



Reversing Cognitive Decline

Groundbreaking Results from a Randomized Controlled Trial of Precision Medicine in Alzheimer's Disease

KAT TOUPS, MD, DFAPA, IFMCP

REGENERATIVE, PRECISION, AND FUNCTIONAL MEDICINE

PSYCHIATRY AND DEMENTIA

EVANTHEA TRIAL: A pragmatic, randomized, controlled trial to evaluate the effectiveness of a precision medicine treatment approach for early-stage dementia and mild cognitive impairment

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- ▶ www.BayAreaWellness.net
- ▶ www.DementiaDemystified.com

**DEMENTIA IS BOTH
PREVENTABLE AND TREATABLE**

**WHEN WE FIND AND CORRECT THE UNDERLYING
CAUSES**

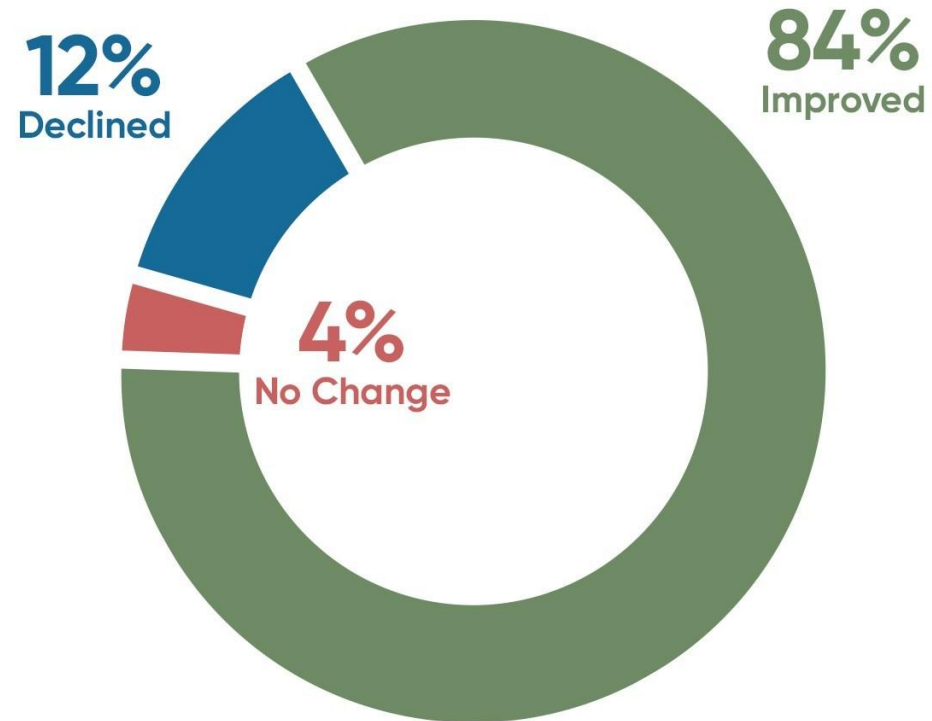


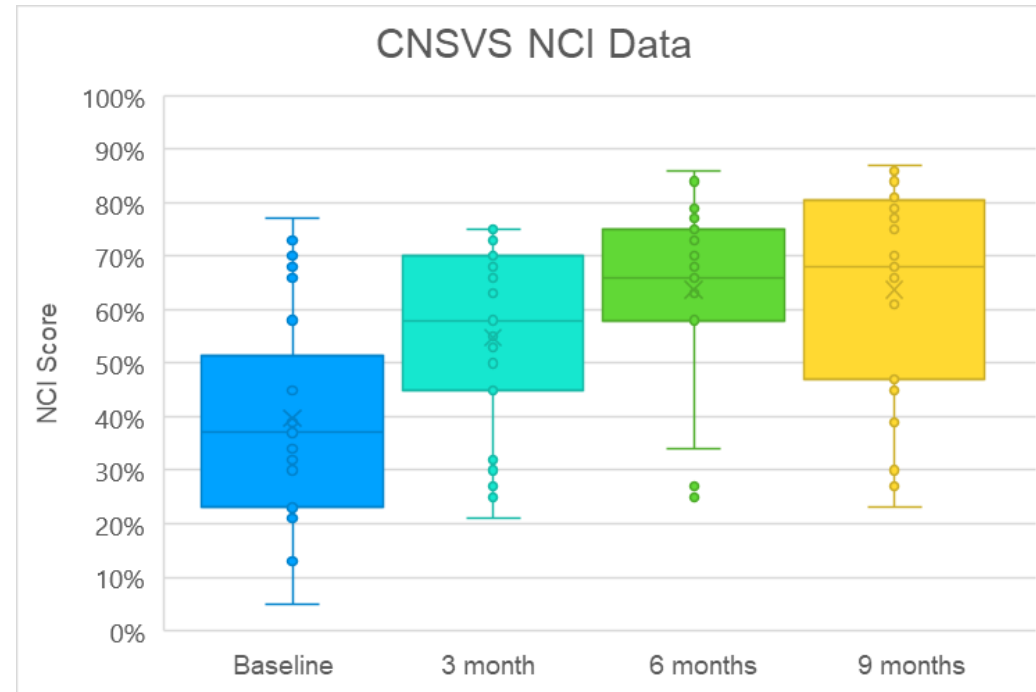
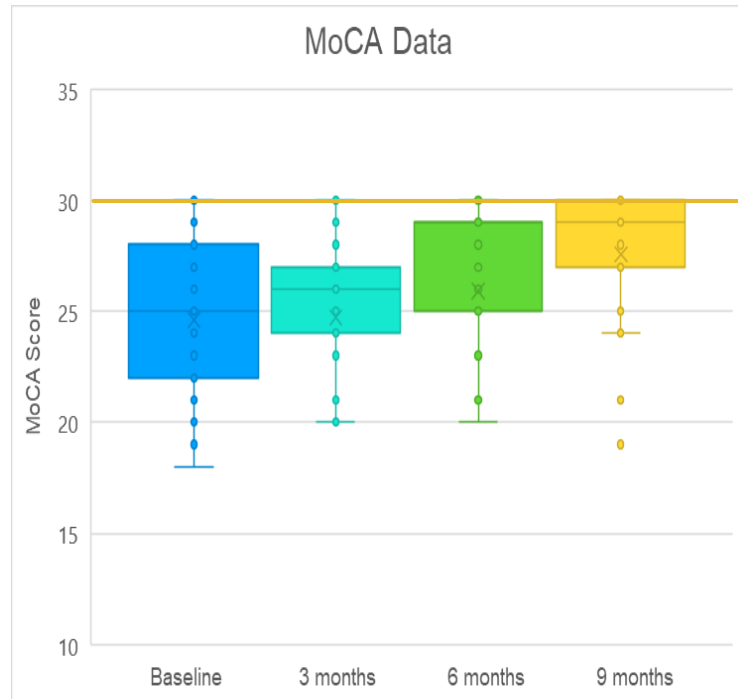
**DEMENTIA IS NOT A DEATH
SENTENCE!**

