# The Surprising Links Between Physical Activity, Brain Health, and Healthy Aging"

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# Example Research Study (1)

- By Yaffee et al. *Arch Intern Med* 2001;61:1703.
- The study measured cognition with MMSE (30 item global test) at start of study (baseline) and again 6-8 yrs later (follow-up) in 5925 women 65+
- Classified women as “decline” if scored 3+ points worse on MMSE at F/U; otherwise “no decline”.
- PA level at baseline measured as blocks walked each week (range 0-672 blocks/wk).
- Classified women into 4 equal sized groups (“quartiles”) of PA: low PA , 2nd, 3rd, & high PA

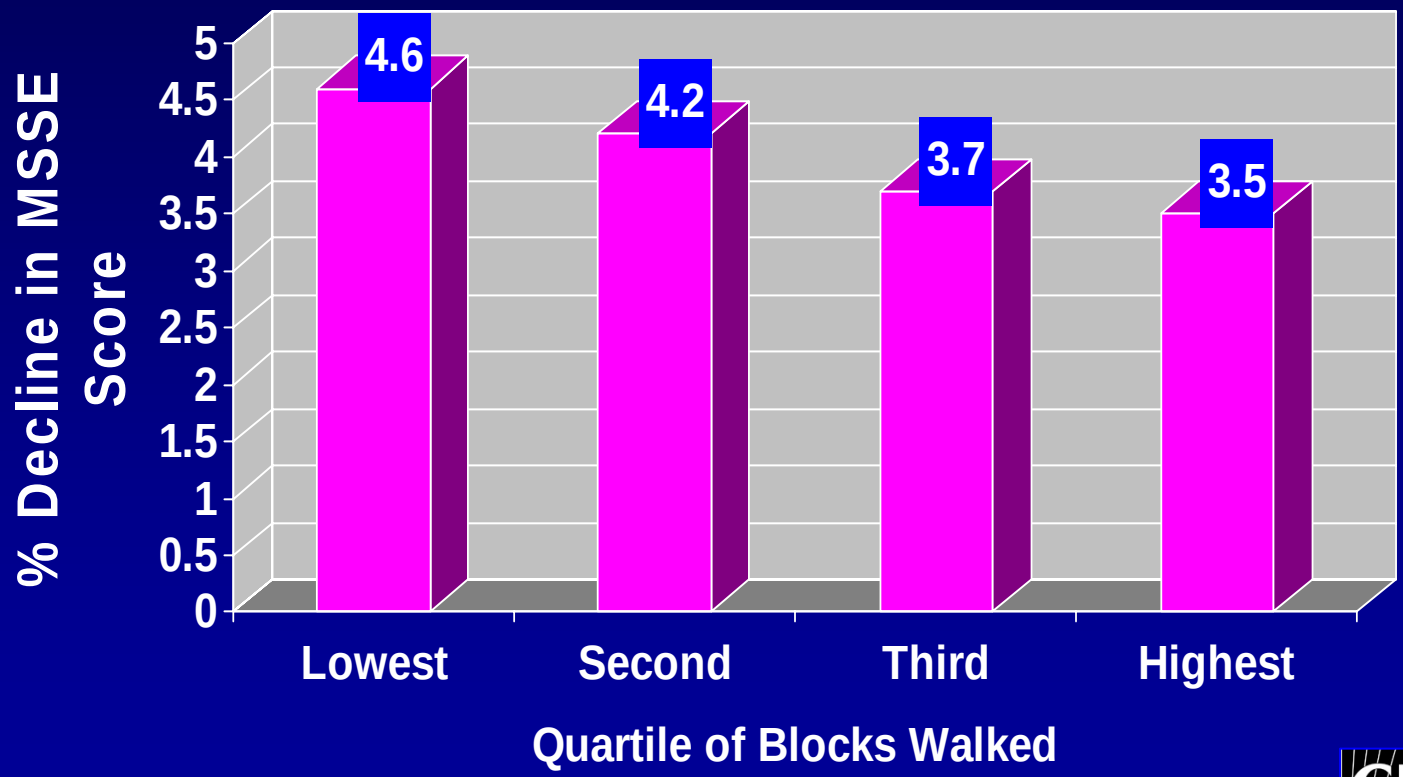
# Example Research Study (2)

- Compared rates of cognitive decline across the PA groups. Statistical methods were also used to adjust for other factors ("confounders") that might account for differences in rates among groups.
- Statistical tests estimated the probability that any observed association between PA and decline is due to chance.
- Generally, when the probability is less than 5% ($p<.05$), chance is deemed an unlikely explanation for the results, and the result is termed "statistically significant".

# Yaffe Study Results

| Physical Activity Level | Percent Women with Decline in MMSE |
|---|---|
| Lowest | 4.6% |
| 2nd | 4.2% |
| 3rd | 3.7% |
| Highest | 3.5% |

# Results of Yaffe Study Bar Chart

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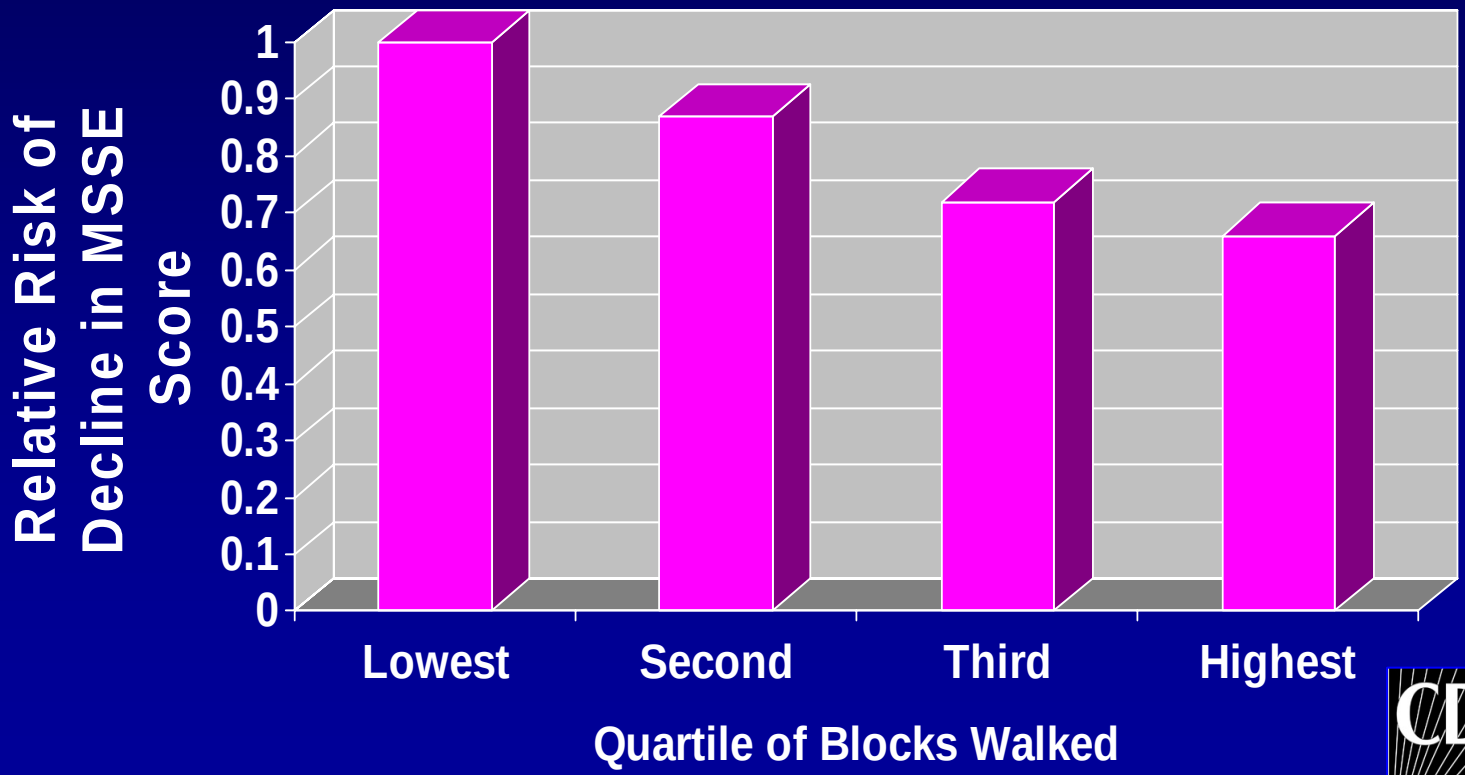
# Oversimplification: Get relative rates (risks) by setting rate in a comparison group = 1.0

