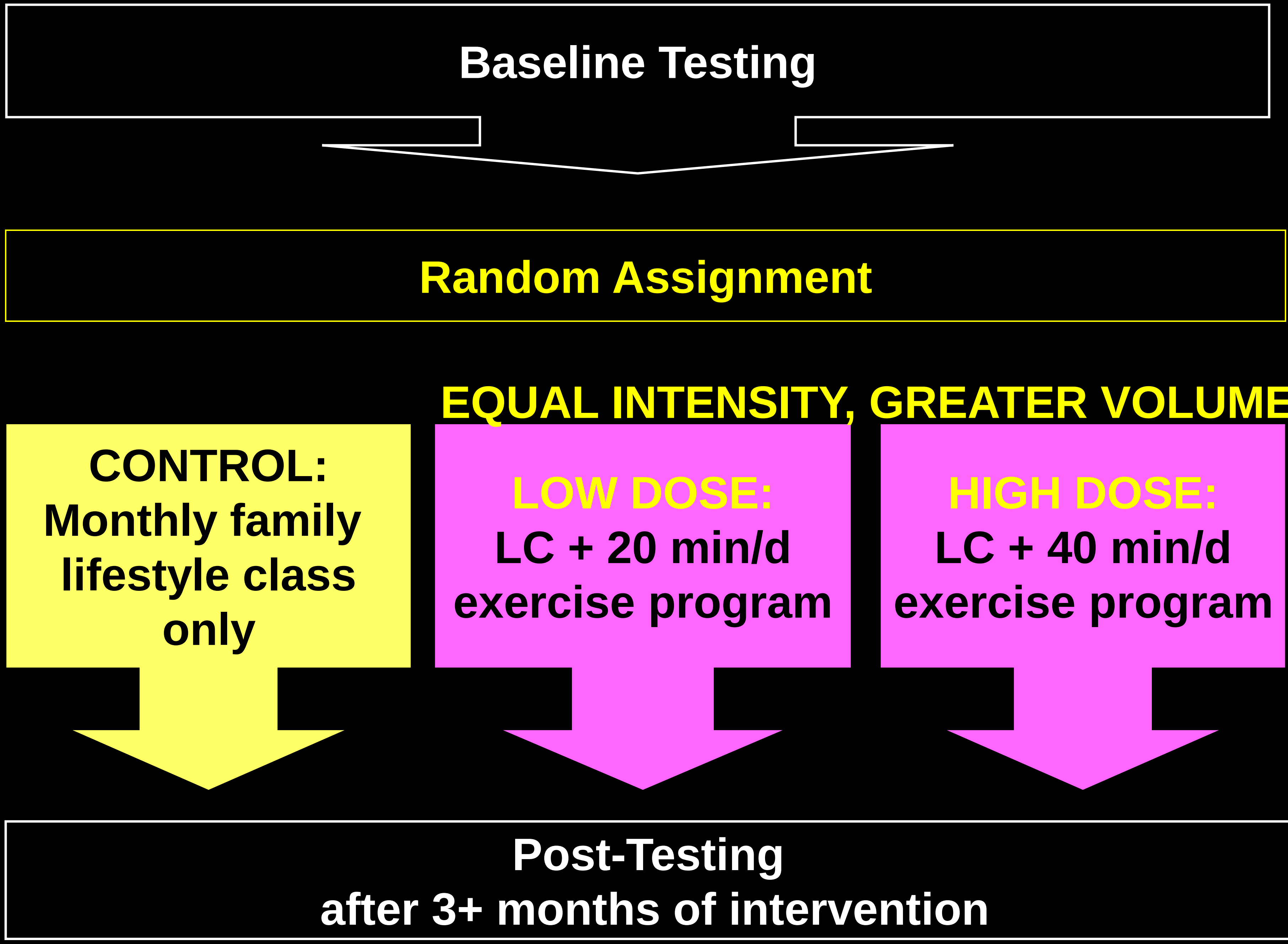
PLAY PROJECT:
HOW MUCH DOES IT TAKE TO REDUCE RISK?

- **Tested 2 doses of a daily after-school exercise program on diabetes risk** (insulin resistance) **in overweight, inactive children**

  58% black **42% male**

  85% obese **28% prediabetic**

  - **0 vs. 20 vs. 40 min/day vigorous 3 mo. after-school aerobic exercise program**