FOUR WINDS CLINICAL TRIAL

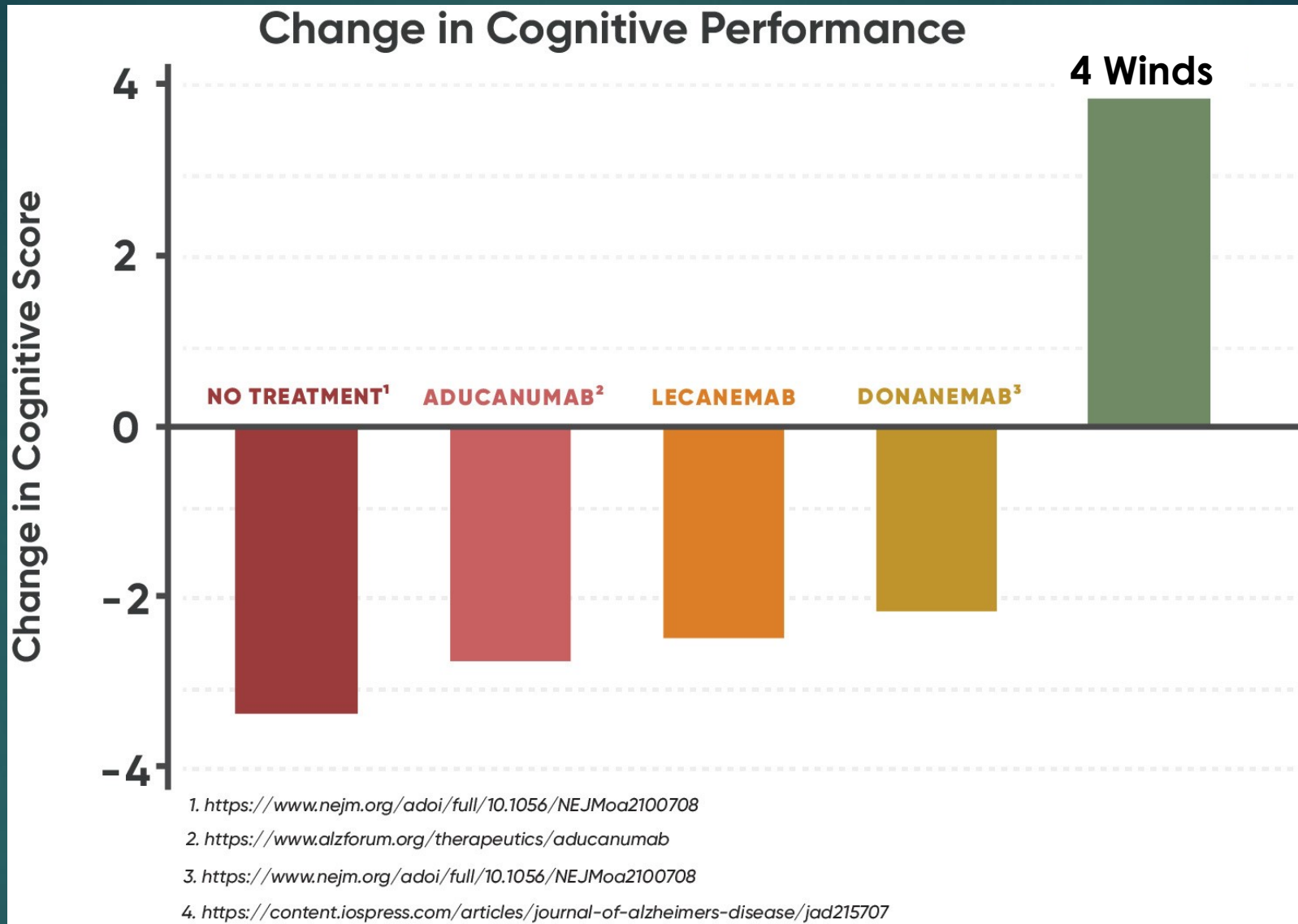
Clinical Trial Results

effect on participants' cognition





4 Winds Clinical Trial Results



4 Winds Clinical Trial Results

BRAIN MRI VOLUMETRIC CHANGES

No brain volume loss or cortical thinning was detected in the trial participants.
(Both of these occur with normal aging.)