(here comparison group =“Lowest PA Level)

Adjusted RR Lowest vs. highest = .66 (p<.05)

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# All Research Studies Have Limitations

- The measure of physical activity (blocks walked)
  - Only measures walking and not other types of aerobic activity
  - Concerns about measurement error
- The measure of cognition
  - Simple summary measure
  - Not designed to measure change in mental status in adults with normal cognition
- We have more confidence in the results of studies where physical activity level is randomly assigned

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# Overview

- Background
- Some “Surprising” aspects
- PA and cognition

# Examples of Types of Health Benefits of Physical Activity

| | Physical | Mental |
|---|---|---|
| Fitness | Muscle Strength | School Performance? |
| Prevention | Heart Disease | Alzheimer Disease? |
| Treatment | Diabetes | Depression |

# Large # Preventive Benefits of PA (more to come?) including:

- Heart Disease
- Stroke
- Hypertension
- Diabetes
- Osteoporosis
- Obesity
- Lipid disorders
- Colon Cancer
- Breast Cancer
- Anxiety
- Depression
- Falls
- Loss of function with age

# Large Number of Therapeutic Benefits including:

- Heart Disease
- Stroke
- Hypertension
- Diabetes
- Osteoporosis
- Obesity
- Lipid disorders
- Depression
- Lung disease
- Osteoarthritis
- Claudication
- Pain
- Back pain
- Dementia
- Syncope
- Constipation

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# Preventive PA Recommendation (Aerobic)

- Meeting PA recommendations = either:
  - 30+ minutes/day (at least 10 minutes per bout) x 5+ days per week for moderate intensity PA
    - Moderate intensity activities expend 3-6x more energy than at rest, e.g. brisk walk)
- OR
  - 20+ minutes/day x 3+ days per week for vigorous intensity PA
    - Vigorous intensity activities expend 6-15+ more energy than at rest, e.g. jogging & running

# Preventive PA Recommendations (Other than Aerobic)

- Strength:
  - Perform activities which maintain or increase muscular strength and endurance at least twice each week
- Balance:
  - Older people at increase risk for falls should do balance training
- Flexibility:
  - Activities that maintain or increase flexibility do not have known preventive health benefits, but are OK to do

# Comments on Aerobic Recommendation

- "Physical Activity" versus "Exercise"
- Accumulation (minimum bout=10 min)
- Dose-response (more is better)
- Minimum volume (= frequency x duration x intensity) = roughly 1000 extra Kcal/week
- Moderate-intensity generally more appropriate for older adults (e.g. less injury risk)

# Moderate-Intensity--Older Adults

- Moderate/vigorous PA is between 50-85% of aerobic capacity reserve;
  - Moderate intensity is roughly an effort of “5-6” on a ten point scale;  vigorous is “7-8”
- “Talk Test”
  - Light = talk and sing
  - Moderate = talk only
  - Vigorous = phrases interrupted by gasps
- “Sweat Test” IMHO is unreliable—affected by:
  - Temperature, clothing, hydration status, gender, genetics, and intensity

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# Common Questions

- Isn't vigorous PA much better?
  - Somewhat better after adjust for volume
- Does all walking count?
  - No. Pace matters. "Brisk" walk is mod.
- Is 3 days/week enough?
  - No, but 3 days is much better than 0.
- Should people with "X" illness do this?
  - Check with doctor. PA is effective Tx for many diseases. Need both prevention and Tx.

# Question:

- **What percent of Americans in 2000 reported a healthy lifestyle,** in that they
  - Did not smoke
  - Regular physical activity 30+ min 5+ days /wk
  - Ate 5 or more fruits and vegetables/day
  - Had a healthy body weight (BMI 18.5-25.0)

- **CHOICES:** 40% 20% 12% 7% 3%

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# Answer:

- **Only 3%** **of Americans in 2000 reported a healthy lifestyle,** in that they
  - Did not smoke
  - Regular physical activity 30+ min on 5+ days /wk
  - Ate 5 or more fruits and vegetables/day
  - Had a healthy body weight (BMI 18.5-25.0)