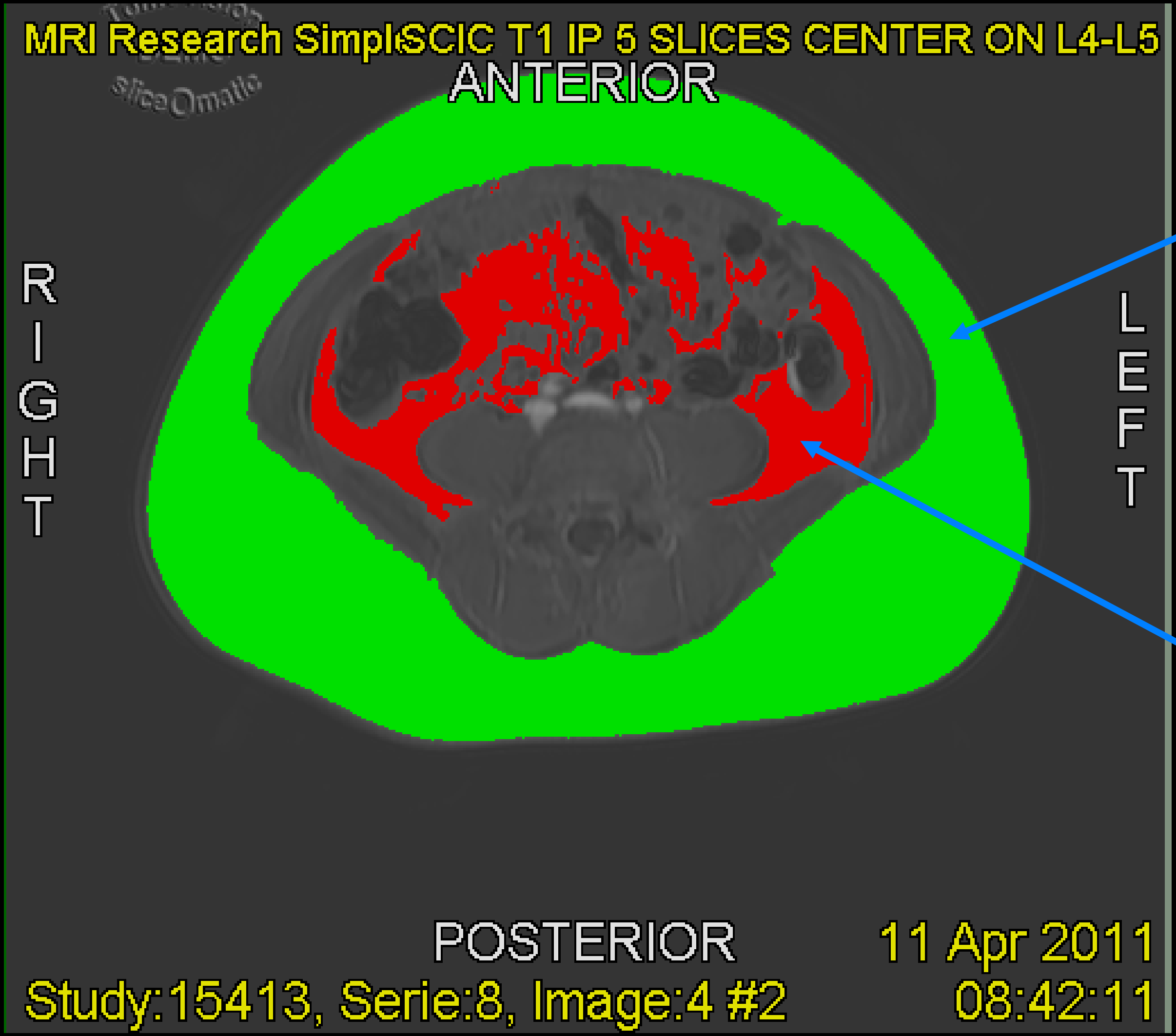


Baseline Testing
Random Assignment
EQUAL INTENSITY, GREATER VOLUME
CONTROL: Monthly family lifestyle class only
LOW DOSE: LC + 20 min/d exercise program
HIGH DOSE: LC + 40 min/d exercise program
Post-Testing after 3+ months of intervention

Oral glucose tolerance test

Insulin Area Under the Curve (AUC): insulin resistance

Visceral adipose tissue



After-school exercise program

- 8 months (5 days/week)
- Vigorous aerobic activities
    - Fun, simple games – this was not PE
    - running games, jump rope, ball games
- Reward effort, not performance
    - Points for average HR>140 bpm
    - Small weekly prizes
- Transportation provided


PROJECT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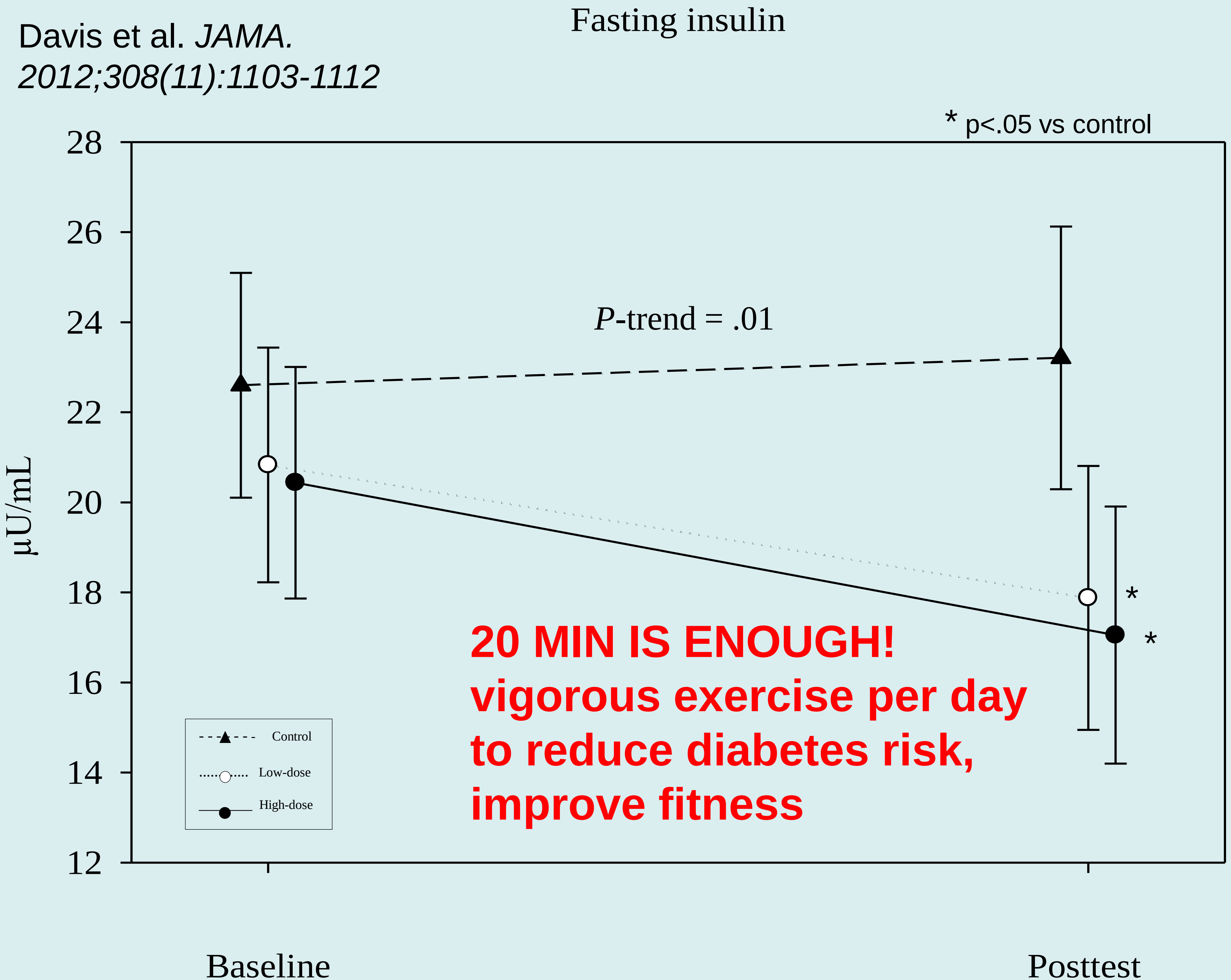
APPROACH

