The Other Side of MS Research:
Cognition and Health Policy

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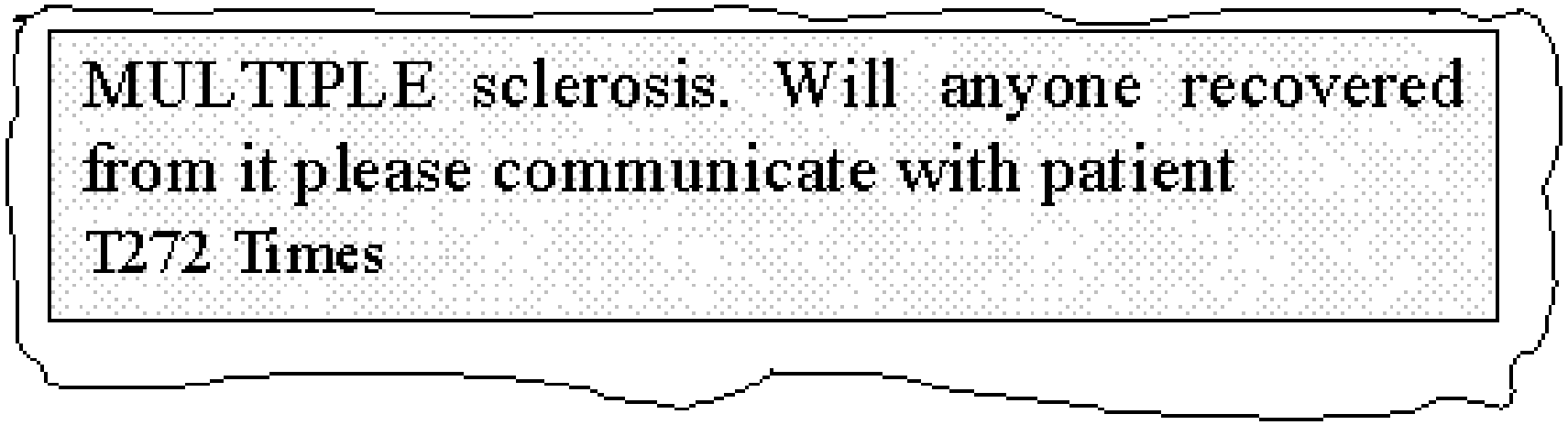
Sylvia Lawry, founder of the Society with her brother, Bernard, late 1940's

Ad in the New York Times – 1945

Looking for help for her brother . . .



The search for a *cure* begins

- Association for the Advancement of *Research* in MS (AARMS) – 1946
- AARMS renamed the National Multiple Sclerosis Society - 1948

Our strategic response – 2011-2015

- ***We are a driving force of MS research and treatment to <u>stop</u> disease progression, <u>restore</u> function, and <u>end</u> MS forever.***
- We develop, deliver and leverage resources to enhance care for people with MS and quality of life for those affected by the disease.
- We are leaders in the worldwide MS movement, mobilizing millions of people to do something about MS now.
- We are activists.
- We develop and align human, business and financial resources to achieve breakthrough results.

The National Multiple Sclerosis Society

Our Vision: *A world free of MS*

Our Mission:
*We mobilize people and resources to drive research for a cure and to **address the challenges** of everyone affected by MS*

Funding Philosophy (1)

- Fund the most promising research regardless of geography
- Funding decisions based on confidential and anonymous review by peers from the scientific community
- Require accountability from the investigators and their institutions
- Attract and train promising young investigators

MS NOW
An MS Research Revolution

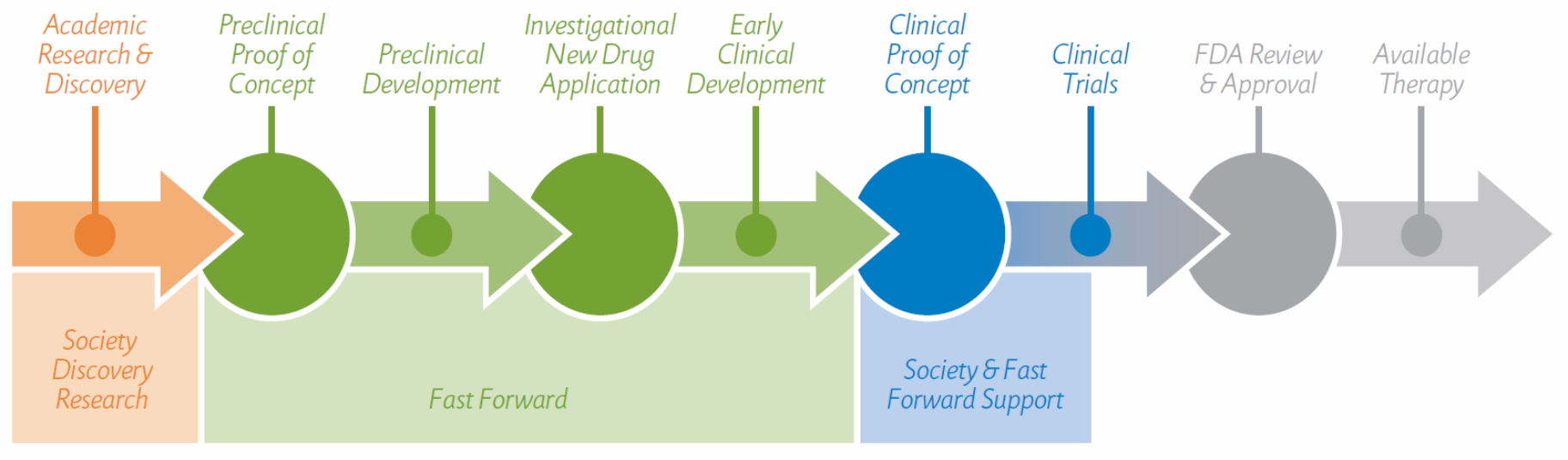
Funding Philosophy (2)