Reeves MJ. Arch Intern Med. 2005;165:854

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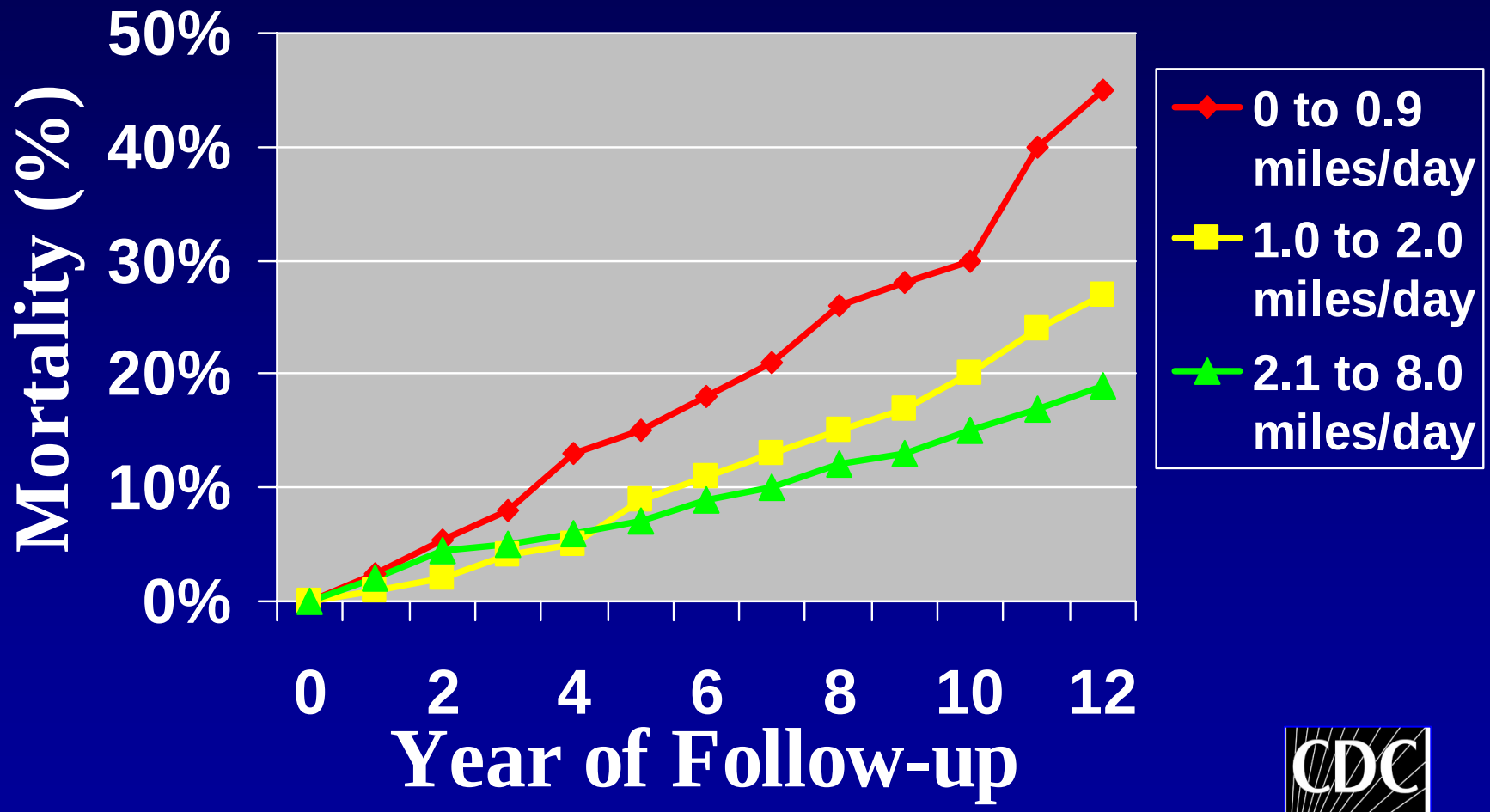
# “Surprises”

- Size of Cumulative Benefit

# Cumulative Mortality by Distance Walked per Day




Hakim NEJM 1998;338:94-9.

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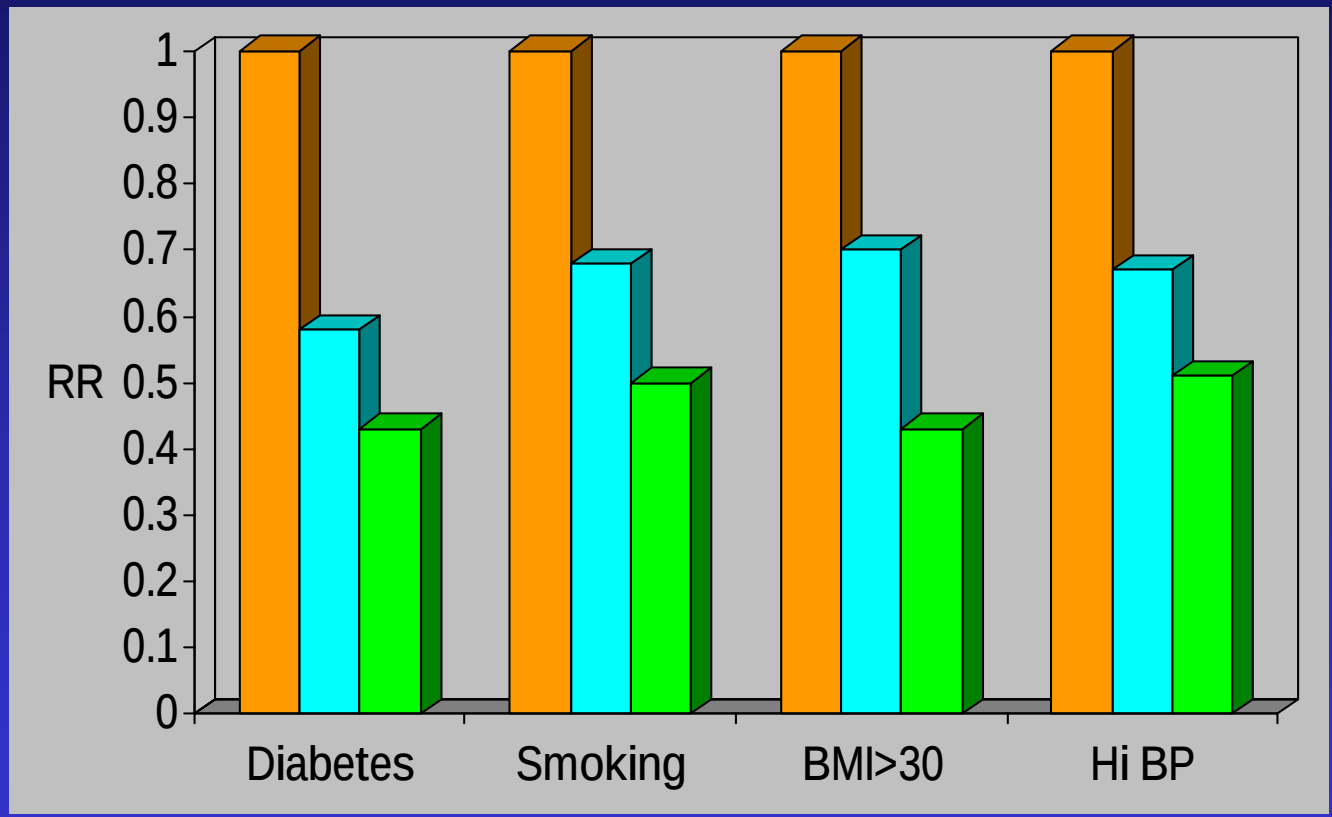
# “Surprises”

- Size of Cumulative Benefit
- Effects of PA independent of other risk factors

# Endurance Capacity (Fitness) and Mortality In Older Men




Myers. NEJM 2002;346;793-801.