GRAY MATTER VOLUMES

- Study Subjects **increased** by a mean of **0.3%**
- Normal Controls **decrease** by **0.83-0.92%**
- Alzheimer's Patients **decrease** **2.20-2.37%**

HIPPOCAMPAL VOLUMES

- Study Subjects **decreased** **1.29%**
- Normal Controls **decrease** **1.41-1.73%**
- MCI or Alzheimer's **decrease** **3.5-4.66%**

OTHER STUDY “SIDE EFFECTS”

WERE IMPROVEMENTS IN:

- ▶ Weight, Waist circumference, BMI
- ▶ Strength and Fitness (including grip strength)
- ▶ Blood Pressure
- ▶ Lipids
- ▶ Glucose levels
- ▶ hsCRP
- ▶ Autoimmunity

EVANTHEA TRIAL: A pragmatic, randomized, controlled trial to evaluate the effectiveness of a precision medicine treatment approach for early-stage dementia and mild cognitive impairment

- ▶ Why is this work important?

ALZHEIMER'S

- ▶ 22% with Alzheimer's (7.4 million)
- ▶ 11% (1 in 9) age 65+ (6.5% in UK – leading cause of death)
- ▶ 35.8% age 85+

MCI

- ▶ 17% age 65+ with MCI

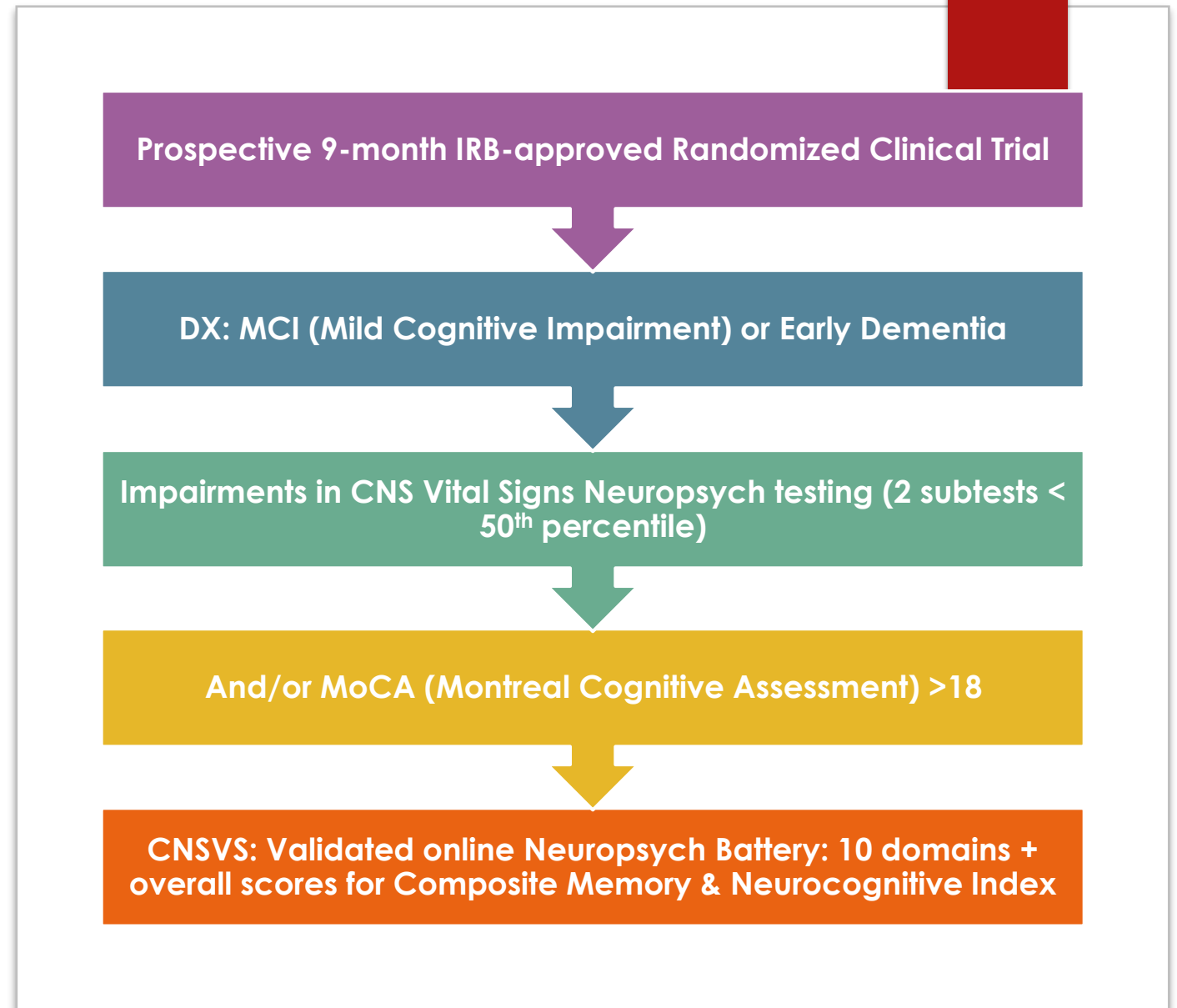
COMBINED MCI and ALZHEIMER'S

- ▶ 30% (11 million) age 65+
- ▶ Rates expected to double in the next 25 years
- ▶ More Distressing: Dementia is afflicting more people at younger ages.