- Identify gaps and opportunities and develop strategies for meeting them
- Incorporate Society priorities and financial considerations into funding decisions
- Leverage support from other agencies and industry
- Connect people and resources

MS NOW
An MS Research Revolution

Another View

A holistic approach is integral to the Society's research strategy



Cognitive Changes

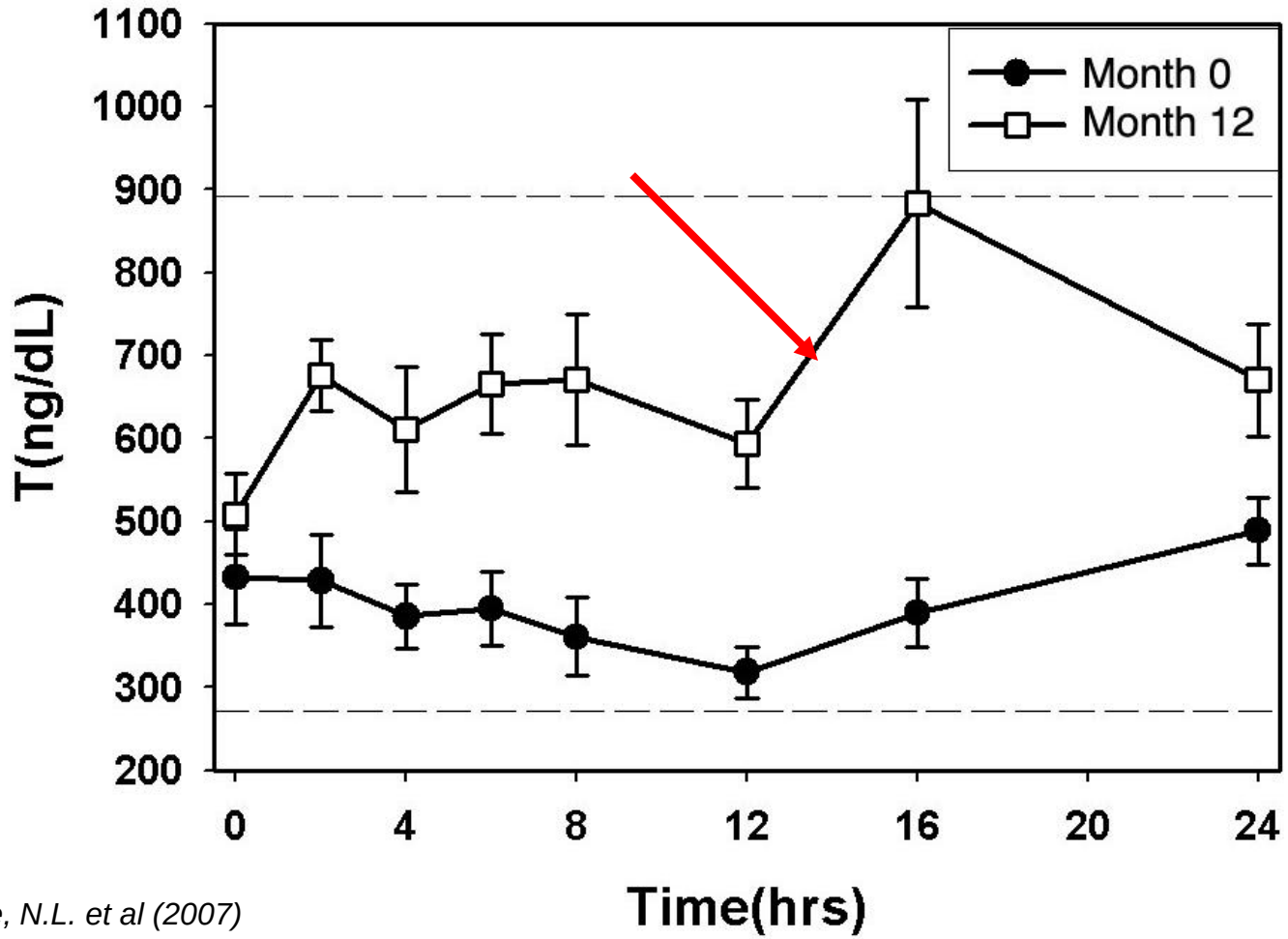
Testosterone pilot study

- PI – Nancy Sicotte, UCLA
- Goal – Test effects of testosterone patch on men with MS
- Subjects – 10 men with RRMS
- Treatment – testosterone patch daily
- Duration – 12 months
- Design – Unblinded pre-post trial

