Advancing Cognitive Training for Older Adults:

Long-Term Results from the ACTIVE Trial and Beyond

ACTIVE

The design of the ACTIVE trial was largely pre-specified by the National Institute on Aging and the National Institute of Nursing Research in RFA-AG-96-001.

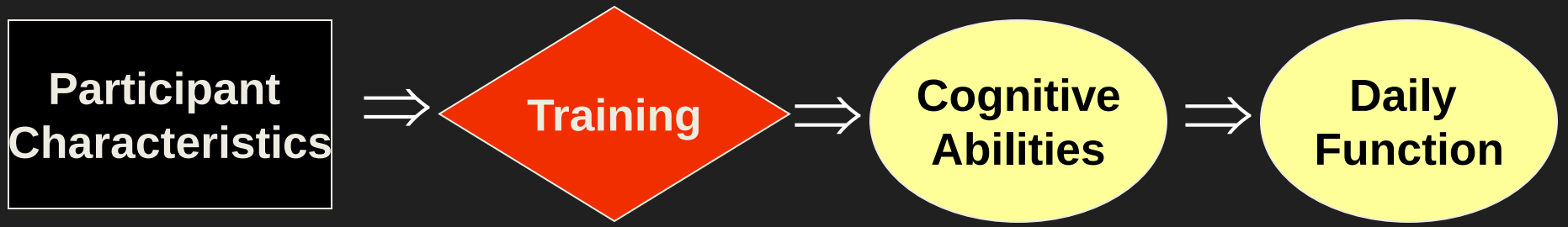
Three major emphases of the request for applications were:

1. Common intervention protocols at multiple sites
2. Primary outcomes: ***functional competence***, focus on everyday independence
3. Focus of interventions: ***basic cognitive abilitie***s.

ACTIVE: Primary Aim

To test the efficacy of three cognitive interventions to improve or maintain the cognitively demanding activities of daily living.

Simplified Conceptual Model



Interventions

Three cognitive training interventions:

- Memory
- Reasoning
- Speed of Processing

Intervention Protocol

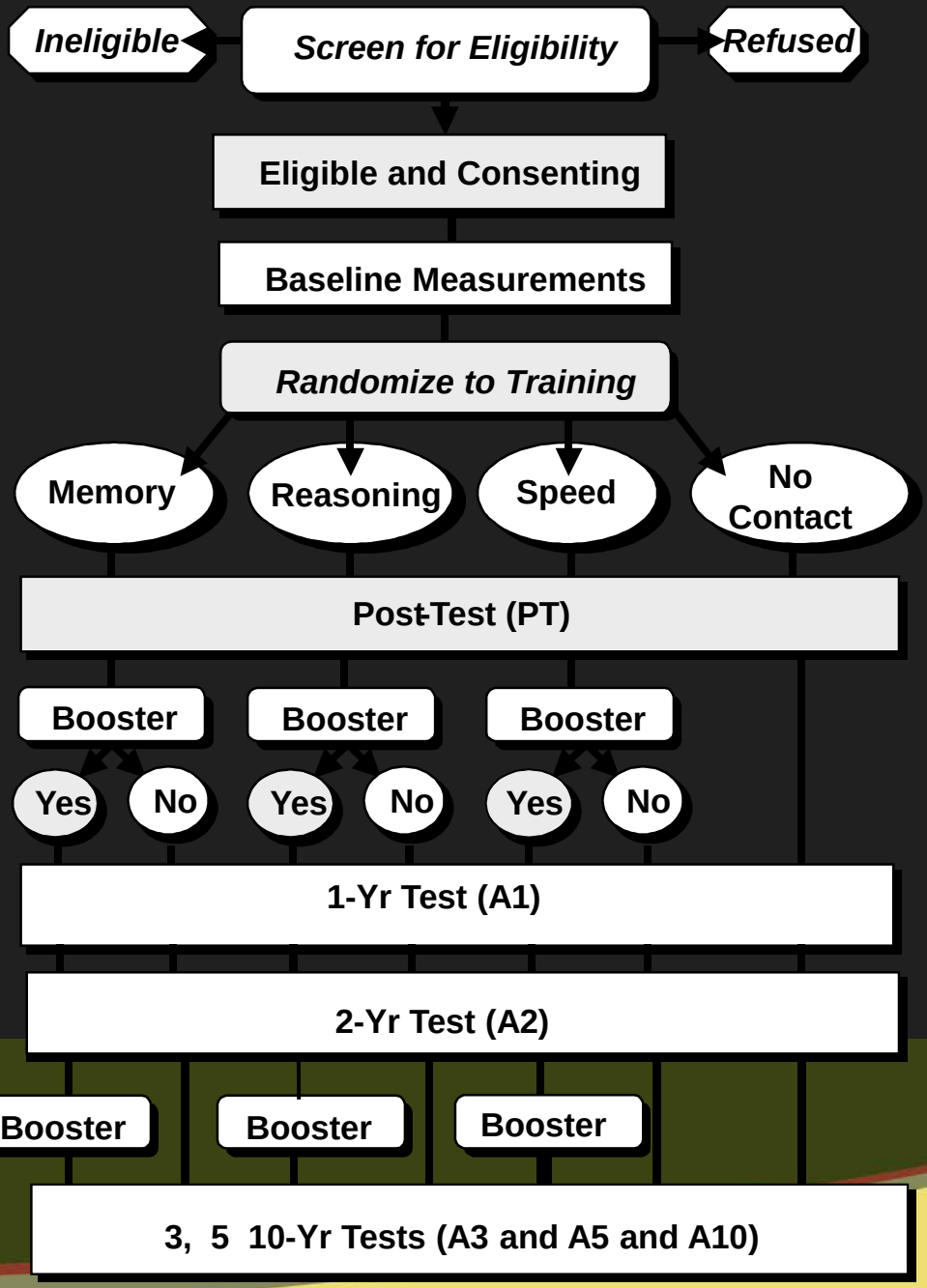
- Initial Training: 10 90-min sessions
- Booster: 4 90-min sessions
  - 1 yr after training
  - 3 yr after training
- Trained in small groups at local facility
- Memory & Reason –
    - strategy-based training

ACTIVE

The ACTIVE study differed from prior cognitive training research in several ways:

1. multi-site, randomized controlled, single-blind trial,
2. intent-to-treat analytical approach that included all randomized participants rather than only those compliant with the intervention,
3. primary outcome measures of everyday functioning, and
4. a more socioeconomically and racially diverse study sample.

Study Design



ACTIVE

ACTIVE Steering Committee

- University of Alabama- Birmingham
  Karlene Ball, Ph.D.
- Hebrew Senior Life, Boston
  John Morris, Ph.D.
- Indiana University
  Fredrick Unverzagt, Ph.D.
- Johns Hopkins University
  George Rebok, Ph.D.
- Pennsylvania State University
  Sherry Willis, Ph.D.
- University of Florida / Wayne State University
  Michael Marsiske, Ph.D.
- New England Research Institutes, Coordinating Center
  Sharon Tennstedt, Ph.D.
- National Institute on Aging
  Jeffrey Elias, Ph.D.
- National Institute of Nursing Research
  Kathy Mann-Koepke, Ph.D.