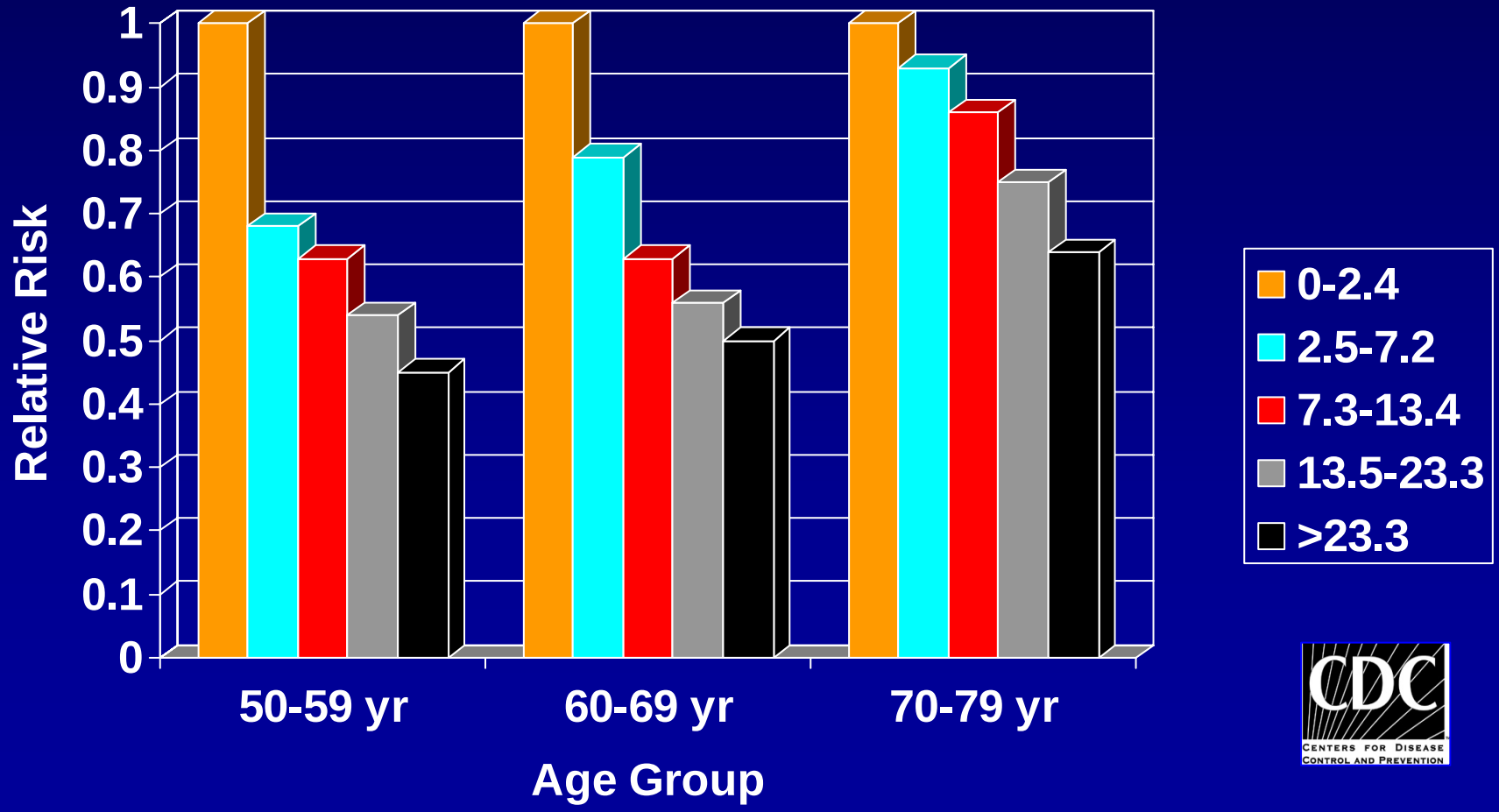
# “Surprises”

- Size of Cumulative Benefit
- Effects of PA independent of other risk factors
- Meaningful benefits from low amounts of PA

# Age-Adjusted Risk of CVD by Quintile of PA score (Met-hrs)

## Women's Health Initiative Observational Study

Manson NEJM 2002;347:716

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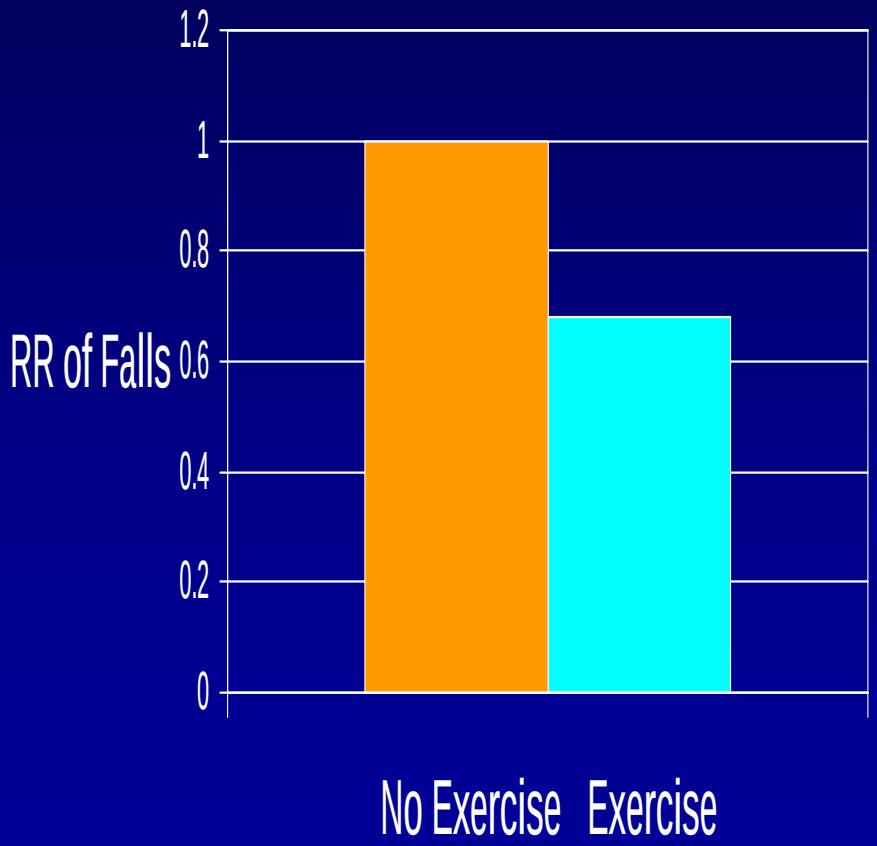
# Effect of Exercise Three Times/week on Fall Risk




- Intervention = individually tailored balance training, resistance training, and walking x 1 yr.