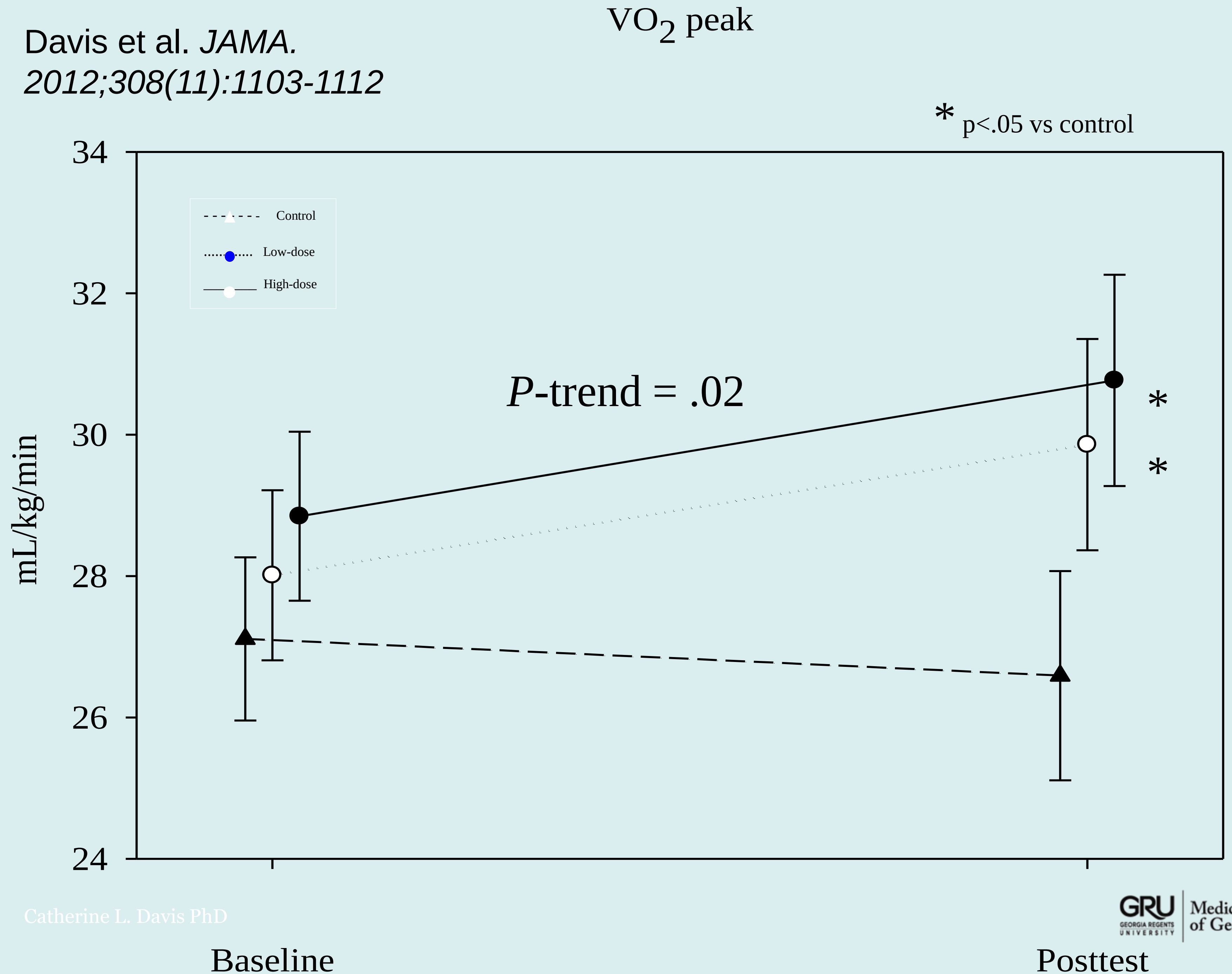
- Overweight and obese children
- Fun, simple games – this was not PE
- Reward effort (heart rate) rather than performance (speed, skill)
- Convenient, no cost