Months -6 to 0	Months 1 to 12
Pre-treatment	Testosterone

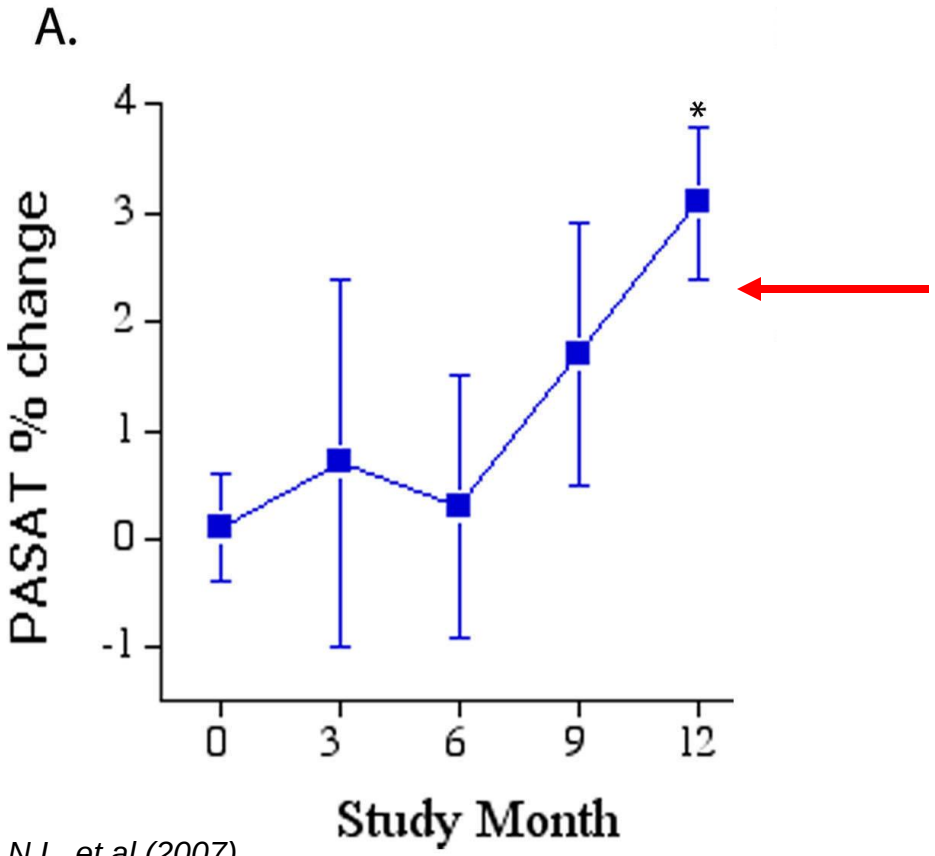
Sicotte, N.L. et al (2007)

Results – Testosterone increased



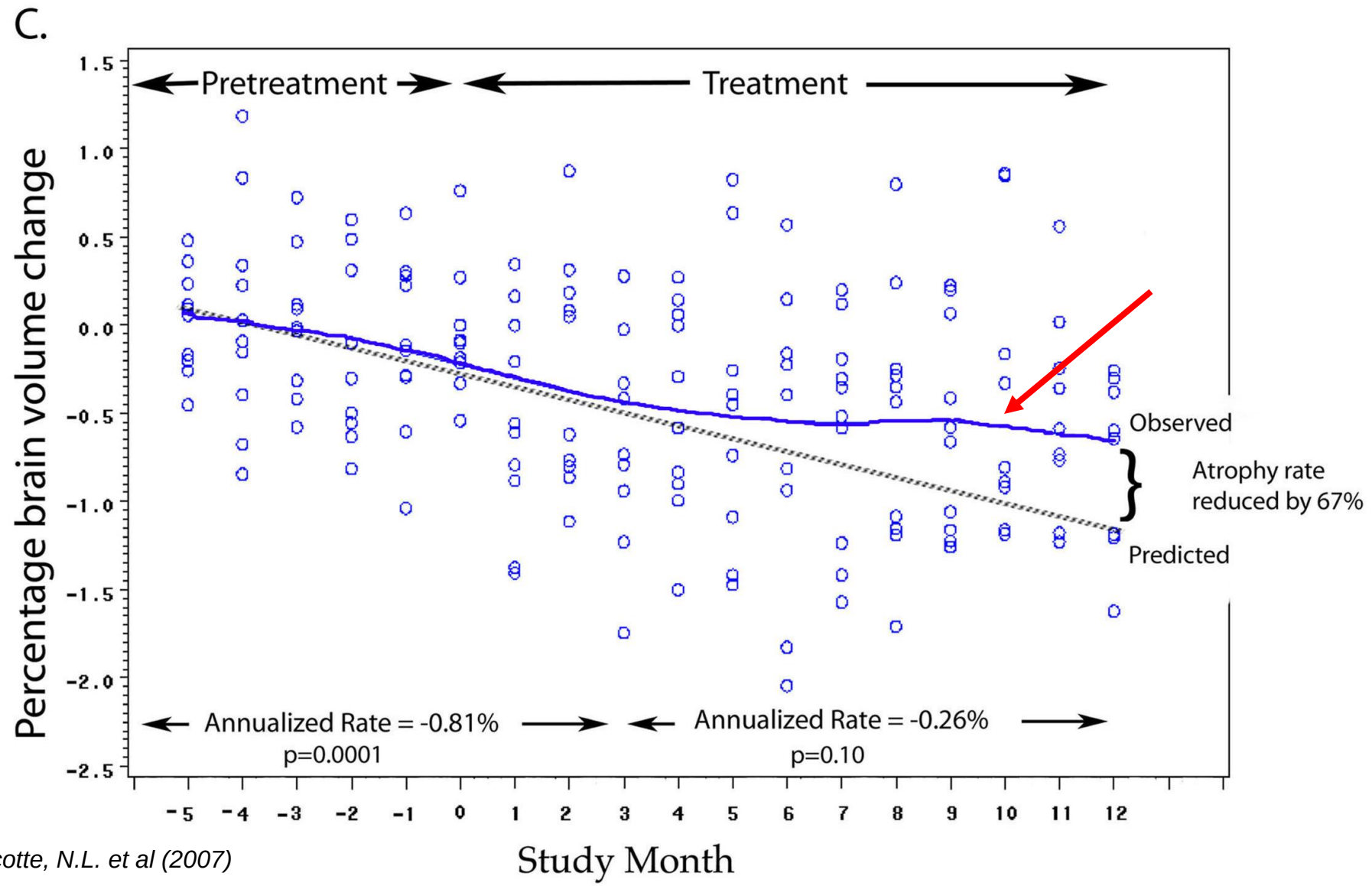
Sicotte, N.L. et al (2007)