Dunedin Falls Study

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# “Surprises”

- Size of Cumulative Benefit
- Effects of PA independent of other risk factors
- Meaningful benefits from low amounts of PA
- Acute Effects of PA

# Acute Effect of Exercise on Resting Blood Pressure

- **Post-exercise reduction in blood pressure is an physiologic response to exercise, including moderate-intensity**
- **Post-exercise decreases in systolic BP of up to 18-20 mm Hg and diastolic BP of up to 7-9 mm Hg occur in people with hypertension, and last up to 16 hours**
- **Also acute reductions of triglycerides and acute increases in HDL-C.**

Thompson. MSSE 2001;33:S438

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# Physical Activity and Brain Health

# Scope of Lifestyle Research on Brain Health

- Intellectual engagement
- Social interaction
- Nutrition
- Physical Activity
- Other (e.g. smoking, alcohol)

# Questions

- What is the evidence that PA has beneficial effects on cognition?
- IF PA improves cognition, what types and amounts of PA are required to get the benefits?
- Is it ever too late for a sedentary person to get the benefits?

# Benefits of PA on Brain Health

| Benefit | Brain Health |
|---|---|
| Fitness | Cognition |
| Prevention | Alzheimer Disease<br>Mild Cognitive Impairment<br>Vascular Cognitive Impairment<br>Stroke |
| Treatment | Dementia |

# Overview of Cognition in Older Adults

- Many dimensions including:
  - Memory (e.g. semantic=facts; episodic=events)
  - Language (e.g. expression, naming)
  - Visual-spatial (e.g. ability to copy designs)
  - Executive (e.g. planning, multi-tasking)
- Small age effect on “crystallized” abilities= skills and knowledge gained through school and experience
- Larger age effect on “fluid” abilities=spatial ability, executive function, information processing

Lindeboom. Eur J Pharm 2004;490:83-86

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# Meta-analysis of Effect of Exercise on Cognition in Adults

**Colcombe. Psychol Science 2003;14:125**

- 18 exercise RCT's published 1966-2001
- Moderate effect of aerobic exercise on measures of cognition (ES=.48)
- Largest effect on executive control (e.g. planning, scheduling, working memory, multi-tasking)
- Larger effect in studies that added strength and flexibility training to aerobic training
- No two studies used the same cognitive tests

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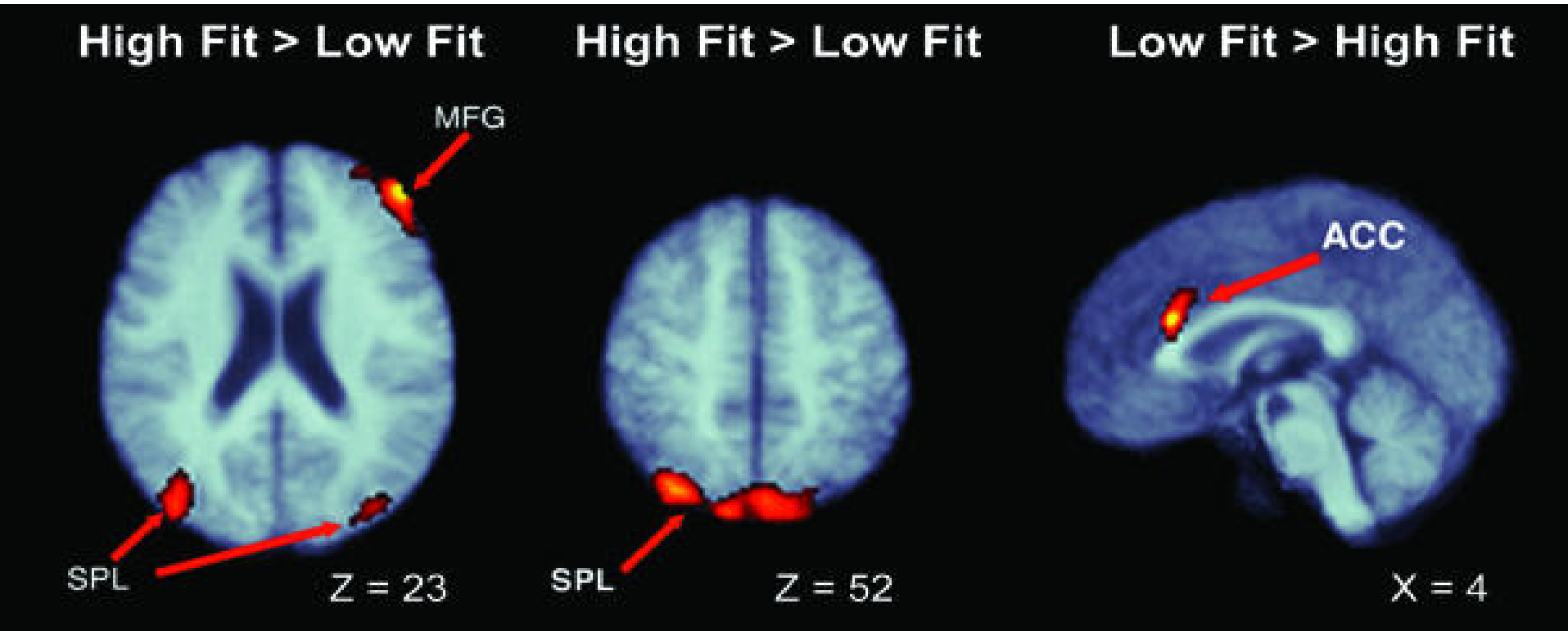
# Study: High fit or aerobically trained adults show greater task-related activity in brain regions involved in attention, and spatial functions.

- From functional MRI. Fitness assessed w 1 mile walk; MFG=middle frontal gyrus; SPL/IPL = superior & inferior parietal lobules; ACC = anterior cingulate cortex; Colcombe.; PNAS 2004;101:3317;