ACTIVE

Targeted Population

- Diverse sample age ≥ 65 years
- Heterogeneous sample
  - Urban and Rural
  - Oversample African American
  - Age 65 – 94
  - Wide SES range
- Cognitive normal
- Living independently
- At risk of loss of independence

ACTIVE

Baseline Characteristics (n=2,802)

- Mean Age: years 73.6 (5.9) Range 65-94
- Gender: Female 75.9%
- Race: African American 26.0% (over sampled)
- Education: H.S. diploma 88.6%
- Marital Status: Married 35.9%
- Cognitive Status: MMSE score 27.3 (2.0)

ACTIVE

Training Effects on Cognitive Abilities

- Immediate effect

Reliable individual effect: Memory 26%, Reason 74%,Speed 87%

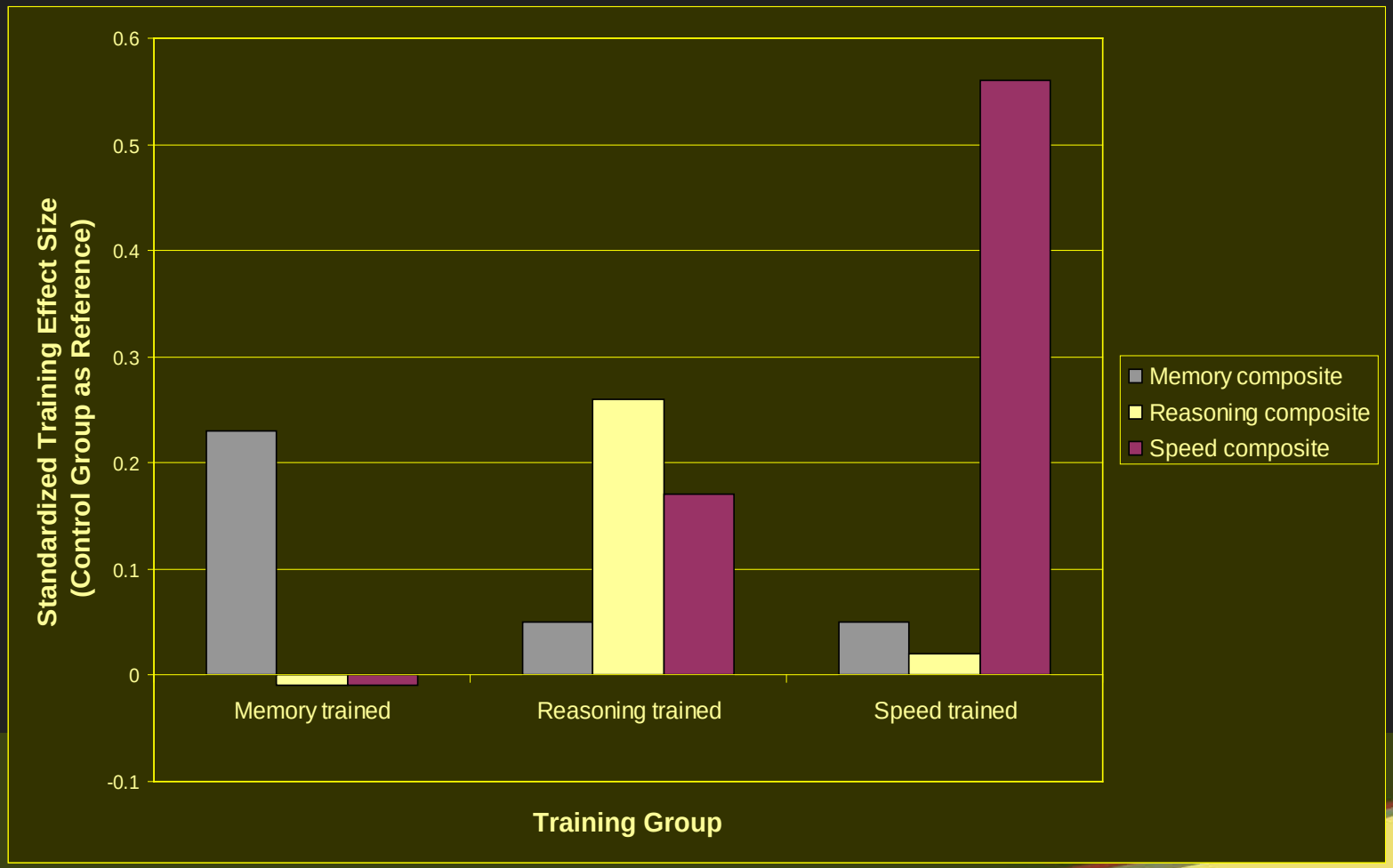
- Durability of Effects

Memory : 5 years

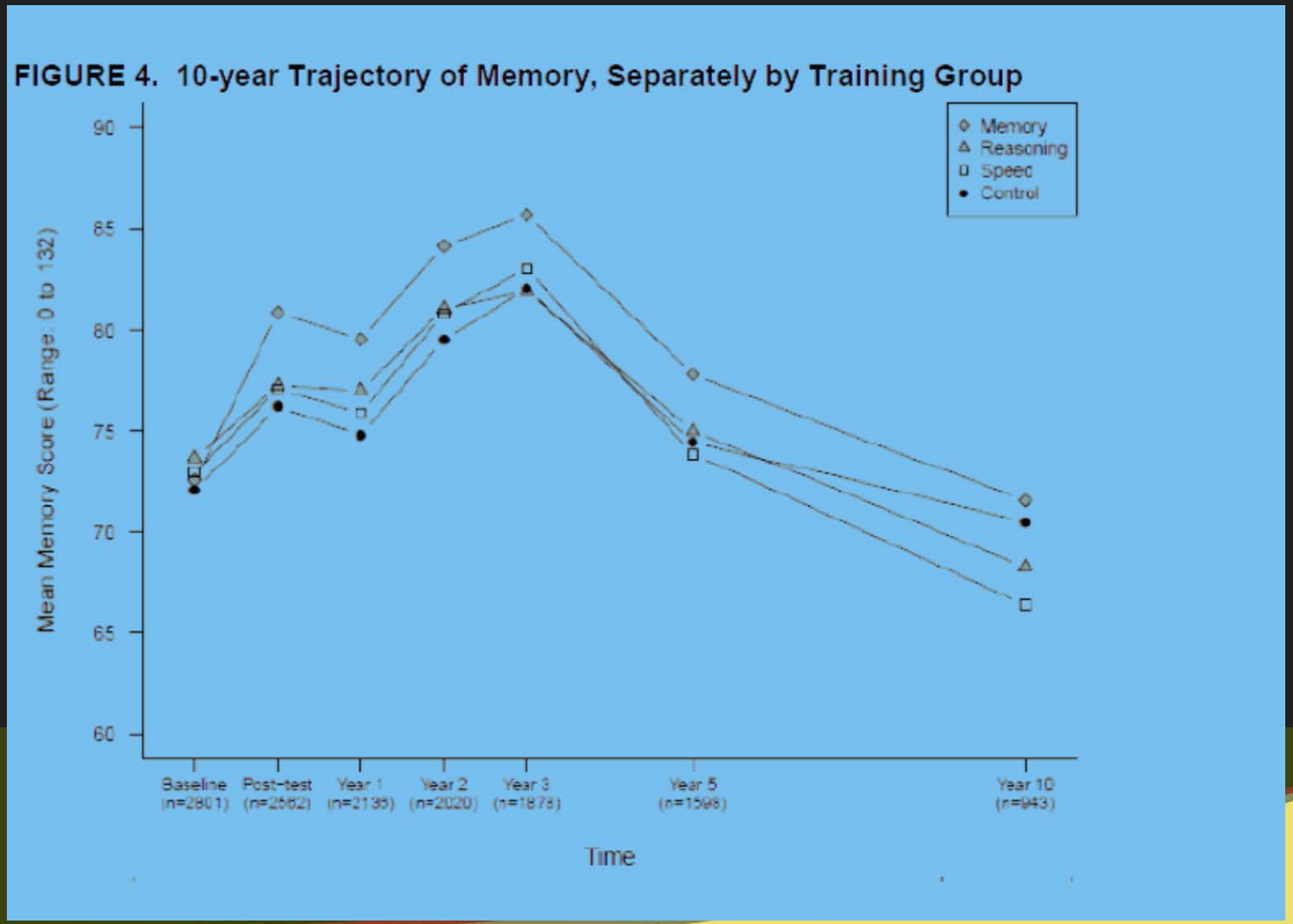
Reason & Speed: 10 years

- Training Specific to Ability Trained

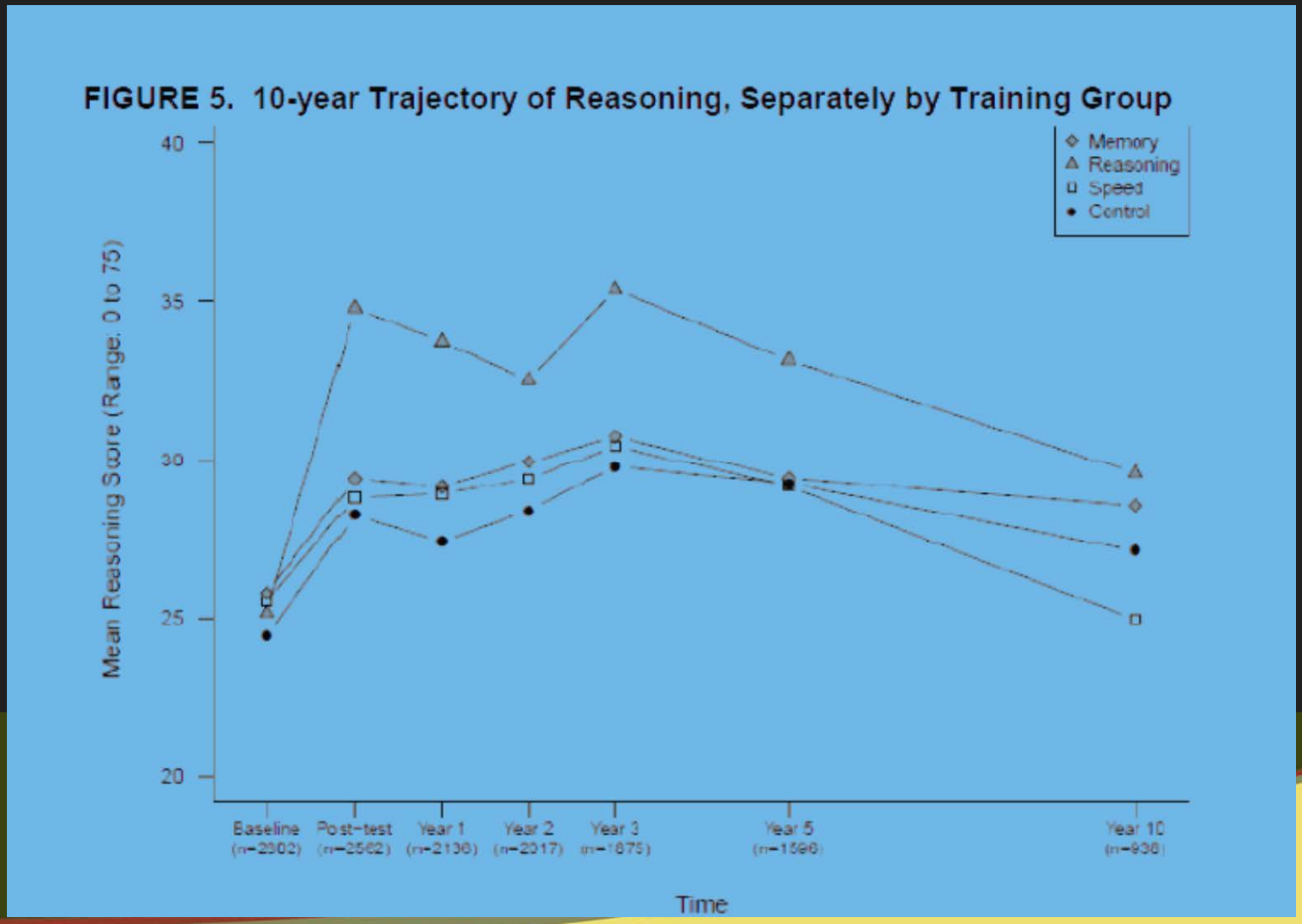
Effect of Training on Cognitive Abilities