Davis et al. *JAMA.* *2012;308(11):1103-1112*



20 MIN IS ENOUGH! vigorous exercise per day to reduce diabetes risk, improve fitness

Davis et al. *JAMA.* *2012;308(11):1103-1112*



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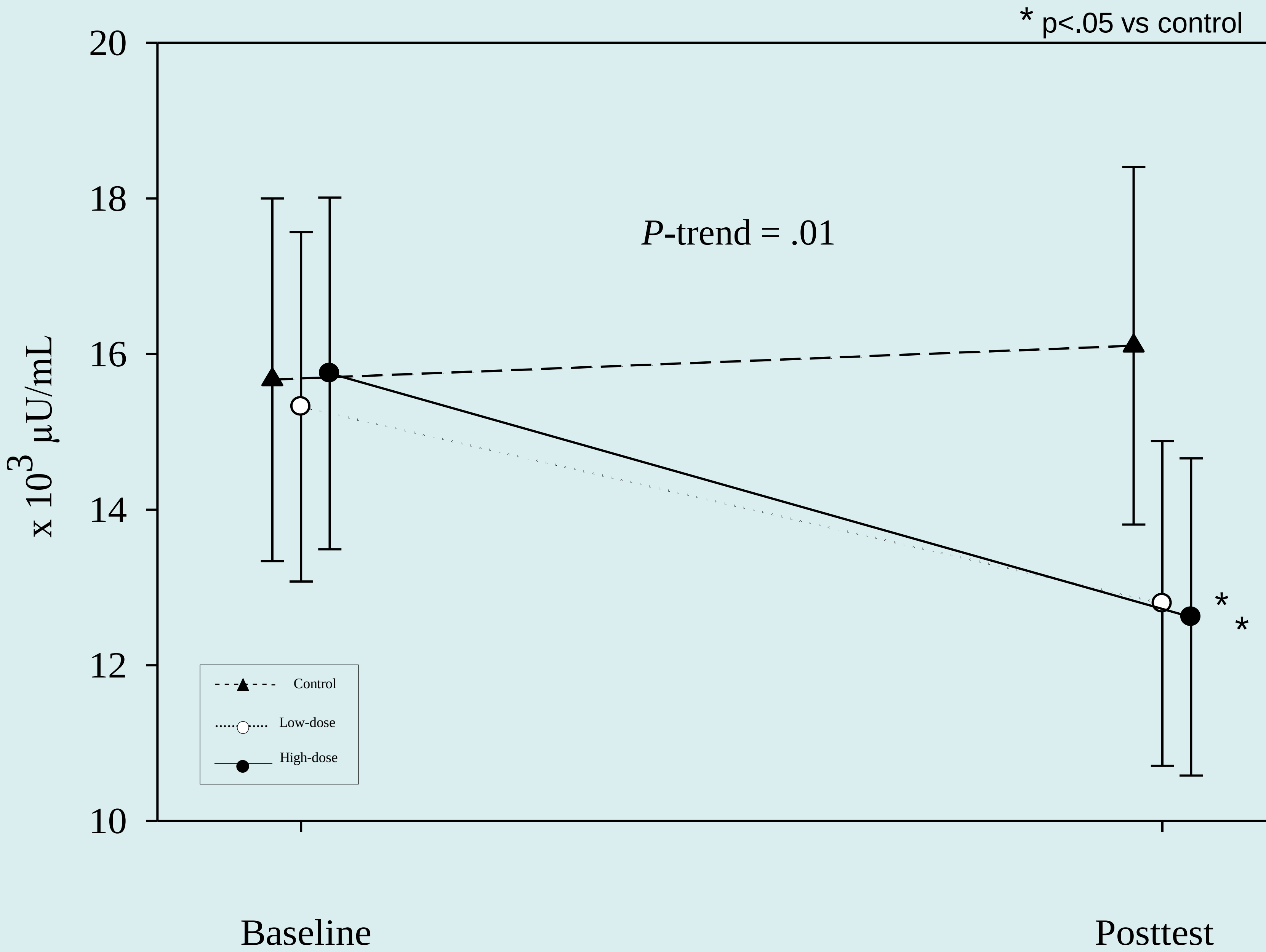
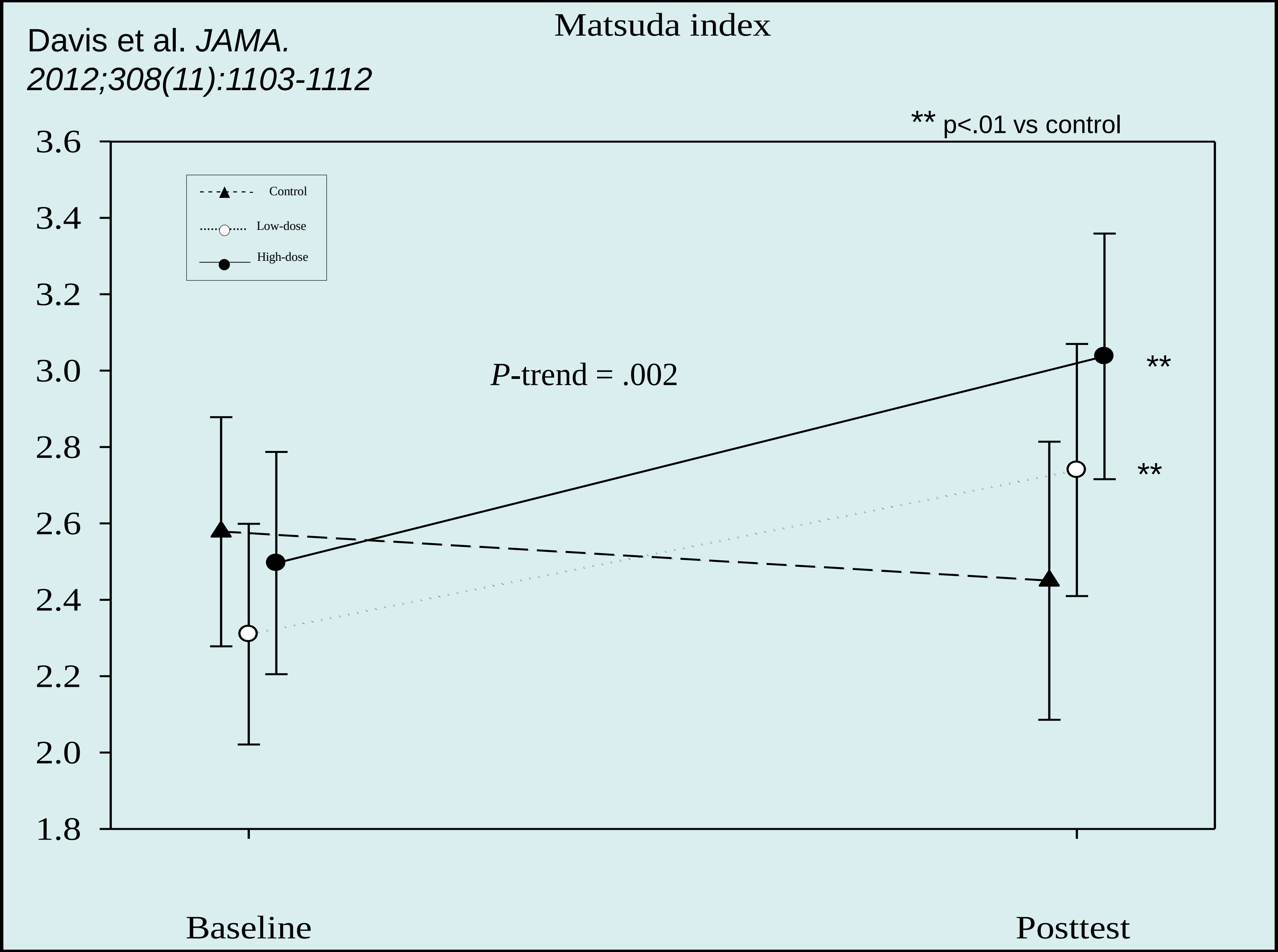
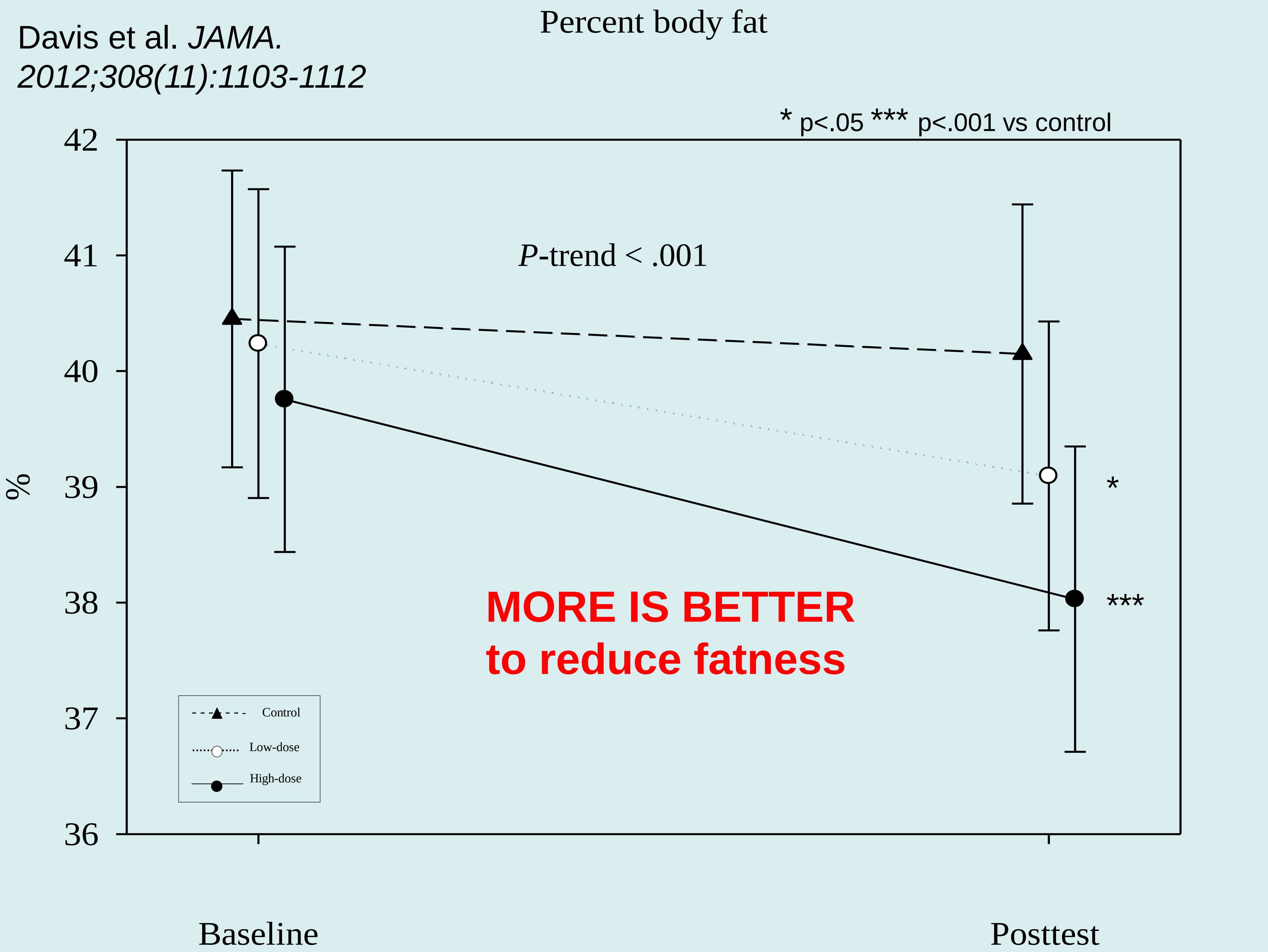
Insulin AUC