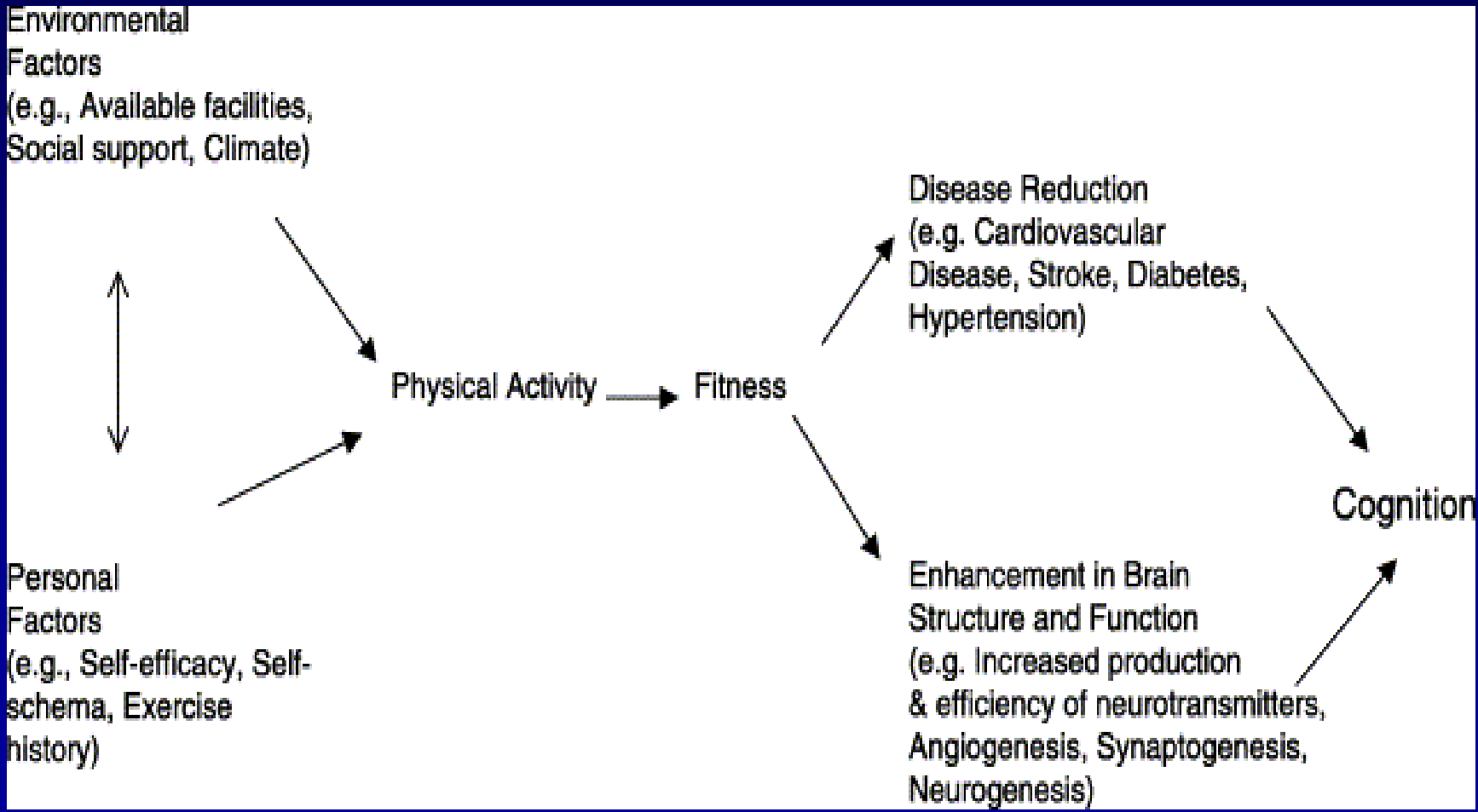


# Aerobically Trained Rats Learn Mazes 2-12 times faster

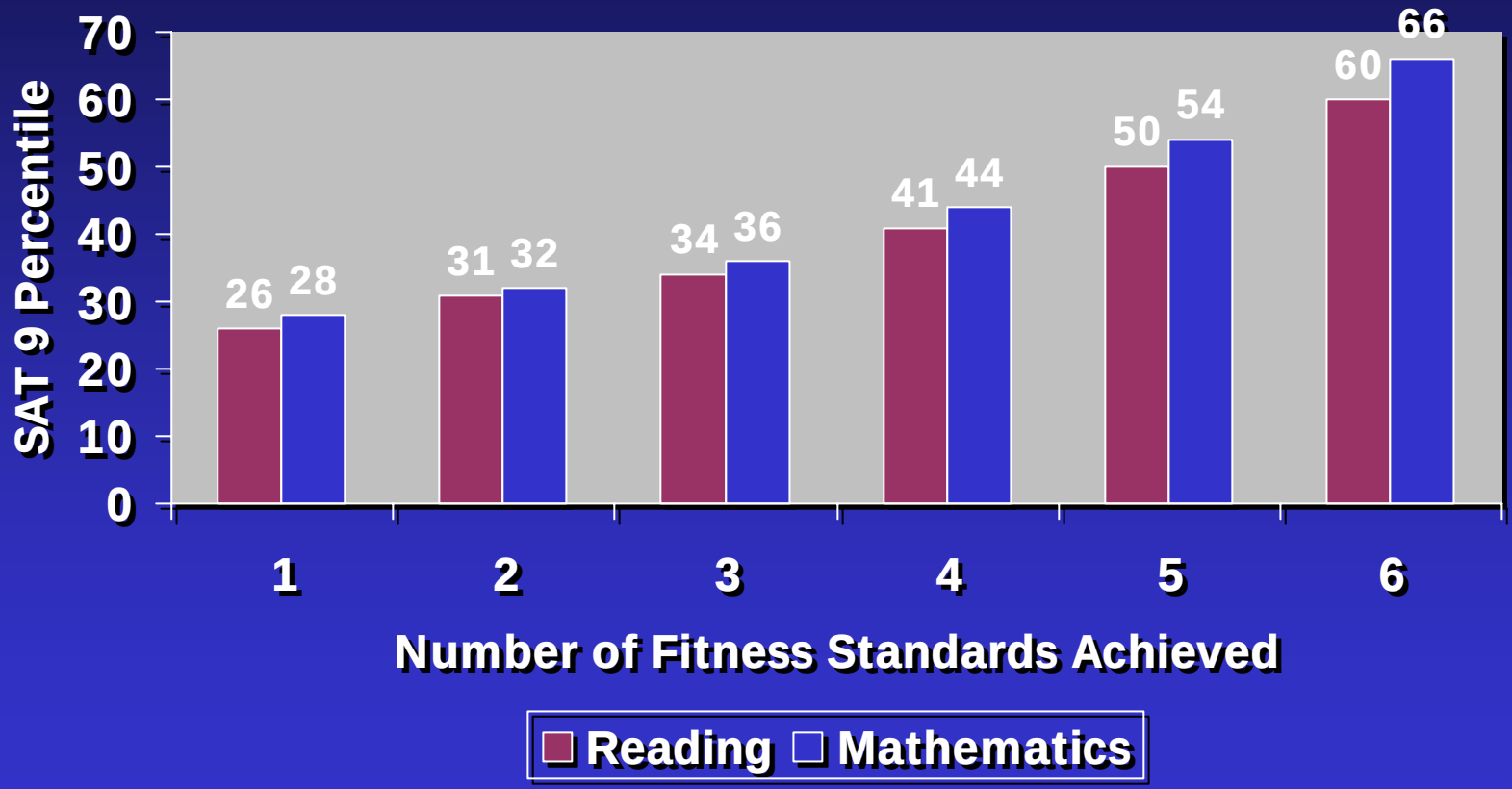
- Exercise-trained aged rats
  - Solve Morris water maze faster
  - New neurons in dentate gyrus of brain along with increases in BDNF (brain derived neurotrophic factor) which is involved in neurogensis (dentate gyrus is in hippocampus—a structure clearly affected by AD)
- In rats, exercise affects neurotransmitters involved in human diseases
  - Dopamine (Parkinsons Disease)
  - Serotonin (Depression)
  - Acetylcholine (Alzheimer Disease)