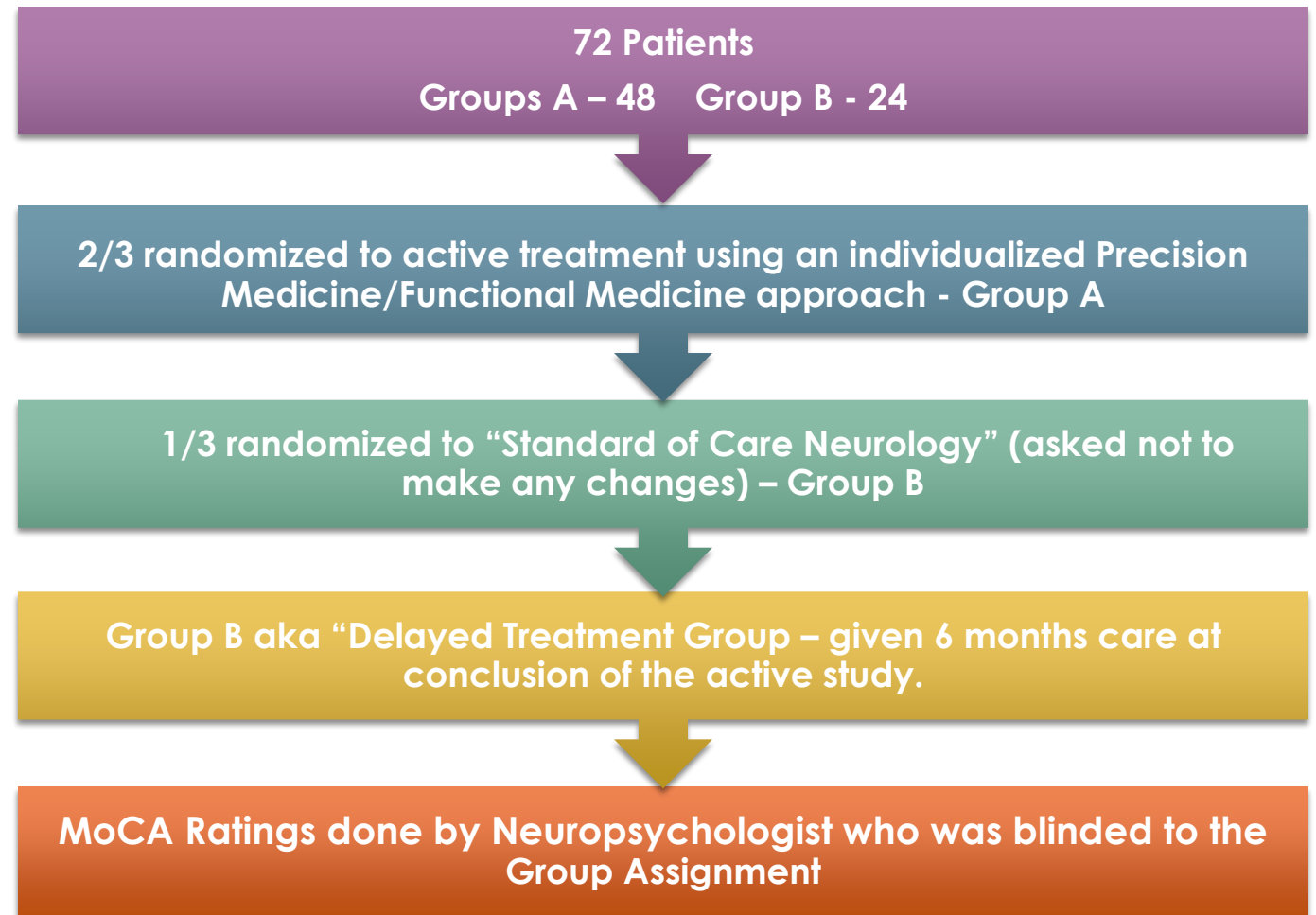
EVANTHEA TRIAL

- ▶ **Sponsor: Alzheimer's Prevention and Reversal Project, Inc. (APRP)**
- ▶ **Funding: Evanthea, LLC with the support of the 4 Winds Foundation**
- ▶ **Senior Advisor: Dale Bredesen , MD**
- ▶ **Lead Investigator: Kat Toups, MD, IFMCP**
- ▶ **Co-Investigators:**
 - ▶ **Nate Bergman, DO, IFMCP**
 - ▶ **Kristine Burke, MD, IFMCP**
 - ▶ **David Haase, MD, IFMCP**
 - ▶ **Ann Hathaway, MD**
 - ▶ **Craig Tanio, MD, IFMCP**