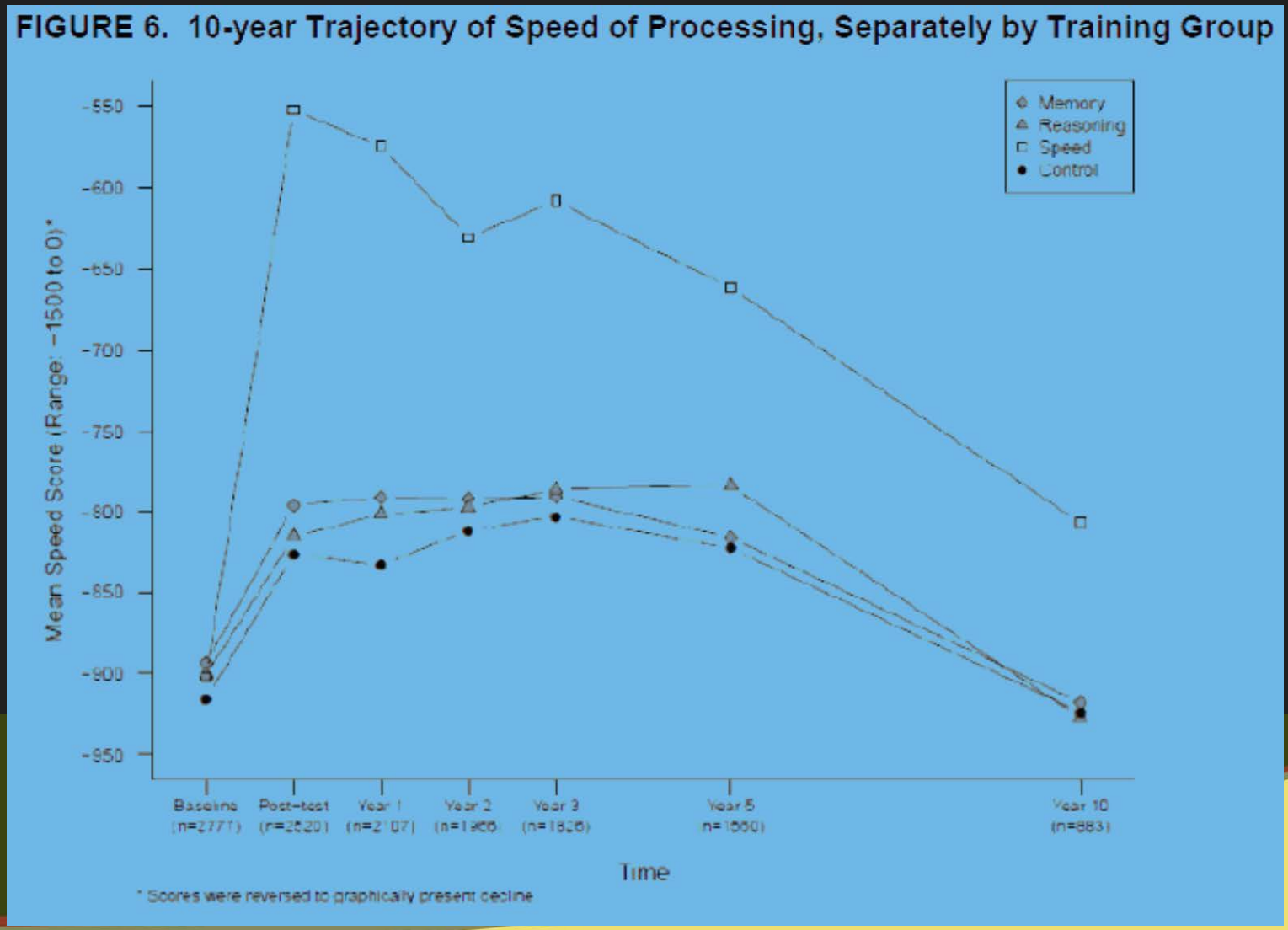
Memory: 10 Yr Trajectory



Reason: 10 Yr Trajectory



Speed: 10 Yr Trajectory



Normal Memory vs Memory Impaired: Impact on Training on Memory, Reasoning, Speed

Normal

Interven	Time	Memory	Reasoning	Speed
Memory	PT	.300***	-.009	-0.050
	A1	.254***	.033	-0.061
	A2	.214***	.052	-0.057
Reason	PT	.001	.477***	0.025
	A1	.013	.416***	-0.026
	A2	-.003	.262***	-0.021
Speed	PT	.004	-.017	-1.488***
	A1	.004	.009	-1.238***
	A2	-.024	-.013	-0.886***

Memory Impaired

Inteven	Time	Memory	Reasoning	Speed
Memory	PT	-.012	-.117	0.105
	A1	-.175	-.163	0.107
	A2	-.100	-.015	0.400*
Reason	PT	-.048	.573***	-0.277
	A1	-.230	.208	-0.155
	A2	-.331	.276*	-0.434*
Speed	PT	-.108	-.111	-1.420***
	A1	-.163	-.097	-1.100***
	A2	-.298	.079	-0.755***

Effects of Booster Training

- Significant Booster Effect:

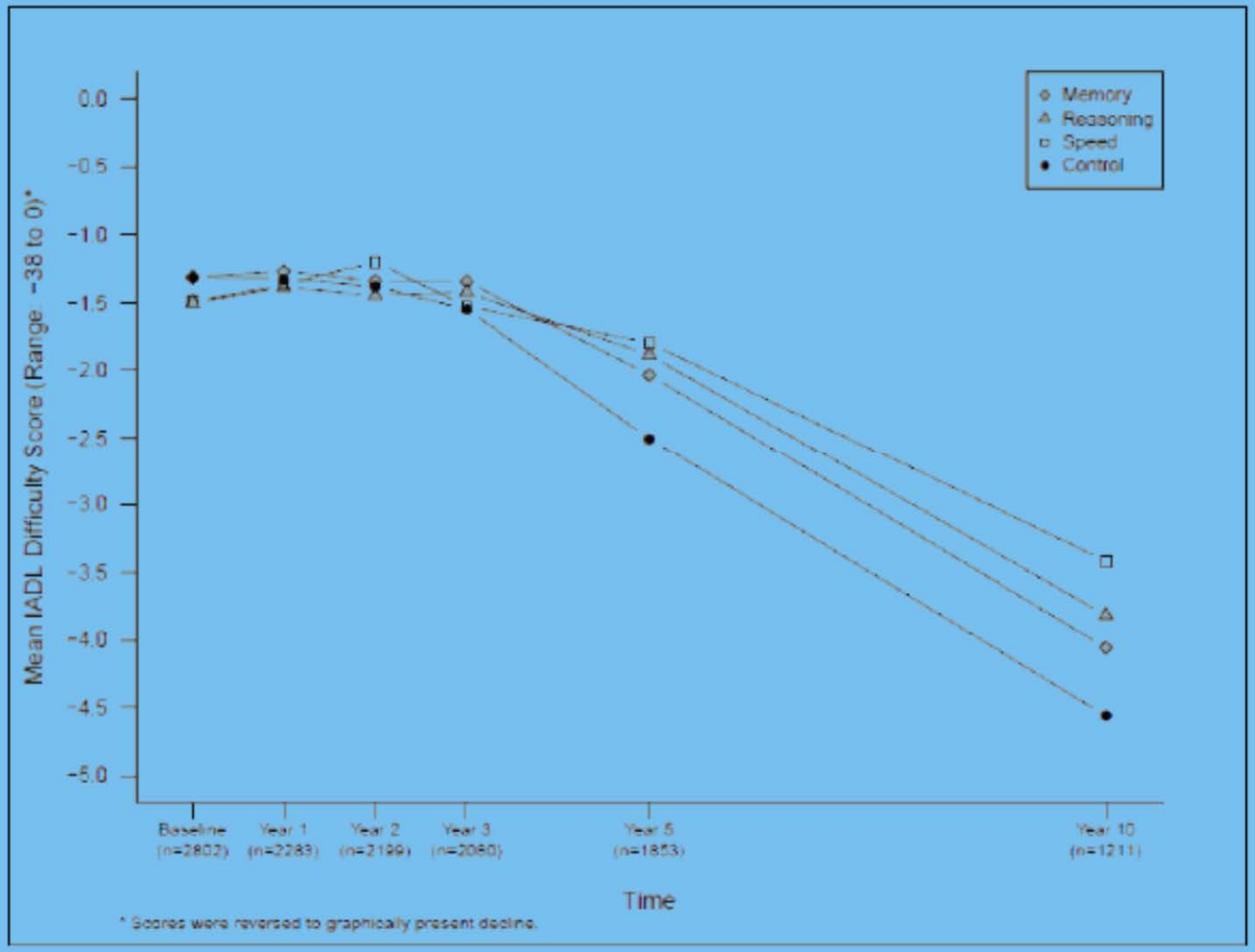
- Speed: Booster Effect through 5 yr follow-up
- Reason & Speed: Booster trhough10 yr follow-up

Training Effects on Daily Function

- Self Reported IADL Difficulty:
- 5 yr Follow –up: Reason report significant less difficulty
- 10 yr Follow-up – All training groups report significant less difficulty

- Training had no effect on performance-based measures of function. However, booster speed training improved performance in Everyday Speed.
- .