Matsuda index
Davis et al. JAMA. 2012;308(11):1103-1112
** p<.01 vs control
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
Control
Low-dose
High-dose
P-trend = .002
**
**
Baseline
Posttest

Davis et al. *JAMA.* *2012;308(11):1103-1112*



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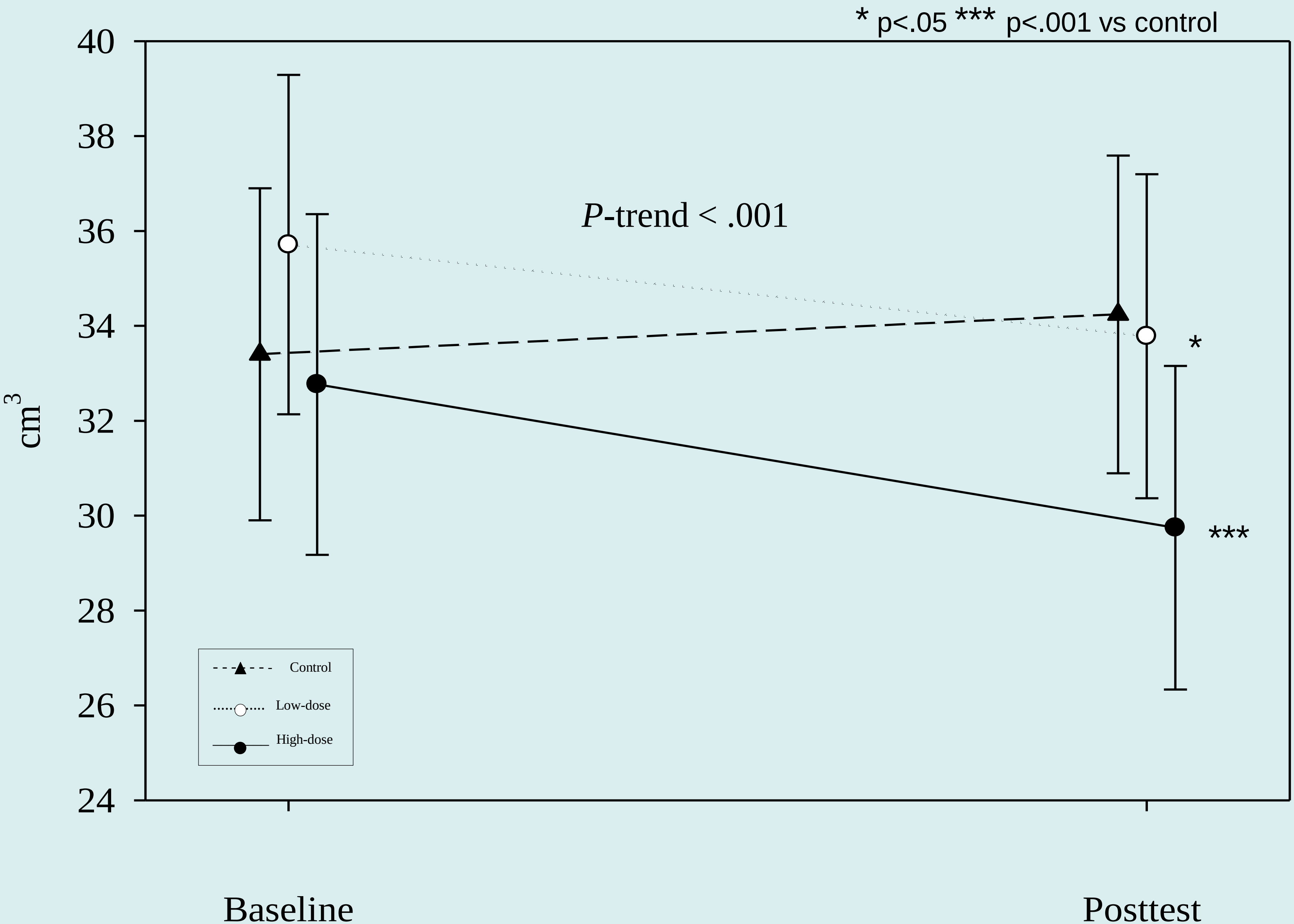
Visceral fat