Results – Cognitive function improved



Sicotte, N.L. et al (2007)

Results – Loss of brain volume slowed



Sicotte, N.L. et al (2007)


Lokomat

Can aerobic exercise improve cognitive functioning in MS?

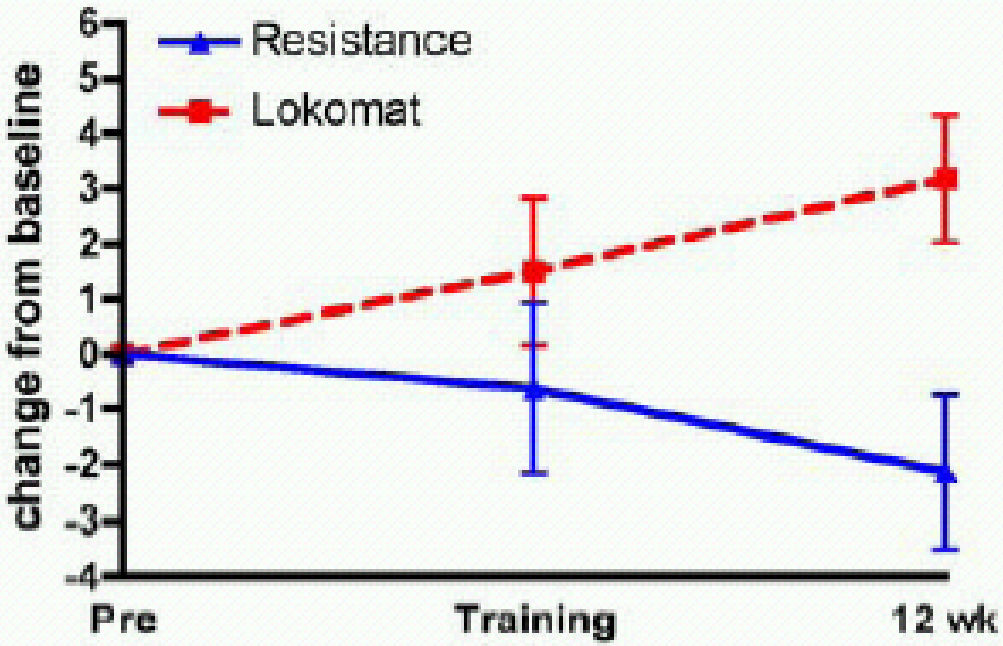


Figure 5: PASAT Scores in subjects with baseline PASAT between 25-55. Group difference p=0.04 at 12 wk follow-up.

Exercise as a strategy to treat cognitive dysfunction in persons with MS

- PI – Barbara Giesser, M.D., UCLA
- Goal – Test effects of aerobic exercise (AE) on cognitive impairment
- Subjects – 60 people with RRMS or SPMS and cognitive impairment
- Treatments – Aerobic exercise (bicycle) vs stretching exercises – 3 30 minute sessions per week for 24 weeks
- Duration – 36 weeks
- Design – Randomized, single-blind, controlled clinical trial

Aerobic Exercise (Bicycle) N = 30	Stretching Exercises N = 33
Weeks 1-24 + 12 week follow-up	Weeks 1-24 + 12 week follow-up

Exercise as a strategy to treat cognitive dysfunction in persons with MS

- Primary outcomes:
  - Processing speed and working memory (PASAT)
- Secondary outcomes:
  - Cognitive function – Attention, processing speed (SDMT), spatial memory (10/36 test), verbal memory (SRT), verbal fluency (word list generation), executive functioning (Stroop)
  - Speed of information processing in the brain (P300 evoked potentials)
  - Immunological function – cytokines; growth factor

The effect of aerobic exercise on cognition in multiple sclerosis

- PI – Charles Bombardier, PhD, University of Washington
- Goal – To determine whether aerobic exercise training significantly improves cognitive functioning in adults with MS
- Subjects – 125 people with MS on disease modifying therapy and with impaired speed of information processing and working memory
- Treatments – Aerobic exercise (bicycle) vs stretching/toning exercises – 3 60 minute sessions per week for 6 months
- Duration – 9 months
- Design – Randomized, single-blind, controlled clinical trial

Aerobic Exercise (Bicycle) N = 63	Stretching/Toning N = 62
Months 1-6 + 3 month follow-up	Months 1-6 + 3 month follow-up