FIGURE 7. 10-year trajectory of Self-rated IADL Trajectory, Separately by Training Group

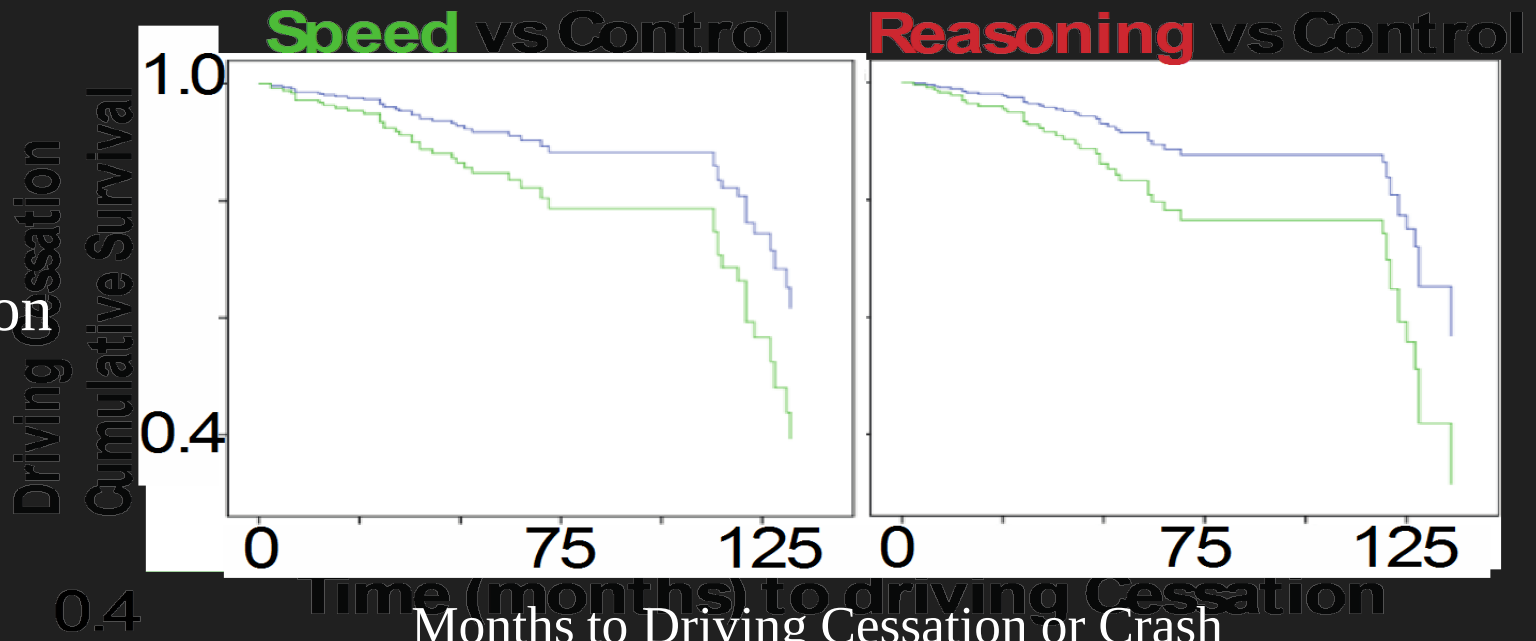


Speed & Reason Effects: Reduced Crashes & Less Driving Cessation

Drive Cessation

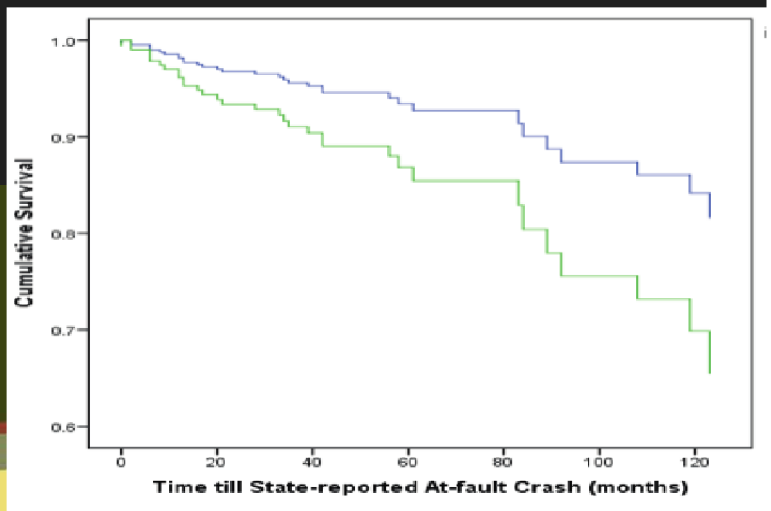
Speed vs Control

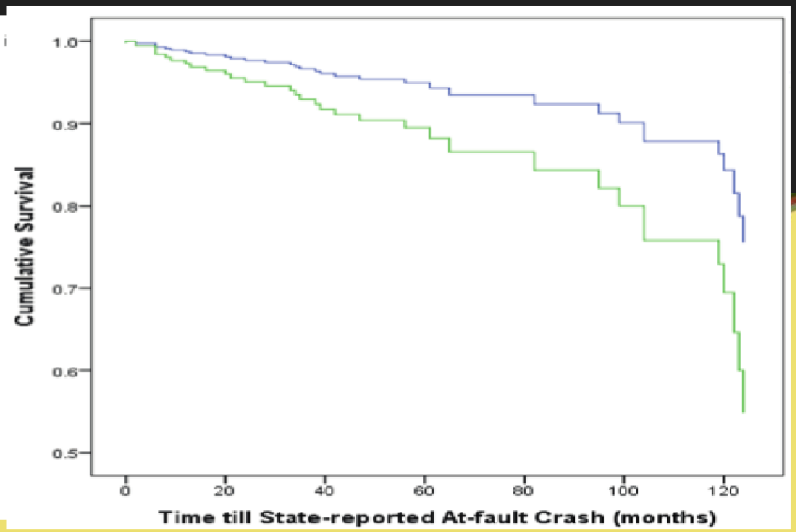
Reason vs control



Crash

Months to Driving Cessation or Crash





Selectivity of Attrition at 5 Years

- Retained 67% (n = 1,877) of initial sample
- Attrition higher if male, older, lower MMSE, lower Reasoning and Memory Scores, less education, and more health problems at baseline
- No differences across treatment groups

Thank you

Goals of Presentation

- To review the 5-year results of the ACTIVE trial and their implications
- To summarize major themes from ACTIVE publications
- To discuss next steps for ACTIVE
- To identify challenges and suggest approaches for future training studies

Excluded

- Age < 65 years
- Substantial cognitive decline
  - ✓ MMSE < 23
  - ✓ self-reported Alzheimer's disease
- Substantial functional decline
  - ✓ Assistance with dressing, personal hygiene, bathing
  - ✓ Specified predisposing medical conditions (e.g., CVA)
- Severe sensory losses
- Communicative difficulties
- Similar cognitive training
- Unlikely availability
- Non-English speaking