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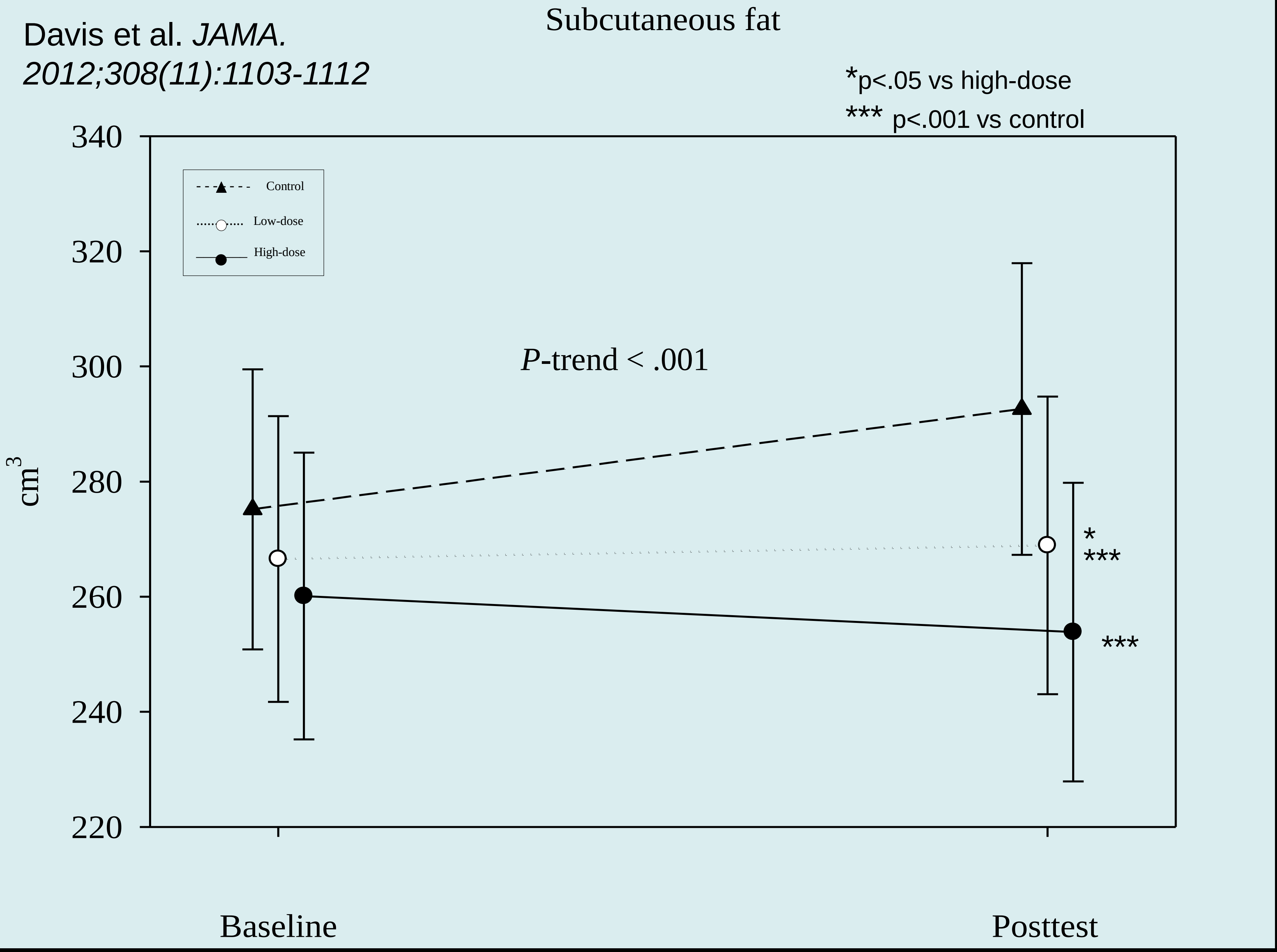