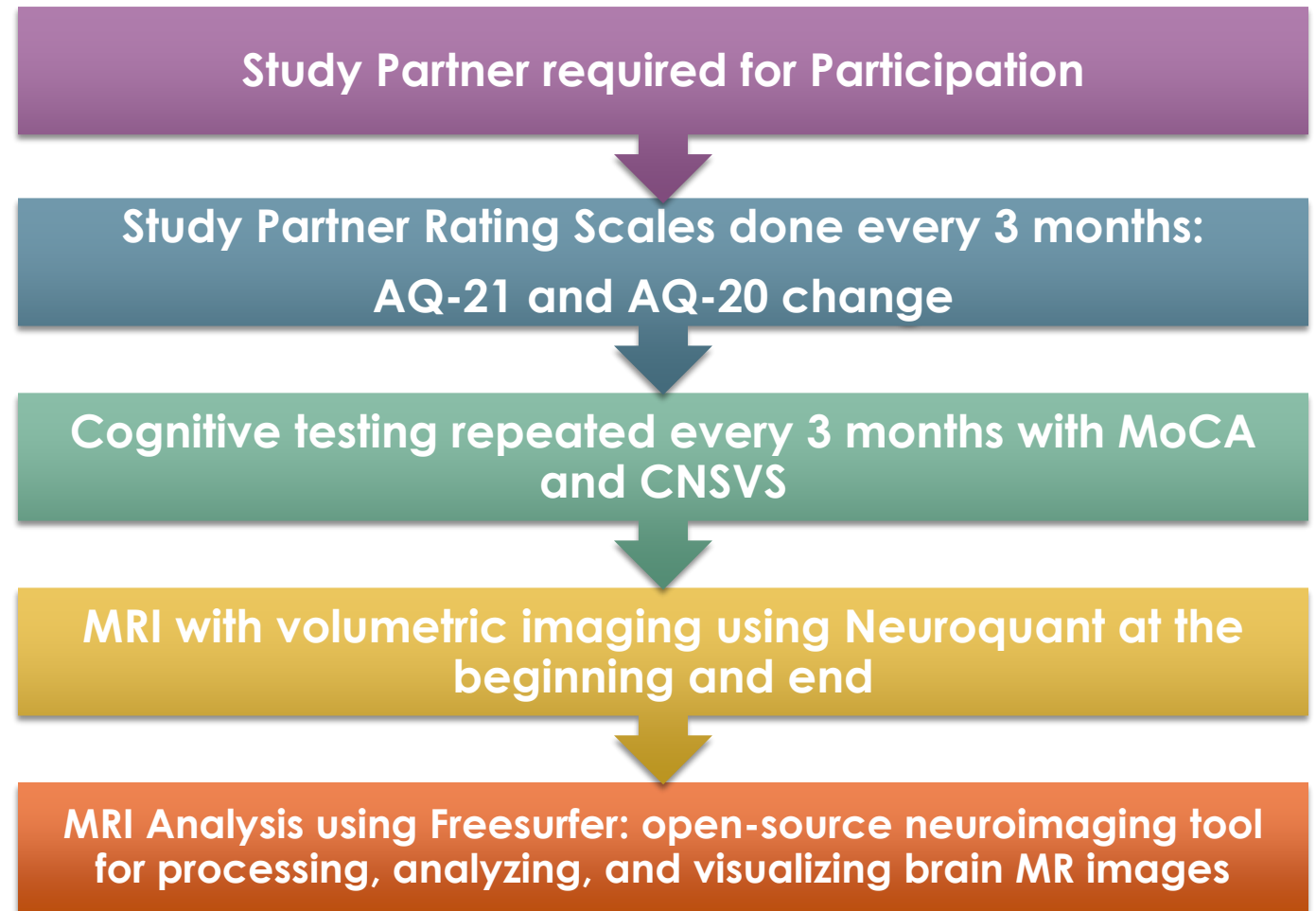
EVANTHEA CLINICAL TRIAL



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ADDITIONAL EVALUATIONS

Hearing Test

Vision Test

Sleep Testing for Apnea and UARS – 3 nights home testing

Mammogram (women)

Dental Pathogens + CBCT (Cone Beam CT Scan) if indicated

EVANTHEA CLINICAL TRIAL

Large Battery of Labs – Cast a Wide Net

Brain Biomarkers

Environmental Toxins (chemical toxins, metals)

Mycotoxins

ERMI/HERTSMI

EVANTHEA CLINICAL TRIAL

STUDY PROCEDURES – TESTING

TESTING – Large battery of tests including:

- ▶ Nutrients, Omega Fatty Acids, Metals (Genova NutrEval)
- ▶ Cardio-metabolic and inflammatory markers
- ▶ Hormones – sex hormones, thyroid hormones
- ▶ Immune Markers – ANA, immunoglobulins, T cell panel
- ▶ Infections – including viruses + tick-borne illnesses (Igenex Lab)
- ▶ Mycotoxins, Chemical Toxins (Real Time Lab)
- ▶ Home Mold Testing – ERMI/HERTSMI (Lis Biotech)
- ▶ Comprehensive Stool Analysis (Genova GI Effects)
- ▶ Genetics (Intellxx DNA)

INFECTIONS LINKED with COGNITIVE DECLINE

- LYME
- BABESIA
- BARTONELLA
- EHRLICHIA/ANAPLASMA
- TICK BORNE RELAPSING FEVER
- EBV + EAD
- HSV 1/2
- HHV-6
- TOXOPLASMOSIS
- MYCOPLASMA
- CMV
- CHLAMYDIA
- SYPHILIS
- HIV
- HEPATITIS
- COVID

BRAIN BIOMARKERS

p-Tau 217

Amyloid (A-beta 42/40)