# Conceptual Model: Physical Activity and Cognition

McAuley. Brain, Behavior, Immunity 2004:18;214



# SAT 9 Score and Physical Fitness California Schools, 2001, Grade 7 (Cross-sectional)



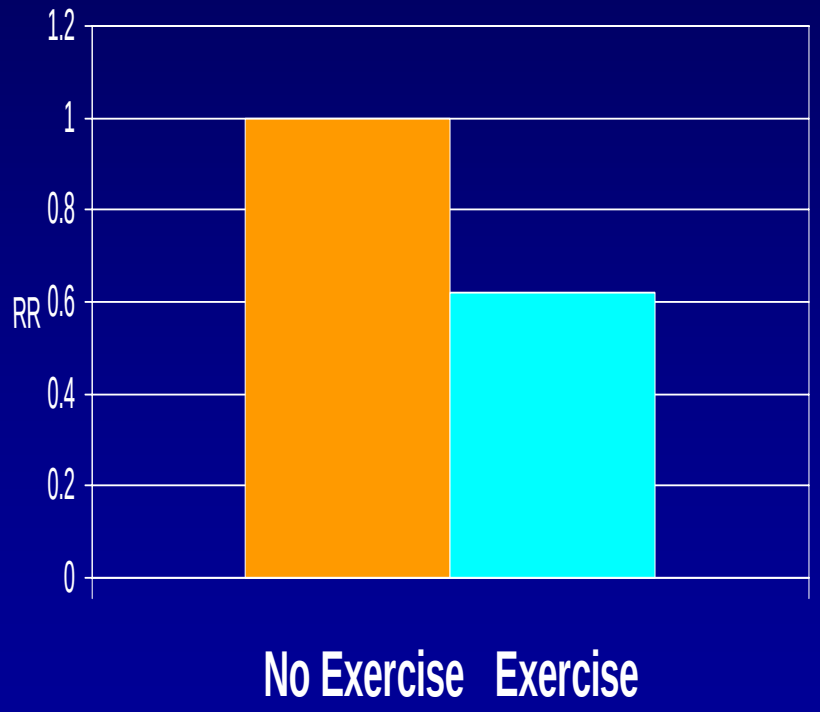

Study by California Dept of Health

# Prevention of Alzheimer Disease

- AD
  - 50-70% of all dementia
  - Early sign=impaired episodic memory; then other cognitive areas involved
  - Brain neurons damaged by deposition of abnormal protein esp amyloid-beta
  - Involves chronic inflammatory processes

# Effect of Regular Exercise Three Times/week on Alzheimer Disease Risk

**Larson Ann Intern Med 2006;144:73-81**




- Not influenced by ApoE gene
- More risk reduction in adults with slower gait speed / lower physical function

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# Mechanisms by which exercise could prevent Alzheimer Disease

- Active mice have decreased brain amyloid-B (Adlard, 2005;Lazarot, 2005)
- Exercise reduces inflammatory markers—could mitigate inflammatory components of AD (Barnes, 2007)
- PA effect on brain blood flow and brain cell volume (Colombe,2006)
- Effects of exercise on neuronal health and function in normal adults also prevent AD

# Summary of AD prevention studies

- Most longitudinal studies report regular PA reduces risk of cognitive decline and dementia by 30-50% (Barnes, 2007)
- A few studies specific to AD
- No randomized trials

# Vascular Dementia

- Subtle progressive worsening of memory and other cognitive function due to vascular disease causing reduced blood flow in the brain
- Different types e.g. multi-infarct dementia
- Distinct from stroke = sudden onset
- AD and VaD can co-occur

# Mild Cognitive Impairment

- Memory deficits with intact daily functioning
- Compensatory strategies (writing reminders) are sufficient
- Not well understood;  increases risk of AD; co-occurs with depression

# Prevention of VaD and MCI by Physical Activity

- Few studies specifically of PA and VaD and MCI.
- Modification of cardiovascular risk factors widely regarded as effective in preventing vascular disease (Haan, 2004)

# Common Symptoms of AD

- Loss of cognitive function
- Loss of physical function
- Behavioral disturbances (e.g. agitation, wandering)

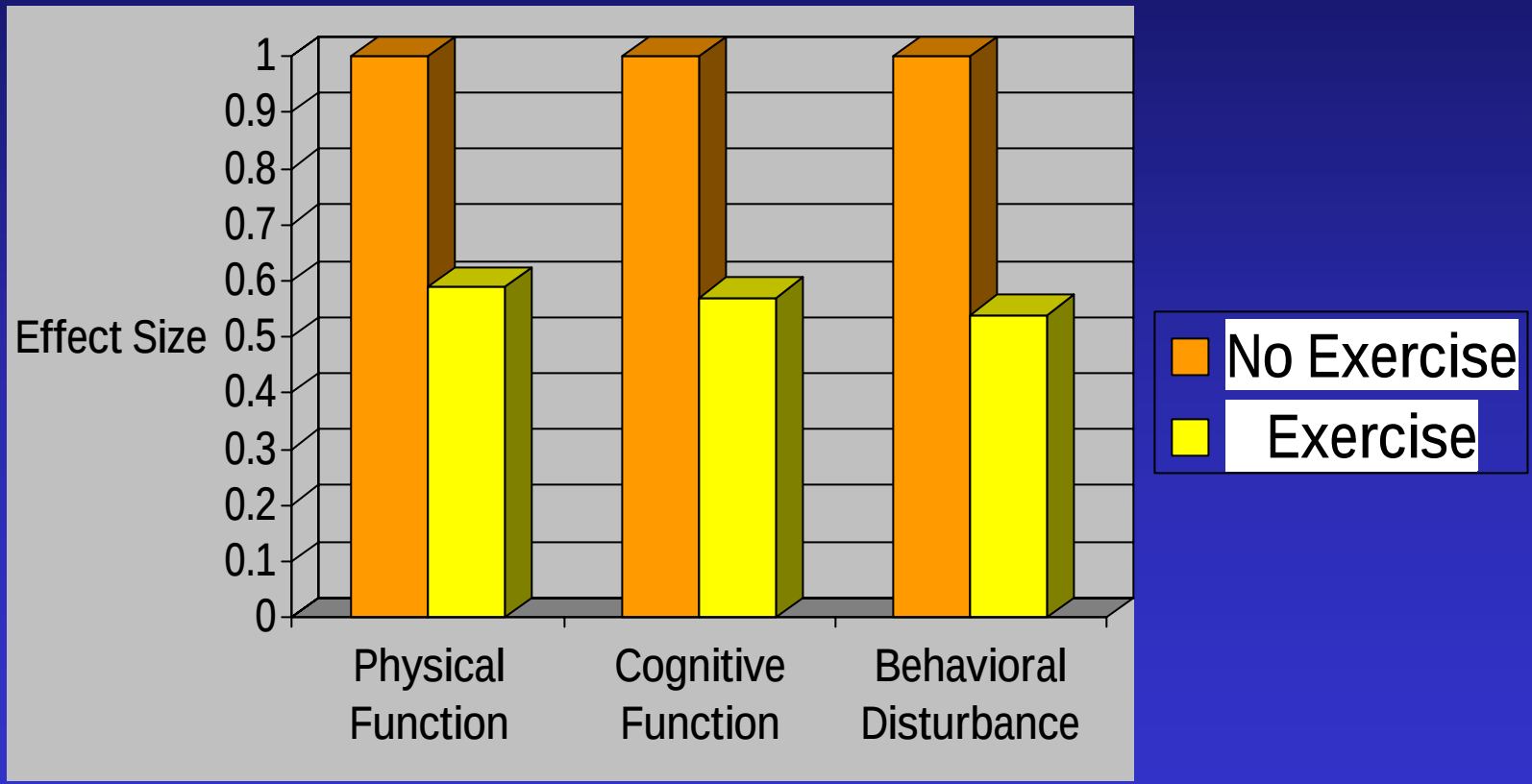
# Study: Effect of Exercise and Behavioral Management in AD