The effect of aerobic exercise on cognition in multiple sclerosis

- Primary outcomes:
  - Processing speed and working memory (PASAT + SDMT)
- Secondary outcomes:
  - Cognitive function – executive functioning, memory, language, spatial processing
  - Patient reported outcomes – perceived cognitive functioning and depression
- Tertiary outcome:
  - Cardioresperitory fitness

A randomized, controlled trial to treat learning impairment in MS

- PI – Nancy Chiaravalloti, Ph.D., Kessler Foundation
- Goal – Test effects of a novel behavioral intervention to improve learning and memory in people with MS
- Subjects – 86 people with MS
- Treatments – 10 sessions of a Story Memory Technique vs. 10 sessions of non-training time with the therapist; half in treatment group got monthly "booster sessions"
- Design – Randomized, double-blind, placebo controlled clinical trial

Story Memory Technique N = 41	Non-training Conversation N = 45
Weeks 1-5 (Treatment)	Weeks 1-5 (Placebo)
Follow-up 6 Months	Follow-up 6 Months

Chiaravalloti. N et al (2013)

A randomized, controlled trial to treat learning impairment in MS

- Primary outcomes:
  - Verbal Memory (CVLT)
  - Everyday Memory (RBMT)
- Secondary outcomes:
  - Subjective report of overall functioning
  - Behavioral symptoms associated with cognitive changes (FAMS)
  - Significant other's report of behavioral symptoms

Figure 2 California Verbal Learning Test (CVLT) learning slope across the 5 learning trials of the CVLT immediately posttreatment, by treatment group ($p < 0.05$)