GFAP (Glial Fibrillary Acidic Protein)

NfL (Neurofilament light chains)

BDNF (Brain Derived Neurotrophic Factor)

EVANTHEA
CLINICAL
TRIAL

BRAIN BIOMARKER TESTING - AMYLOID

Amyloid - AB42/40

- Looks at ratio of AB42/40 in plasma. This correlates with amyloid deposition in the brain
- Amyloid accumulates outside of neurons to form protective amyloid plaques in response to hostile provocations.
- Amyloid has **antimicrobial effects**. Supports the brain's innate immune system by trapping and neutralizing microbes (bacteria, viruses, and fungi).
- Lower ratios indicate increased amyloid accumulation and Alzheimer's risk. Lower scores are worse.
- Low amyloid levels can occur 20 or more years before symptoms, so amyloid screening is useful even before symptoms are present.
- Quest, LabCorp, NeuroCode, Precivity AD
- Sometimes covered by insurance

BRAIN BIOMARKER TESTING - pTau

Phosphorylated Tau (pTau) – 217 (most sensitive form of Tau)

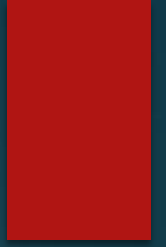
- Indicates an accumulation of hyperphosphorylated tau protein inside of neurons, forming neurofibrillary tangles (classic marker of Alzheimer's).
- Tau is also released when there is brain injury and damage to neurons.
- pTau may have some indirect antimicrobial effects (particularly HSV-1, HIV).
- Much more sensitive than plasma amyloid for detecting neurodegeneration.
- P-tau elevations can start with very early cognitive symptoms, though not as early as amyloid.
- Tau levels can be useful to detect early cognitive decline/dementia and can also be useful for tracking disease progression and *improvement*.
- Two markers available: pTau -181, pTau-217 (217 more sensitive in early AD)
- Quest, LabCorp, and NeuroCode all test pTau-181 and pTau-217
- Sometimes covered by insurance

BRAIN BIOMARKER TESTING - GFAP

Glial Fibrillary Acidic Protein (GFAP)

- Non-specific marker of astrocyte/glial reactivity (in neurodegeneration or head trauma).
- Marker of early astrocyte injury (astrogliosis) that correlates well with amyloid and tau levels.
- Elevated GFAP indicates ongoing damage to the axons from vascular disease, head trauma, infections, or any neurodegenerative process.
- It indicates neuroinflammation, and the reactive astrocytes may release inflammatory cytokines, ROS, and glutamate. This can all lead to **disruption of the blood-brain barrier**.
- So, amyloid and tau are more indicative of the plaques and tangles prevalent with AD.
- GFAP indicates neurodegeneration, but it is less specific.
- Can be an indicator of AD, but also FTD, MS, Parkinson's, and TBI, as well as small vessel disease. An **early-stage indicator of neurologic damage** – years before symptoms.
- Quest, LabCorp and NeuroCode all offer GFAP testing.

BRAIN BIOMARKER TESTING - NfL



Neurofilament Light Chains (NfL)

- Released from injured or degenerating myelinated axons or neurons – into the extracellular fluid and then into the CSF and blood.
- This is another general marker of axonal/neuronal injury, rather than linked to a specific disease like AD. Another marker of neurodegeneration.
- Can be elevated in AD, FTD, ALS, MS, Parkinson's, TBI.
- Also stroke, a-fib, MI, chronic kidney disease, diabetes, and pregnancy.
- This marker is the only one shown to be useful for ALS.
- 10% lower levels in PM, so always best to test repeat brain biomarkers at the same time of day.
- Falsely lowered levels with obesity (BMI > 30)
- Overnight fasting is recommended for all the brain biomarkers. Lipemia interferes with the assays.
- Quest, LabCorp and NeuroCode all offer NfL testing.

BRAIN DERIVED NEUROTROPHIC FACTOR (BDNF)

- ▶ BDNF is involved with helping neurons to make new synaptic connections.
- ▶ So, BDNF is essential for neuroplasticity.
- ▶ We hoped see the BDNF levels increase with all of the things our patients were doing to enhance neuroplasticity, like exercise and Heartmath meditations (the two best validated things to increase BDNF), brain training, optimizing sleep and HRV, photobiomodulation, and targeted nutrients.

EVANTHEA CLINICAL TRIAL

WEARABLES & TRACKING

OURA RING – sleep and HRV

CGM (Continuous Glucose Monitor)

CRONOMETER – food intake tracking

BRAIN HQ & HEARTMATH

KETONE MONITORING – Keto Mojo

EVANTHEA CLINICAL TRIAL

STUDY PROCEDURES - DIET

Ketogenic Diet with ketone levels of 1 – 4

Grain Free, Dairy Free, whole foods organic Paleo-type diet
(vegetables, healthy fats, a little free-range meat/chicken/fish)

Time Restricted Eating / Intermittent Fasting –
restrict calories to 8 – 12 hours a day

Avoid eating 2 - 3 hours before bedtime

EVANTHEA CLINICAL TRIAL



STUDY PROCEDURES - OTHER



SLEEP OPTIMIZATION – including assessment and treatment of Sleep Apnea, Oura Ring for tracking



EXERCISE – aerobics, strength, stretching, balance training + HIIT (High Intensity Interval Training) – 45”



BRAIN TRAINING for Neuroplasticity – Brain HQ – 15”