Teri. JAMA 2003;290;2015

- 153 community-living AD patients
- Exercise + education of caregivers on management had beneficial effects:
  - Physical function
  - Depression
  - Less often placed in institution due to behavior disturbance (trend)

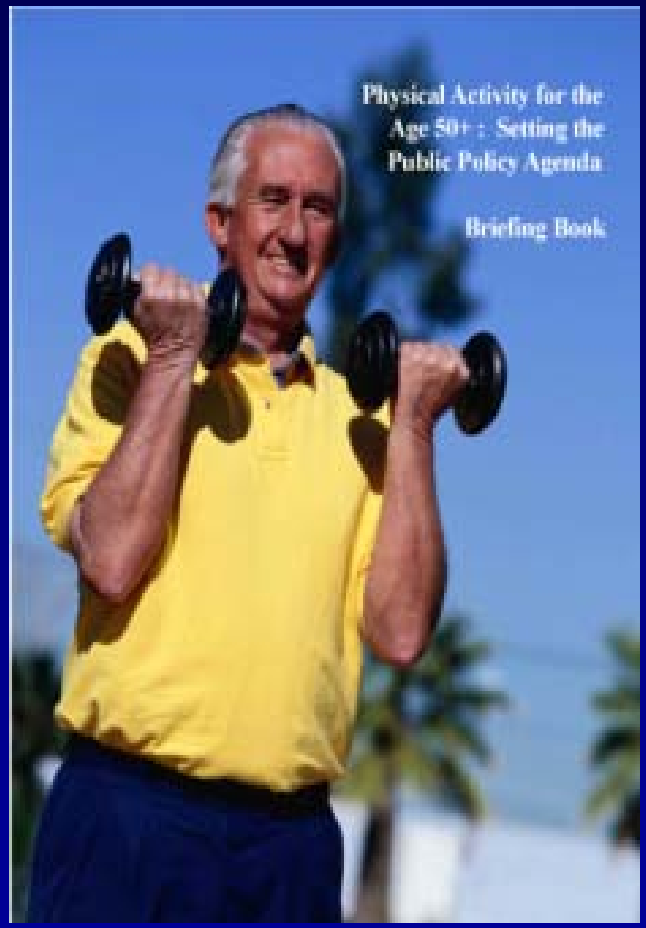
# Meta-analyses of RCTs of Effects of Exercise in Dementia

**Heyn. Arch Phys Med Rehabil 2004;85:1964**




**Also, exercise caused significant increases in aerobic fitness, strength and flexibility**

# To Obtain the (Probable) benefits of PA on cognition:




- Follow the preventive physical activity recommendations
- Aerobic training has the most evidence for benefit, but some evidence for benefits of strength training

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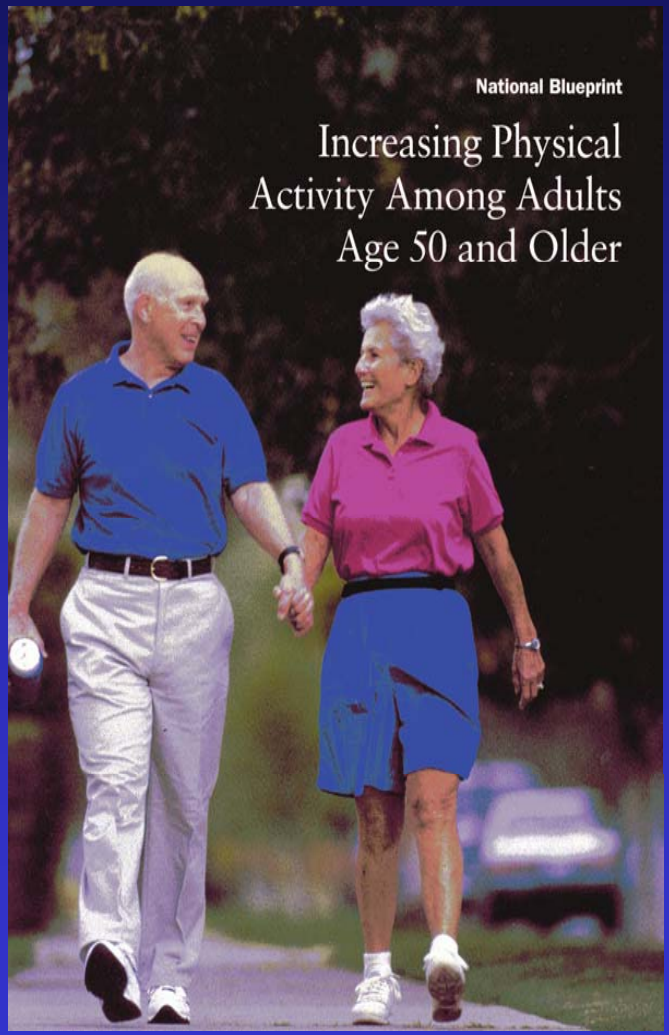
# Never too late to benefit?

- **Benefits of PA on cognition observed:**
  - In previously sedentary older adults
  - In adults doing less than recommended amounts of PA (e.g. 3 days/week)
  - In adults with reduced physical function
  - In adults with reduced cognitive function (e.g. diagnosed with AD)
  - In adults doing moderate-intensity PA

# Summary of PA and Cognition

- **IMHO, evidence is not conclusive, but probably PA, esp aerobic PA:**
  - **has a moderate effect on cognition in healthy and cognitively impaired adults**
  - **prevents or delays development of cognitive impairment, including impairment caused by AD**
- **Much remains to be learned e.g.:**
  - **What types of PA are optimal? What are the mechanisms? How much variation exists in effect of PA on cognition?**




- **We already have more than enough reasons to engage in regular physical activity**
- **It looks like we're going to have one more BIG reason**

*"The human body is the only machine that breaks down when it is not used"*

**Attributed to Thomas Cureton, Professor, UIUC ("Father of Physical Fitness")**

http://www.drnick.com/fitquips/archive/fq_bodymachine_cureton.htm

http://www.ahs.uiuc.edu/alumni/newsletter/cureton.htm