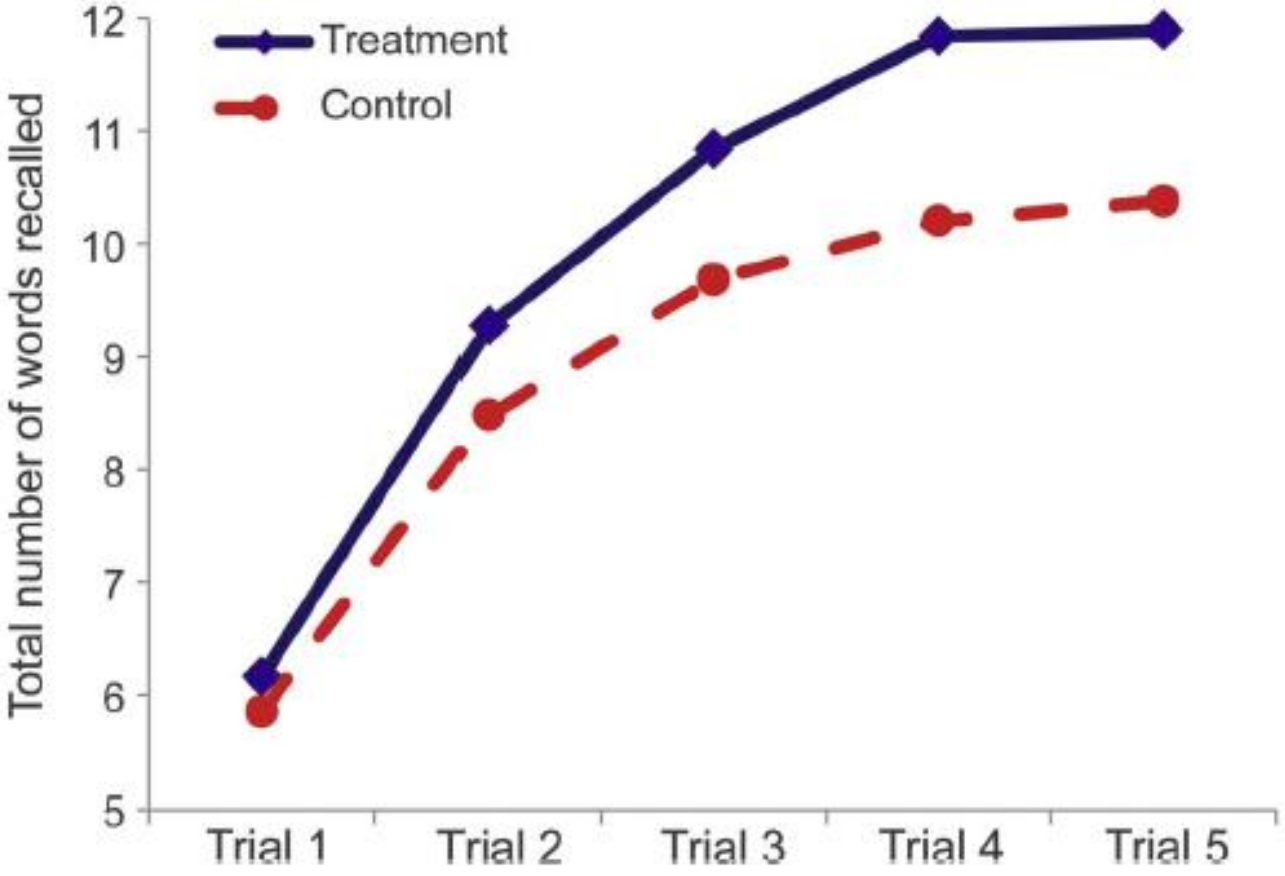
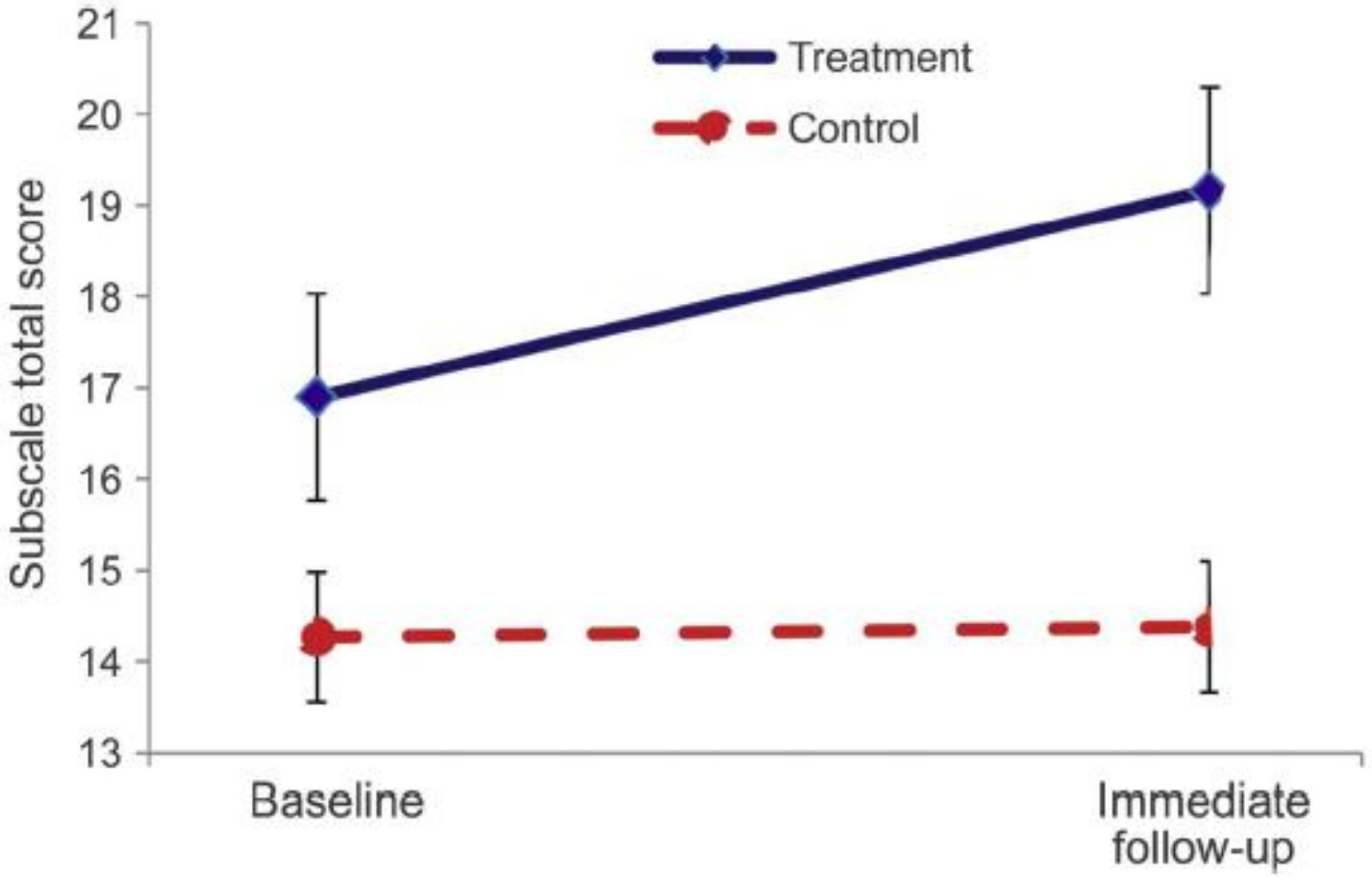