ACTIVE

Five-Year Results from the ACTIVE Trial

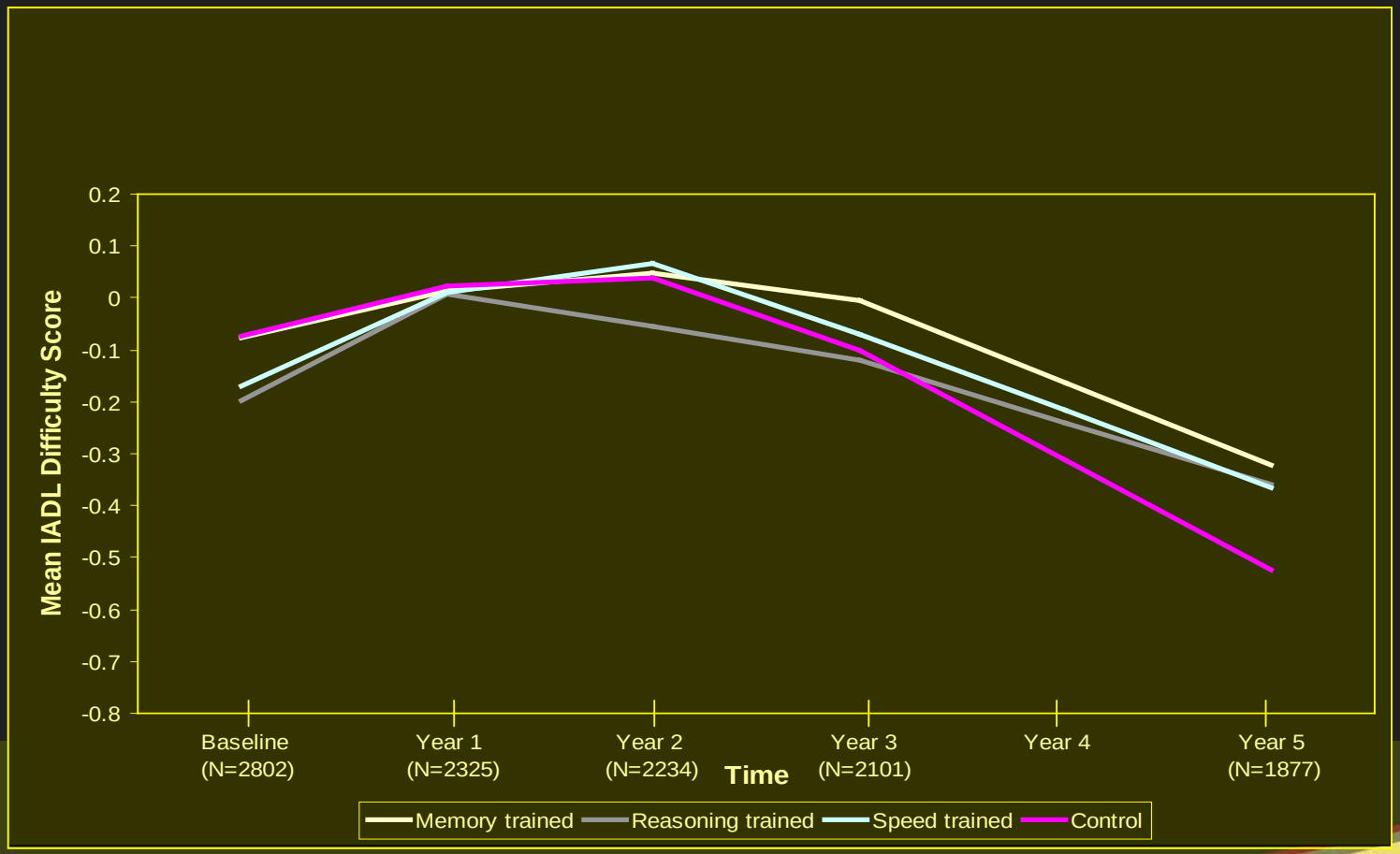
- Published in lead article in *JAMA*, December 20, 2006
- *JAMA's* most read/most e-mailed article
- Extensive media coverage – *NPR, New York Times, Washington Post*
- *The Washington Post's* most viewed and most e-mailed story

Sample: Unique Characteristics

Unusually heterogeneous sample for cognitive aging

- Minority elders (WSU, IU, JHU)
- Low income elders (PSU)
- Very old adults (HRCA)

Effect of Training on Function: Self-Reported IADLs



ACTIVE

Cognitive Abilities

Reasoning

- Word Series
- Letter Series
- Letter Sets

Memory

- Auditory Verbal Learning Test
- Hopkins Verbal Learning Test
- Rivermead Paragraph Recall

Visual Processing Speed

- Useful Field of View

Daily Function

Everyday Problem Solving

- Observed Tasks of Daily Living
- Everyday Problems Test

ADL / IADL Functioning

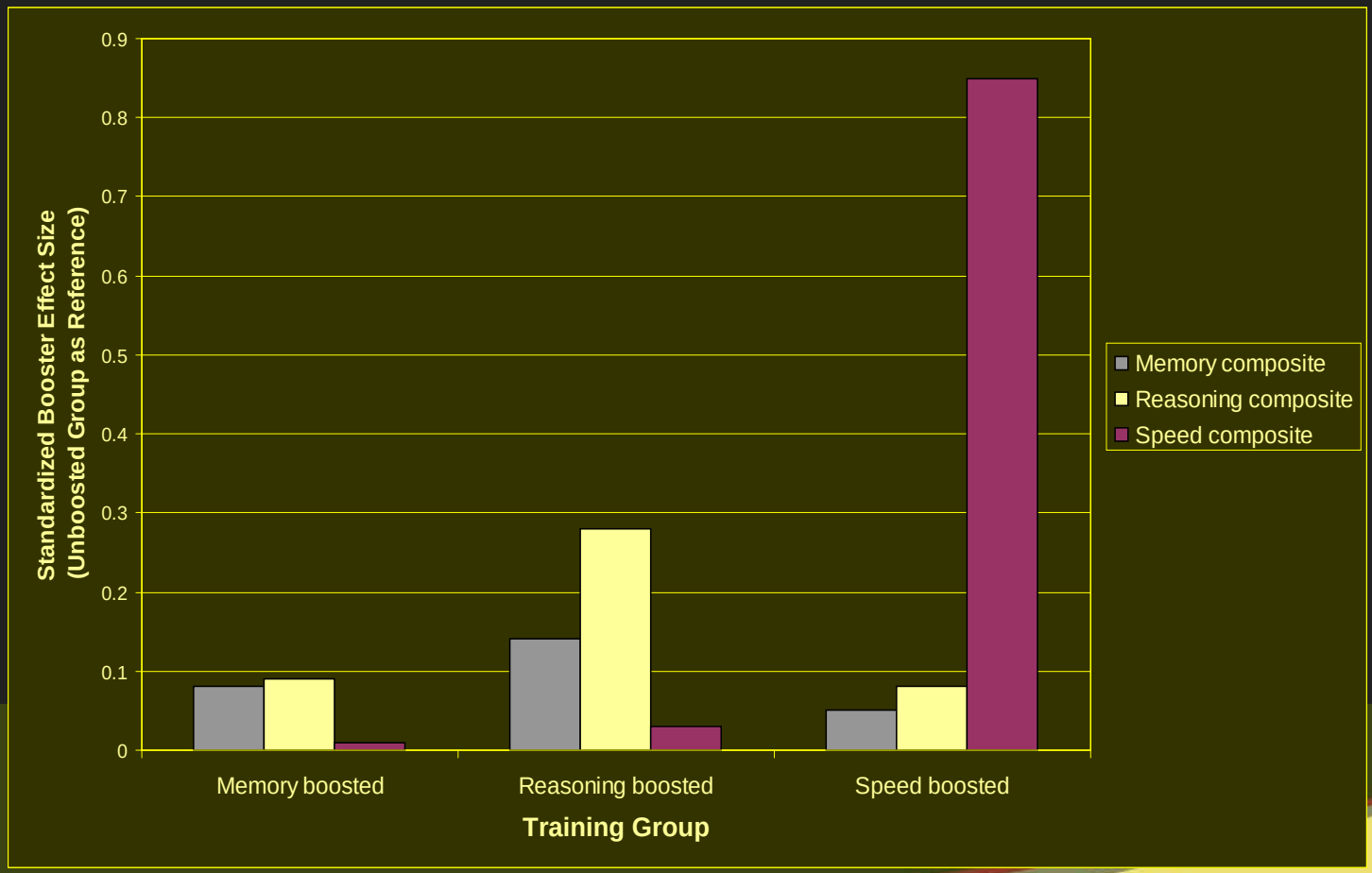
- Perceived IADL Performance
- Perceived IADL Capacity
- Perceived ADL Performance