MINDFULNESS TRAINING/STRESS REDUCTION – HeartMath – 10”



DENTAL HEALTH – Dentalcidin Toothpaste and Dental Rinse from Bio-Botanical Research

EVANTHEA CLINICAL TRIAL



KETOGENIC DIET

- ▶ Ketosis: High Fat/Low Carb/Moderate Protein diet – can be helpful with dementia.
- ▶ The ageing brain can have a bioenergetic dysfunction with abnormal glucose utilization and mitochondrial dysfunction.
- ▶ Shifting from burning glucose to burning fat is a work-around for this. Enhances metabolic flexibility.
- ▶ Ketosis can help with increased energy, brain clarity, and sometimes memory in adults. Changes can be rapid for some people.
- ▶ Follow advanced lipids after 3-4 months on a Keto diet, especially for people with Apo E4 alleles, but this is not a contraindication.

EVANTHEA CLINICAL TRIAL

STUDY PROCEDURES – TREATMENT

- ▶ We used some basic nutrients for nutritional and mitochondrial support, plus some nootropic support.
- ▶ All thyroid and sex hormones were optimized, including Estrogen (ideally 80 – 120), Progesterone, Testosterone (men and women), Pregnenolone, and DHEA-S.
- ▶ Beyond that, treatments for each patient were individualized, based on their findings with the testing and assessments.

EVANTHEA CLINICAL TRIAL

STUDY PROCEDURES – OPTIONAL TREATMENTS

PBM: Photobiomodulation (Auragen,
Neuronic)

Neurofeedback

HBOT (Hyperbaric Oxygen Therapy)

EWOT (Exercise with Oxygen Therapy)

Cold Laser brain treatments (Aspen laser)



DEMOGRAPHICS

- ▶ Age: 45 – 77
- ▶ Male – 27 (37.5%)
- ▶ Female – 46 (62.5%)

APO E STATUS

	GROUP A (49)	GROUP B (23)
▶ 2/3	3 (6%)	1 (4%)
▶ 2/4	0 (0%)	1 (4%)
▶ 3/3	24 (49%)	9 (39%)
▶ 3/4	19 (39%)	9 (39%)
▶ 4/4	3 (8%)	3 (13%)

SPONSOR ACKNOWLEDGEMENTS

We gratefully acknowledge the following companies for providing donated or discounted products or services in support of this study.

Abbott Freestyle Libre

Auragen – Reversal Systems

Biocidin

Bioharvest Vinia Resveratrol

Brain HQ

Cerbo, LLC

Cronometer

CNS Vital Signs

Genova

Heartmath

Igenex

Infectolab

IntellXX DNA

Ketone Aid KA1

Keto Mojo

Lis Biotech ERMI

My Periopath

NeuroCode

Neuronic

Northeast Bio Labs

OmegaQuant

Oura Ring

Patient Safety, Inc sleep studies

Real Time Labs

TruDiagnostics

US Enzymes

Vireo Systems Creatine

None of the sponsors had input into the study design, data analysis, or interpretation of results.



EVANTHEA TRIAL: Precision Medicine Treatment of Alzheimer's Disease: Successful Randomized Controlled Trial

- **Search: Preprint Kat Touns**
- <https://www.preprints.org/manuscript/202512.2694>
- Over 15,000 downloads since 12/30/25

FOUR WINDS STUDY PUBLICATIONS

Journal of Alzheimer's Disease

- ▶ **Toups, Hathaway, Gordon, et al. Precision Medicine Approach to Alzheimer's Disease: Successful Pilot Project**
Journal of Alzheimer's Disease – 2022; 88(4): 1411–1421.
<https://content.iospress.com/articles/journal-of-alzheimers-disease/jad215707>
Published: 16 August 2022

ADDITIONAL PAPERS – Journal of Alzheimer's Disease

- ▶ **Precision Medicine Approach to Alzheimer's Disease: Rationale and Implications**

Bredesen, Toups, Hathaway, et al.

Journal of Alzheimer's Disease, vol. 96, no. 2, pp. 429-437, 2023

<https://content.iospress.com/articles/journal-of-alzheimers-disease/jad230467>

- ▶ **Longitudinal White and Gray Matter Response to Precision Medicine-Guided Intervention for Alzheimer's Disease**

Chaw, Raji, Toups, et al.

Journal of Alzheimer's Disease, vol. 96, no. 3, pp. 1051-1058, 2023

<https://content.iospress.com/articles/journal-of-alzheimers-disease/jad230481>



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WWW.DEMENTIADEMYSTIFIED.COM

DEMENTIA DEMYSTIFIED RESOURCES - 1

HEARTMATH

▶ www.HeartMath.com

BRAIN HQ BRAIN TRAINING

▶ www.BrainHQ.com

CNSVS – CNS Vital Signs NeuroPsych Battery Online used to evaluate cognitive performance

▶ <https://www.cnsvs.com>

MoCA – Montreal Cognitive Assessment Testing

▶ <https://mocacognition.com/>

DEMENTIA DEMYSTIFIED RESOURCES - 2

NeuroQuant – Volumetric MRI Testing

- ▶ <https://Cortechs.ai>
- ▶ Search for location near you that offer NeuroQuant scans.
- ▶ Reports to Order: Triage Brain Atrophy, Age-Related Atrophy, Multi-Structure Atrophy

Home Dust Testing for Mold/Mycotoxins

- ▶ www.LisBiotech.com – Order ERMI dustcloth (includes HERTSMI scoring)
- ▶ Mycometrics.com – Order ERMI dustcloth
- ▶ www.MyHouseMakesMeSick.com – to score the Mycometrics testing for a Moldiness Index of your home. You upload the scores from Mycometrics testing to this program for a General Moldiness Index called a HERTSMI-2 score.