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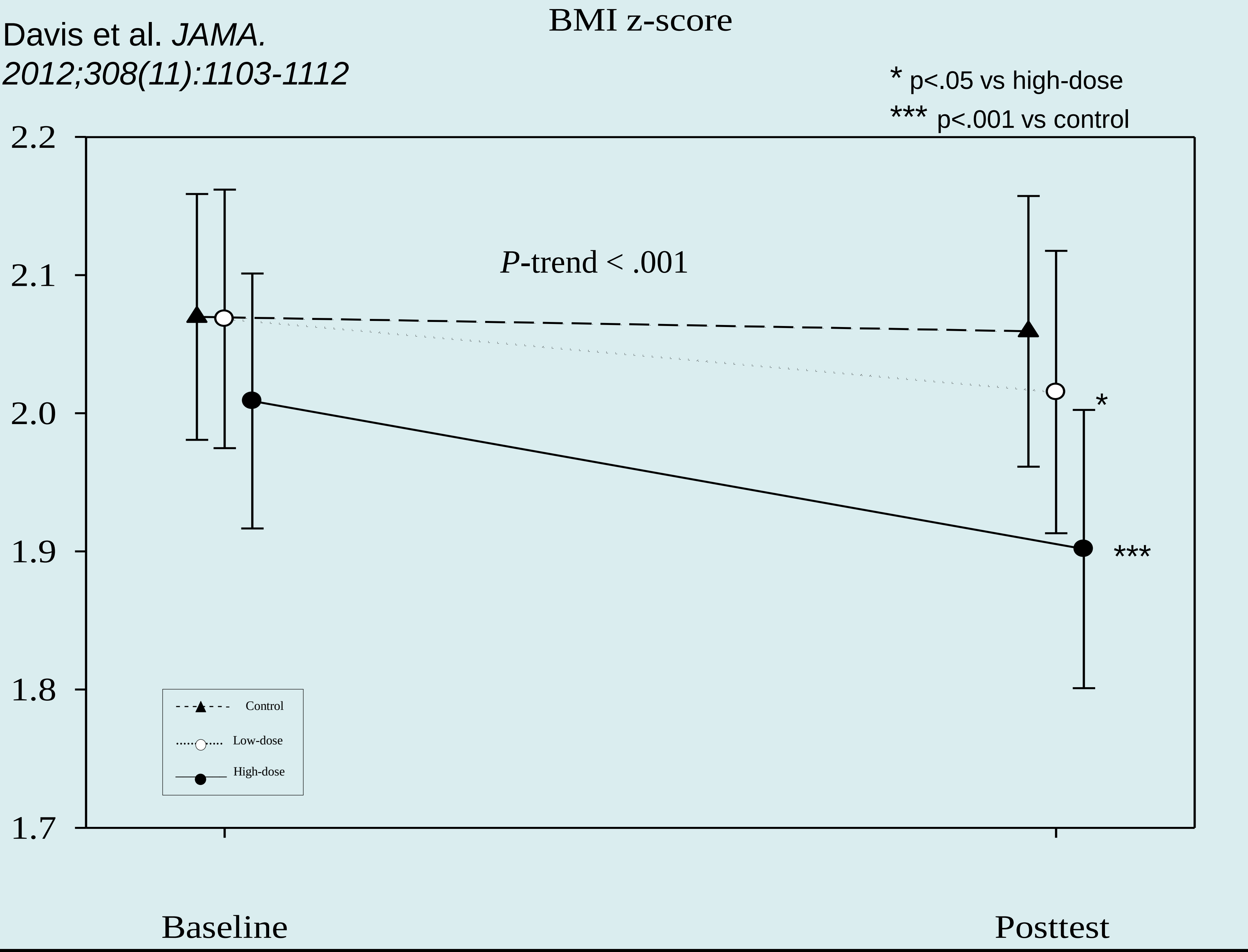


PLAY PROJECT IMPLICATIONS

- **20 min/d aerobic activity can reduce diabetes risk. *Could fit into school day***
  - ***Optimized PE (SPARK)***
  - ***Classroom PA (Mahar 2006, Donnelly 2009, Kibbe 2011)***
  - ***Recess with adult play leaders (Howe, 2012)***
  - ***Power Up for 30! program led by Georgia SHAPE*** *(georgiashape.org)*
- **40 min/d will require after-school time**

SMART Study questions

- Are these benefits unique to exercise interventions?
- Will this approach work to reduce risk for arteriosclerosis, NAFLD and NASH in overweight children?
- Would effects be greater over a longer period of time (School year vs semester; 8 vs 3 months)?

Exercise Trials with Liver Fat Outcomes in Children

- **Mostly uncontrolled pre-post trials**
  - Pacifico et al. 2013, Pozzato et al. JPGN 2010, Van der Heijden et al. 2010
- **A few small randomized controlled trials in adolescents have mixed results**
  - **Lee et al. 2012 (45 obese teen boys)**
    - **aerobic or resistance exercise ↓liver fat**
  - **Lee et al. 2013 (44 obese teen girls)**
    - **aerobic, but not resistance exercise ↓liver fat**

    Why were genders analyzed separately?
  - **J. Davis et al. 2011 (38 overweight Latina teens)**
    - **no effect of combined aerobic/resistance exercise on liver fat**

Study Objective: Isolate effects of exercise

- To compare cognitive effects of after-school exercise training (40 min/day over 8 months) vs a sedentary attention control condition in overweight children.
  - **Effect of exercise *per se***
  - Intent-to-treat analyses

- Ancillary study: arterial stiffness (PWV), liver fat (MRI), liver stiffness (Fibroscan), inflammation (ALT, AST, CRP) outcomes

SEDENTARY CONTROL CONDITION

- Attention control
  - Different room in same building
  - Same buses, same snacks
  - Teachers rotated between conditions

- Sedentary recreation
  - Board games
  - Crafts
  - Teacher-led group activities
  - Points for cooperation, proper use of materials, clean up
  - Points calibrated so groups got equal rewards

SMART Study Participants

175 healthy overweight, sedentary 8-11 yr olds recruited from Augusta, GA schools

- 61% female, 87% Black
- 9.7 ± 0.9 yrs
- **BMI ≥ 85th percentile**
  - **74% obese**
  - **BMI** **26 ± 5** kg/m^2 (96 ± 4 %ile)
  - **Percent body fat** **38 ± 7** %
  - **Peak VO_2** **30 ± 6** ml/kg/min
  - **92% Needs Improvement-Health Risk**
- Groups similar at baseline

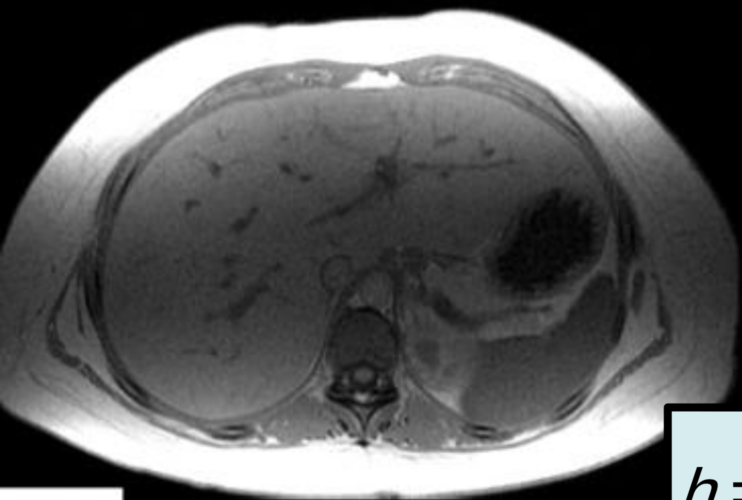
Results

- 89% study retention rate at posttest (*n* = 155)

- Exercise group had 59% attendance rate
    - Heart rate average 161 ± 7 beats/min
    - 6.8 ± 1.6 METs
    - 10 refused posttest