Everyday Speed

- Complex Reaction Time
- Timed IADL Test

ACTIVE

Effects of Booster Training



ACTIVE

Major Areas of ACTIVE Publications (published, in press, submitted)

1. Short-term and long-term evaluations of training effects and real-world transfer / Effects of training on quality of life
   - Ball et al., *JAMA*, 2002
   - Wolinsky et al., *J of Gerontol: Psych Sci*, 2006
   - Wolinsky et al., *J or Gerontol: Med Sci*, 2006
2. Predictors of training responsiveness / Individual differences in training response / Applications of new methods for the study of longitudinal change (growth models, mixed effects longitudinal models)
   - Jones et al., *Exp Aging Research*, 2005
   - Unverzagt et al., submitted
3. Cognitive status and its association with training outcomes and functional changes
   - Crowe et al., *International J of Geriatric Psychiatry*, in press
   - Cook et al., submitted
4. Race/ethnicity effects on test performance, test bias and cognitive change
   - Aiken Morgan et al., *Exp Aging Research*, in press
   - Aiken et al., submitted

ACTIVE

Major Areas of ACTIVE Publications (published, in press, submitted) – cont.

5. Physical factors / morbidity as predictors of cognitive function and change
   - Kuo et al., *J of Am Geriatr Soc*, 2005
   - Kuo et al., *J of Am Geriatr Soc*, 2006
6. Measurement studies (functional status, self-reported medications)
   - Owsley et al., *Gerontology*, 2002
   - Caskie et al., *Gerontologist*, 2004
   - Diehl et al., *J of Applied Gerontology*, in press
   - Edwards et al., *Arch of Clin Neuro*, 2006
7. Mental health and well-being
   - Gallo et al., *Aging and Mental Health*, 2003
   - Yen et al., submitted

New Challenges for Advancing Cognitive Training

- Are there new ways to train people so that results generalize to multiple areas of daily function?
- What should be the accepted transfer target(s)?
- What is the expected time course?
- What is the best way to extend cognitive training to the cognitively impaired?
- Can we match interventions to individual risk profiles?

ACTIVE

Next Steps for ACTIVE

- Proposed follow-up at 10 years to assess:
  - Protective effects on cognitive abilities, daily function, quality of life, driving safety, and health service use
  - Individual difference factors that moderate response to intervention, including low cognitive function, engagement, and APOE genotype
  - No additional intervention (booster training)

Next-Step Training Approaches

- Multi-faceted interventions that combine skill-based training and other behavioral and non- behavioral intervention techniques
- Hybrid approaches that target cognitive and functional abilities
- High-intensity, high-exposure interventions
  - activity-based (e.g. Baltimore Experience Corps)
  - life-style management
  - web-based, computerized
  - in-home, self-administered

ACTIVE

Primary Analysis: Mixed Effects Model

- Dependent Variables: cognitive abilities and daily function
- Independent Variables: basic design features
  - ✓ treatment group
  - ✓ booster training
  - ✓ field site
  - ✓ replicate within site
  - ✓ time x training (net effect of trial)
  - ✓ time x booster (non-specific effects of additional social contact in booster)
  - ✓ time x training x booster (training-specific effects of booster)

ACTIVE

Effect of Training on Cognitive Abilities

Abilities	Memory	Reasoning	Speed	Control
Memory				
Mean change BL to 5 years	-1.0	-4.8	-5.3	-4.0
Effect size (99% CI)	0.23 (0.11, 0.31)	0.05 (-0.07, 0.17)	0.05 (-0.17, 0.17)	
Reasoning Change				
Mean change BL to 5 years	4.3	8.1	4.2	5.2
Effect size (99% CI)	-0.01 (-0.01, 0.08)	0.26 (0.17, 0.35)	0.02 (-0.06, 0.11)	
Speed				
Mean change BL to 5 years	-19.1	119.6	241.8	-96.1
Effect size (99% CI)	-0.01 (-0.15, 0.13)	0.15 (0.01, 0.29)	0.76 (0.62, 0.90)	