Nasal MARCoNS Infection Testing - MicrobiologyDx

- ▶ <https://microbiologydx.wixsite.com/dlmmicro>

DEMENTIA DEMYSTIFIED RESOURCES - 3

Lyme and Co-Infection Testing Companies

- ▶ Igenex
- ▶ InfectoLab
- ▶ MDL

Home Dental Pathogen Testing

- ▶ My PerioPath (OralDNA.com)
- ▶ SimplyPERIO – tests viruses as well as bacteria
- ▶ DirectDiagnostics.com
- ▶ Bristle Health

DEMENTIA DEMYSTIFIED RESOURCES - 4

Testing Chemical Toxins and Heavy Metals

- ▶ Real Time Labs EPP – Environmental Pollutants Panel (Chemical Toxins)
- ▶ Mosaics Diagnostics (Great Plain Labs) – Chemical Toxins and Glyphosate (Roundup) level
- ▶ Toxic metals testing – Whole Blood (Quest, LabCorp, Genova)

* When ordering RBC Mercury at Quest, get the quantified option. The Metals panel only reports Hg as < 4.

DEMENTIA DEMYSTIFIED RESOURCES - 5

Micronutrient and Metals Testing

- ▶ Quest panels for: Antioxidants, B Vitamins, Minerals, and Heavy Metals
- ▶ LabCorp: Trace Minerals panel; Heavy Metals testing
- ▶ Genova NutrEval tests for all kinds of nutrient levels (including mitochondrial nutrients and omega fatty acid levels), some metal and chemical toxin levels, organic acids, and more.
- ▶ NutrEval covered by Medicare with appropriate diagnostic codes/indications

DEMENTIA DEMYSTIFIED RESOURCES - 6

HOME SLEEP APNEA STUDY COMPANIES

- ▶ **Patient Safety, Inc**

<https://www.marketing.PatientSafetyInc.com/>

- ▶ **WatchPAT One**

<https://www.itmar-medical.com/>

DEMENTIA DEMYSTIFIED RESOURCES - 7

PHOTOBIOMODULATION DEVICES

- ▶ **Auragen**

<https://reversalsolutions.com>

<https://reversalsolutions.com/pages/comparison-chart-1>

- ▶ **Vielight**

<https://www.Vielight.com>

- ▶ **Neuronic Neuradiant Helmet**

<https://www.neuronic.online/>

GENERAL RESOURCES FOR MORE INFO - 8

- ▶ FOUR WINDS PAPER: Precision Medicine Approach to Alzheimer's Disease: Successful Pilot Project – Kat Toups, Ann Hathaway, Deborah Gordon, Dale Bredesen, et al.
- ▶ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9484109/>
- ▶ ApoE4 Website by Julie Gregory – a Nutritionist with ApoE4 +/- who healed with Dr. Bredesen's approach
- ▶ [ApoE4.info](https://www.apoe4.info/)
- ▶ PAPER: Reversal of Cognitive Decline in Alzheimer's Disease – Dale Bredesen, et al.
- ▶ <https://pubmed.ncbi.nlm.nih.gov/27294343/>
- ▶ BOOK: The Ageless Brain: How to Sharpen and Protect Your Mind for a Lifetime – Dale Bredesen, MD
- ▶ BOOKS: The End of Alzheimer's and other books by Dale Bredesen, MD

GENERAL RESOURCES – 9

DECODING DEMENTIA eBook

- ▶ Free eBook: Decoding Dementia - Kat Toups, MD
- ▶ 22-page guide with actionable insights for assessment and treatment of cognitive decline
- ▶ www.DementiaDemystified.com

SOCIAL MEDIA INFO – ADDITIONAL DEMENTIA AND FUNCTIONAL PSYCHIATRY CONTENT

- ▶ **FACEBOOK PAGE: KAT TOUPS, MD - FUNCTIONAL MEDICINE PSYCHIATRY AND DEMENTIA**
<https://www.facebook.com/BayAreaWellness.net/>
Lots of posts about the brain and neuroscience, including Dementia and Nutritional Psychiatry
- ▶ **YOUTUBE CHANNEL – KAT TOUPS, MD**
<http://youtube.com/KatToupsMD>
Videos of talks on Dementia, as well as Functional Medicine Psychiatry topics

BASIC DEMENTIA PROTOCOL IN A NUTSHELL

- 1) Find and correct/remove/re-balance any underlying causes that are contributing to the cognitive decline/dementia (including infections, toxins, lack of hormones, metabolic, nutrient deficiencies).
- 2) Diet: Paleo/Mediterranean Ketogenic Diet with Time-Restricted Eating
- 3) Exercise: 40 – 60 minutes/day (6 days/week) – strength, aerobics, balance, HIIT
- 4) Mindfulness/ Meditation/ Tai Chi or Qigong/ Guided Meditation/ HeartMath: 15+ minutes/day
- 5) Brain Training: Brain-HQ 15+ minutes/day
- 6) Sleep: 8 hours/night, before midnight
- 7) Supplements as indicated by symptoms and testing to support processes affecting the brain and cognition
- 8) Optimize all Hormones

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