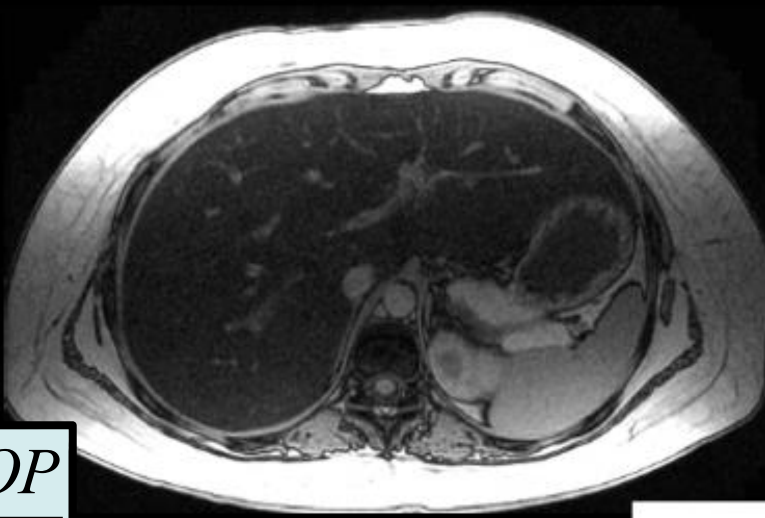
- Control group had 64% attendance rate
    - 10 refused posttest

Dixon Method (2-point) Fat-Water MRI
(scaled to Lipoquant for interpretability)

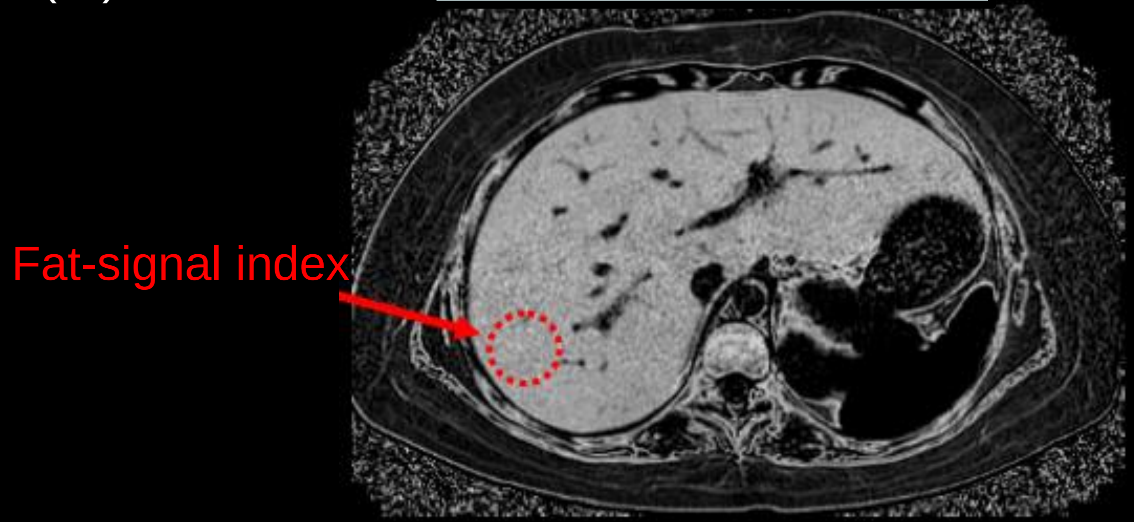


In-Phase (IP) = W + F

$$h = \frac{F}{W+F} = \frac{IP - OP}{2IP}$$



Opposed-Phase (OP) = W - F



Images courtesy of Dr. S. Reeder, U. Wisconsin Madison

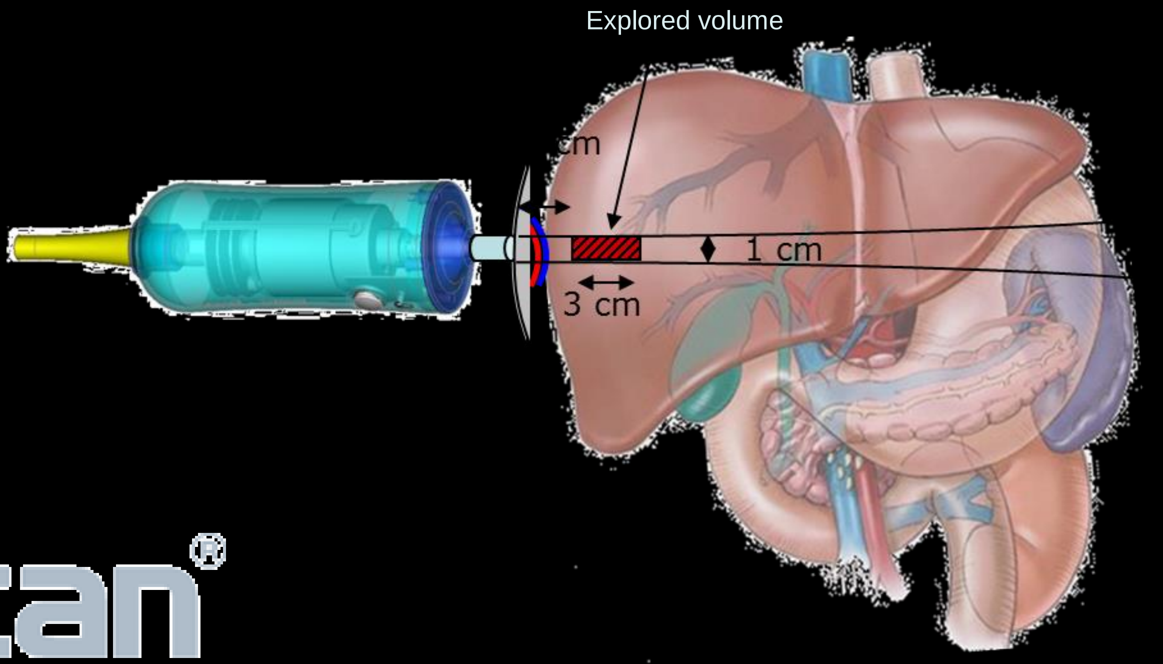
Liver Stiffness via Transient Elastography

Fibroscan®, Echosens, Paris, France

- Liver stiffness measurement consists in creating an elastic shear wave within the liver, measuring its speed of propagation and calculating the corresponding stiffness expressed in kilopascals (kPa).

To do so, a probe is placed between the rib bones in proximity to the right lobe of the liver. The operator, assisted by a time-motion mode ultrasonic image, locates a 5-cm deep portion of liver parenchyma free of large vascular structures. When the measurement is triggered, the vibrator gives a painless push to the tissue, creating an elastic shear wave.

Transient Elastography



FibroScan®

Thank You!

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