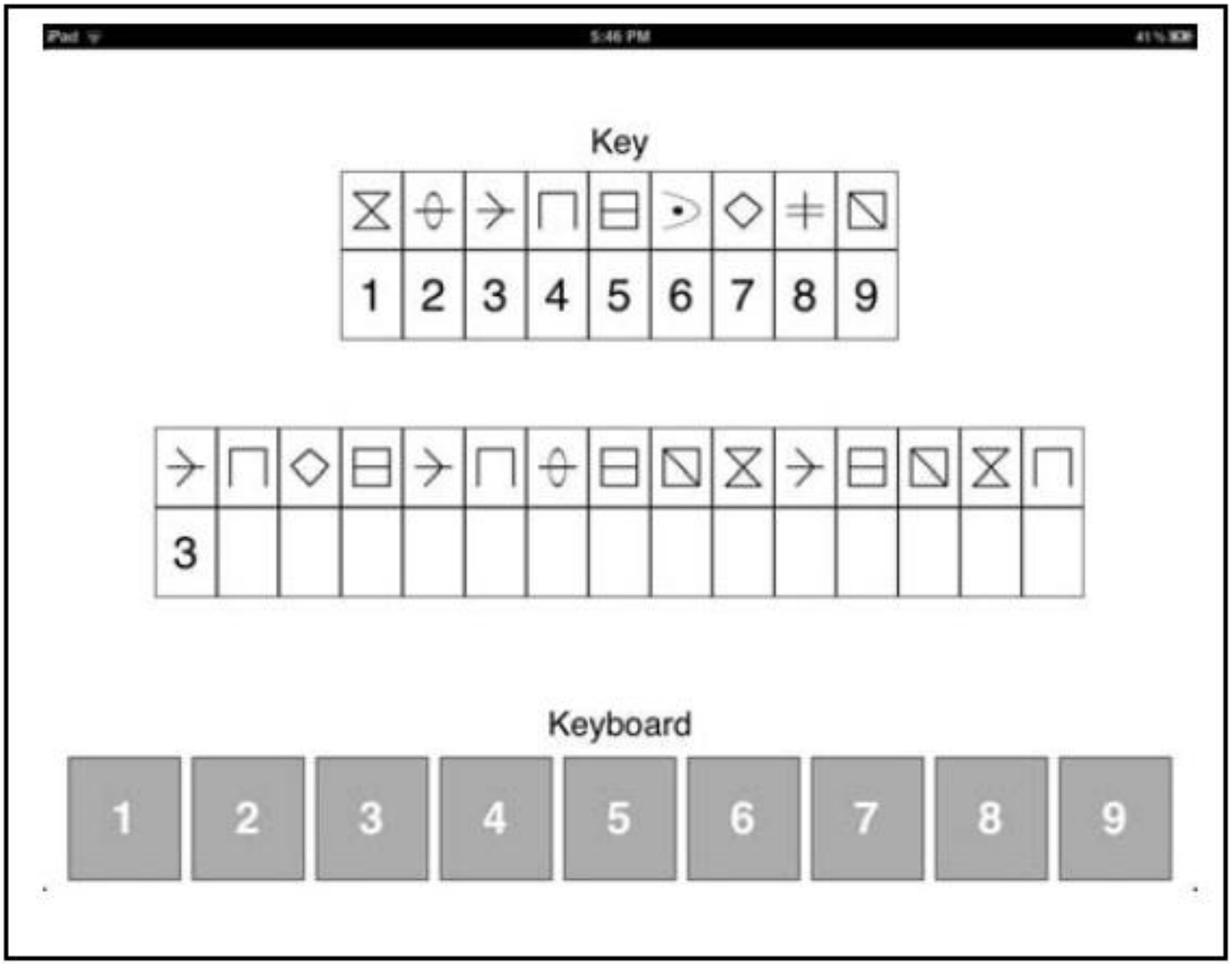
Figure 3 **Baseline and immediate follow-up Functional Assessment of Multiple Sclerosis general contentment scores for the treatment and control groups ($p < 0.05$)**



Validation of an iPad App for Assessing Cognition in MS

- PI – Stephen Rao, PhD, Cleveland Clinic
- Goal – Evaluate the equivalence of an iPad administered test (PST) to a standard test of cognitive dysfunction widely used in MS (SDMT) and evaluate the reliability and validity of the PST
- Subjects – 70 people with MS and 70 controls
- Protocol (Phase I) – 10 patients and 10 controls are given ad iPad, stylus, and noise-cancelling headphones and complete the PST; adjustments are made in the procedure
- Protocol (Phase II) - 60 patients and 60 controls complete the PST and the Brief Repeatable Battery of Tests

STOP. RESTORE. END.



STOP. RESTORE. END.

Validation of an iPad App for Assessing Cognition in MS

- Primary outcomes:
  - Comparison of the number of correct items on the PST vs the SDMT
- Secondary outcomes:
  - Evaluate the test-retest reliability of the PST and the Brief Repeatable Battery of Tests
  - Evaluate the ability of the PST to detect cognitive dysfunction
  - Compare the PST and the BRBT to other MS measures (neurological function, walking, dexterity, MS course

A Randomized Controlled Trial of Intellectual Enrichment to Build ***Cognitive Reserve*** in MS

- PI – Victoria Leavitt, PhD, Kessler Foundation
- Goals
  - Improve cognitive efficiency and memory through a 12-week cognitive enrichment program
  - Show altered brain function on fMRI following treatment, shifting toward a pattern of enrichment-related neural activity
- Subjects – 16 people with MS and cognitive impairment
- Protocol – Double-blind, randomized, controlled trial lasting 12 weeks; subjects engage in online activities using an iPad one hour per day for 12 weeks. E-mail and Facetime contact with investigators

Treatment N = 4	Control N = 4	Wait List N = 8
Intellectual Enrichment	Educational Videos	No Intervention

What is ***Cognitive Reserve*** ?

"The concept of ***cognitive reserve*** provides an explanation for differences between individuals in susceptibility to age-related brain changes or pathology . . . whereby some people can tolerate more of these changes than others and maintain function. Epidemiological studies suggest that lifelong experiences, including educational and occupational attainment, and leisure activities in later life, can increase this reserve."

Stern, Y. 2012

Games	Reading/Writing	Novel Hobby
Changes bi-weekly:	Changes daily:	Select one:
Executive skills (planning/organization) Cut-the-Rope, Fling!, Max & Magic Marker	Etiquette Monday: **Read** a letter to an etiquette column. **Writing:** You are 'Mr/Ms Manners.' Respond to the letter.	Reading music Foreign language Gardening Astronomy American Sign Language
Processing speed Diner/Garden/Hotel Dash, Flight Control	Movie Tuesday: **Read** a personal essay. **Writing**: You are a Hollywood agent. Pitch the idea for a movie screenplay.	
Memory Memoryblock, Matching game	Wedding Wednesday: **Read** a wedding announcement. **Writing:** You are the mother/father in-law. Compose an email to the couple detailing your thoughts about their nuptials.	
Language Jumbline, Word-a-day, Boggle	Haiku Thursday: Read an emotionally evocative essay. **Writing:** Compose a haiku based on the essay.	
	Famous Friday: **Read** a bio of a noteworthy person. **Writing**: You are Barbara Walters. Formulate 10 questions for your big interview.	