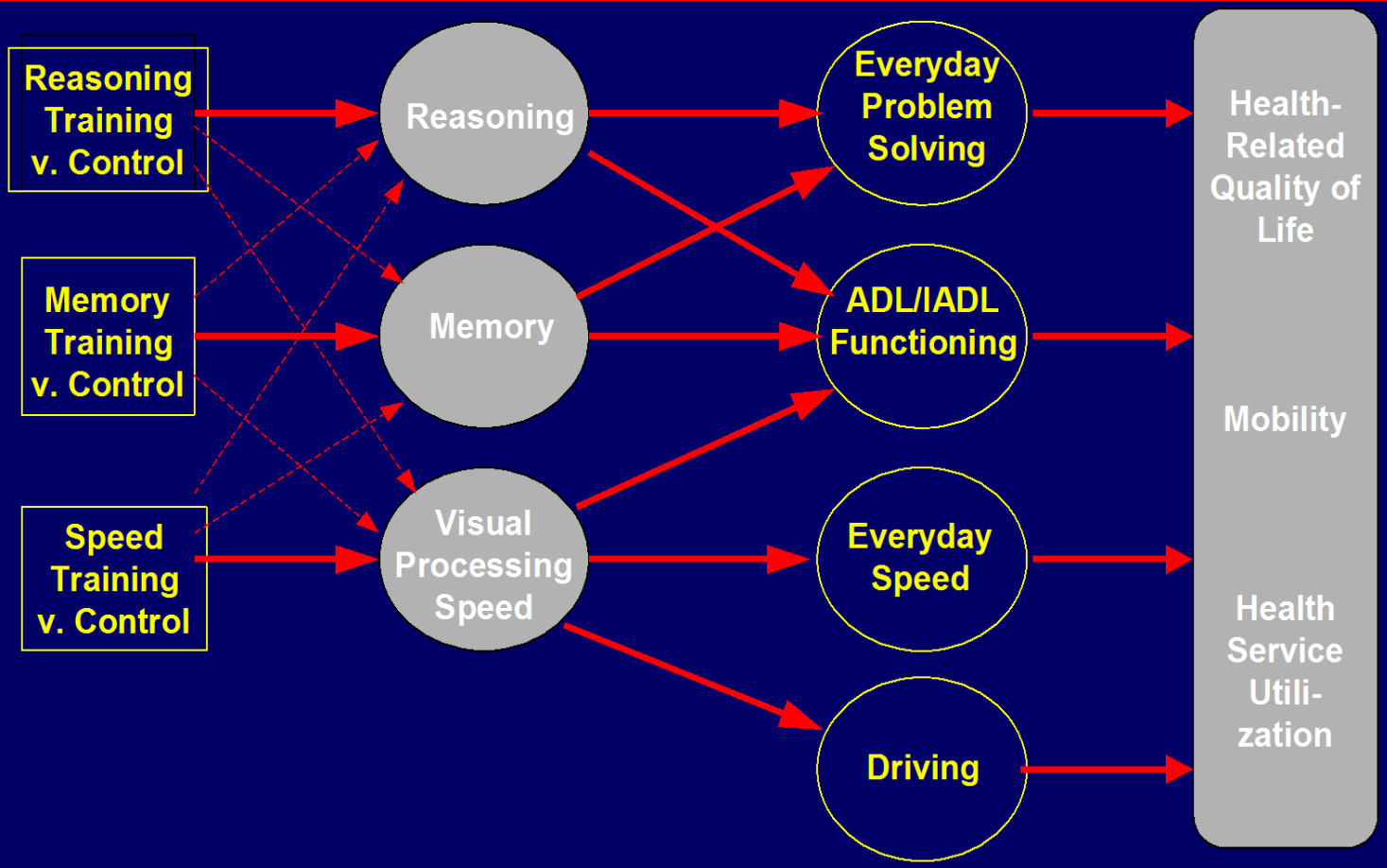
ACTIVE

Effect of Training on Function

Function	Memory	Reasoning	Speed	Control
IADL Difficulty				
Mean change BL to 5 years	-0.7	-0.4	-0.3	-1.2
Effect size (99% CI)	0.20 (-0.06, 0.46)	0.29 (0.03, 0.55)	0.26 (-0.002, 0.51)	
Everyday Problem Solving				
Mean change BL to 5 years	1.5	1.8	1.5	2.4
Effect size (99% CI)	0.15 (-0.28, 0.02)	-0.08 (-0.21, 0.05)	-0.05 (-0.18, 0.07)	
Everyday Speed				
Mean change BL to 5 years	0.1	0.3	0.2	0.1
Effect size (99% CI)	0.04 (-0.09, 0.17)	0.09 (-0.04, 0.22)	0.08 (-0.05, 0.21)	

ACTIVE

Hypothesized Model of Effects



ACTIVE

A Taxonomy of Behavioral and Non-Behavioral Intervention Strategies (adapted from Baltes)

Goal	Level	Target	Type	Mode	Setting
Enrich Prevent Remediate Compensate	Individual Small group (e.g., n =3-5) Large group (e.g., n > 5) Neighborhood Community	Cognitive ability (e.g., memory, attention, executive function) Cognitive complaints Efficacy beliefs Functional skills	Cognitive training-practice Cognitive rehabilitation Pharmaco-therapy Life-style modification (e.g., exercise, health habits, diet, stress reduction) Cognitive engagement Biomedical	Single component Multiple component (e.g., cognitive training + pharmaco-therapy; Cognitive training + exercise therapy)	Laboratory Clinic Hospital Home School Workplace Community center Internet Multiple settings (e.g., Clinic + Internet; clinic + home)

Technology-Based: In-Home Video Training Study

- Developed and evaluated a modification of the standardized Speed of Processing training protocol for home use.

- Emphasis on accessibility and affordability.

Standard versus Home-based Training

- **STANDARD**
  - Lab-based
  - Trainer-facilitated
  - Computer-based
  - 8-10 sessions
  - 5 weeks
- **HOME-BASED**
  - Home-based
  - Self-administered
  - Videotape-based
  - 8-10 sessions
  - 5 weeks

FIGURE 2. Study Design

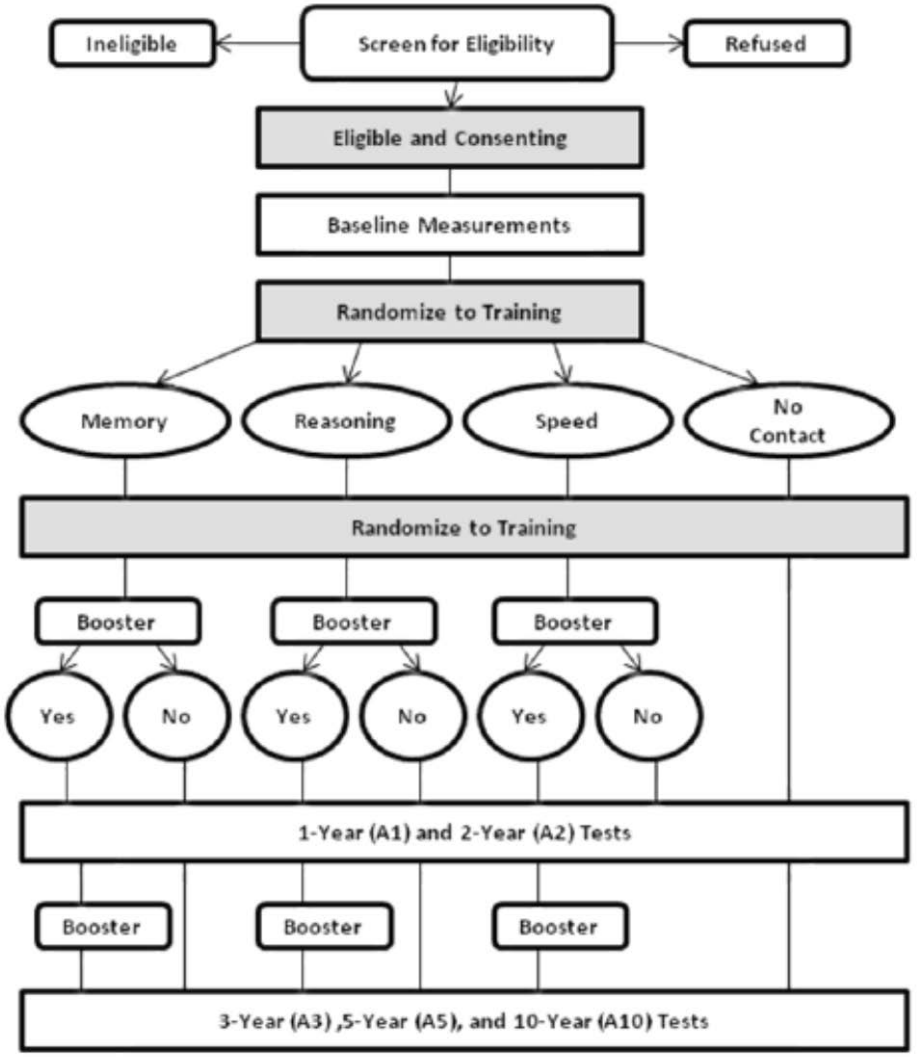


TABLE 3. Training Effect Size for Memory-normal and Memory-impaired Participants by Intervention Group and Composite Measure

Intervention	Time	Composite Outcome Measures					
		Memory-normal			Memory-impaired		
		Memory	Reasoning	Speed	Memory	Reasoning	Speed
Memory	PT	.300**	-.009	-.050	-.012	-.117	.105
	A1	.254**	.033	-.061	-.175	-.163	.107
	A2	.214**	.052	-.057	-.100	-.015	.400*
Reasoning	PT	.001	.477**	.025	-.048	.573**	-.277
	A1	.013	.416**	-.026	-.230	.208	-.155
	A2	-.003	.262**	-.021	-.331	.276*	-.434*
Speed	PT	.004	-.017	-1.488**	-.108	-.111	-1.420**
	A1	.004	.009	-1.238**	-.163	-.097	-1.100**
	A2	-.024	-.013	-.886**	-.298	.079	-.755**

Note. PT = post-test, A1 = first annual assessment, A2 = second annual assessment.

* $p < .05$

** $p < .001$