A Randomized Controlled Trial of Intellectual Enrichment to Build ***Cognitive Reserve*** in MS

- Primary outcomes:
  - Verbal memory, visual memory, processing speed, working memory, visuospatial skill, executive functioning, and verbal fluency
  - Functional MRI
- Secondary outcomes:
  - Blinding
  - Level of interest and enjoyment with treatment
  - Perceived benefits
  - Comfort using the iPad

Health Care Delivery and Policy

Health, disability, and life insurance experiences of working-age persons with MS

- PI – Lisa Iezzoni, MD, MPH, Harvard Medical School
- Goal – Explore the problems faced by persons with MS concerning the three major types of insurance coverage
- Subjects – Nationwide sample of 983 persons with MS from high poverty areas vs. all other areas
- Protocol – Half-hour telephone interview covering insurance experiences, demographics, medical history, health care utilization and cost
- Sample characteristics – 79% female, 86% Caucasian, 69% married, 72% college educated, 40% employed
- Insurance status – 96% had health insurance, (40% public), 68% had life insurance, 57% had disability insurance (36% public)

Health, disability, and life insurance experiences of working-age persons with MS

- 27% reported that after being diagnosed with MS health insurance concerns had affected employment decisions
- 27% postponed seeking needed care due to costs
- 22% delayed filling Rx's, skipped doses, or split doses due to costs
- 27% reported considerable worries about affording basic necessities such as food, utilities, and housing
- 16% had considerable difficulty paying for health care
  - Of these, 21% had actually spent less on food, heat, and other necessities due to health care costs

Iezzoni & Ngo (2007)

Specialized housing needs in multiple sclerosis: a comprehensive analysis

- PI – Malachy Bishop, PhD, University of Kentucky
- Goal – Assess the current and anticipated specialized housing needs of persons with MS in the USA and develop a new instrument to assess specialized housing needs
- Subjects – 5082 People with MS and 103 health care professionals (64 social workers, 16 MS center directors, 23 NMSS chapter programs staff)
- Protocol – Survey questionnaire completed by phone, mail, or online covering demographics, housing-related questions, cognition, MS symptoms, quality of life
- Sample characteristics – 78% female, average age = 54, 96% Caucasian, 67% married, 59% college educated, 36% employed, 20% urban, 26% rural, 54% suburban, 95% had health insurance,
- Housing – 77% owned their home, 16% renting, 4% living in someone else's home, 1% in assisted living, NH, other

Specialized housing needs in multiple sclerosis: a comprehensive analysis

- 42% need assistance in the home (36% receive, 6% do not)
- 71% with mobility limitations, 38% need an assistive device
- 17% reported accessibility needs at home that were not met
  - Most frequent was bathroom
- Needed but unaffordable modifications – bathroom, entrance ramp, shower, grab bars, stair-lift, kitchen, wider doorways
- Had experienced housing discrimination – 11%
- Not confident they can live independently in current residence in the future – 30%, or afford to do so – 26%

Specialized housing needs in multiple sclerosis: a comprehensive analysis

- Recommend improving access to information about:
  - Specialized, especially accessible housing
  - Financial assistance for housing modifications
  - Universal design and “aging in place”
  - Financial assistance for housing purchase or renting
  - Resources for personal care or home health support
  - Legal rights and protections related to disability and housing
  - Specialized transportation
  - HUD housing resources
  - SSDI and SSI disability insurance programs
  - Organizations such as independent living centers
  - Options and rights concerning rentals
- Recommend working to increase the availability of specialized housing with recreational facilities

Patient and physician perspectives concerning decision making regarding treatment with multiple sclerosis disease-modifying therapies

- PI – Robert Buchanan, PhD, Ohio State University
- Goal – To improve the decision-making process for treatment with MS disease-modifying therapies (DMT) by developing an understanding of how physicians and patients approach these decisions, the facilitators and barriers they face, and any unmet decision-making needs.
- Subjects – 1,000 people with MS from 10 MS centers, 500 neurologists (surveys) 60 people with MS and 60 neurologists (in-depth interviews)
- Protocol – The study will utilize quantitative and qualitative approaches, including focus groups, national and in-depth interviews. Data collected in the focus groups will identify key issues to include in the national surveys.

Patient and physician perspectives concerning decision making regarding treatment with multiple sclerosis disease-modifying therapies

- Perspectives of patients and physicians concerning how they decide which medication (if any) to take and strategies to maintain adherence to treatment
- Types of information they need to make the decision of which DMT to take
- What role each takes in the decision-making process and what demographic and medical factors are associated with different types of rols
- Procedures for shared decision-making
- How decisions are currently make
- The role of family members in decision making
- Testing and refinement of decision aids, the Decision Board

There are many side to MS research

- Stop – Restore – End
- Addressing all of the challenges faced by people with MS
- Holistic approach to MS research
- Not only ending MS but ending the challenges of MS