



## What's New in Dementia Research and Care?

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Constituent Services

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## Today's Conversation

- Who We Are
- Alzheimer's Association International Conference 2015 Overview
- Dementia and Alzheimer's Disease Facts
- Risk Factors
- Biomarkers
- Interventions
- Prevention Trials
- Questions

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## Our vision is a world without Alzheimer's disease



**Our mission:**

- Advance research
- Provide care and support
- Increase Concern & Awareness
- Public Policy & Advocacy Efforts

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## Alzheimer's Association International Conference (AAIC) 2015


- The world's largest Alzheimer's research conference
- Just took place in Washington DC
- Over 4500 researchers from 65 countries
- 489 speakers in 87 sessions
- 1225 poster presentations
- 8 corporate symposia and 106 ancillary meetings
- 135 exhibitors



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## AAIC 2015: Dementia Care Research and Practice Track

- Two-day track
- 2 plenary speakers
- 11 dementia care research sessions
- 4 dementia care practice session
- 132 poster presentations



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## Dementia & Alzheimer's Disease

- Dementia is the loss of memory due to changes in the brain
- Alzheimer's is the most common form
- Definite diagnosis used to require autopsy
- Many mixed cases
- Many memory disorders are reversible and not truly dementia

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## The Alzheimer's Epidemic Continues to Grow...

**5.3** million Americans of ALL Ages will have Alzheimer's in 2015

**6** TH LEADING CAUSE OF DEATH IN THE U.S.

**\$1.1** TRILLION IN 2015  
**\$226** BILLION IN 2010

Total cost of care for those with Alzheimer's, with more than two-thirds paid by Medicare and Medicaid.

Of the top 10 causes, Alzheimer's is the only one that cannot be prevented, cured or even slowed.

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## Baby Boom Generation = Generation Alzheimer's

- More than 28 million Baby Boomers will develop Alzheimer's between 2015 and 2050
- 37% will have Alzheimer's before they die
- In 2040, 10.3 million Boomers will have the disease – nearly twice as many as total today
- In 2050, half of Baby Boomers will have Alzheimer's

Year	Prevalence
2015	1.2%
2030	7.0%
2040	26.0%
2050	50.1%

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## Hope In Research

- 6<sup>th</sup> leading cause of death across all ages
- 5<sup>th</sup> leading cause of death for those aged 65 and older
- Only cause of death among the top 10 in America without a way to prevent, cure or even slow its progression.

Change in the Number of Deaths: 71% Between 2000-2013

Cause of Death	Change
Alzheimer's Disease	+71%
HIV	-52%
Stroke	-23%
Heart Disease	-18%
Cancer	-11%
Prostate Cancer	-7%
Brain/Cancer	-2%

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## National Plan to Address Alzheimer's disease

Goals:


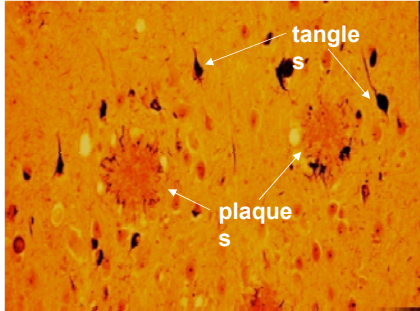
- Prevent and Effectively Treat Alzheimer's Disease by 2025
- Enhance Care Quality and Efficiency
- Expand Supports for People with Alzheimer's Disease and Their Families
- Enhance Public Awareness and Engagement
- Improve Data to Track Progress


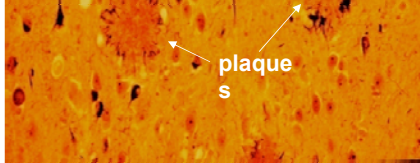
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## Risk Factors

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## Alzheimer's Disease

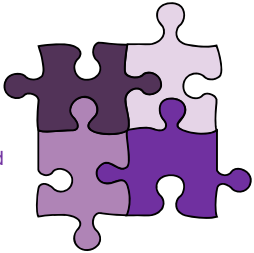



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THE SPRINGER SPENDINGER

## Risk Related to Cognitive Decline & Alzheimer's



- Age: The greatest known risk factor
- Heart-head connection
  - Increased risk suspected if high blood pressure, heart disease, stroke, diabetes and high cholesterol
- Head injury
- Family history
  - Risk and deterministic genes



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## Risk Factors for Alzheimer's Disease, Dementia & Cognitive Decline


- Type 1 Diabetes (T1D) and Dementia
  - First study to report the dementia risk, including Alzheimer's, in older adults with T1D.
  - The researchers used a healthcare database of more than 490,000 people. 230 of them had T1D.
  - People in the study with T1D were 93% more likely to get dementia (73% after adjustment for heart health risk factors) compared with people without diabetes.

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## Early Life Risk Factors for Alzheimer's Disease, Dementia & Cognitive Decline



- School Performance and Occupation
  - 1<sup>st</sup> Study**
    - Risk elevated 21% in people who were in the lowest 20% of childhood grades.
    - Risk reduced 23% among individuals in occupations characterized by high complexity with data and numbers.
    - Lowest risk (39% reduction) found in group who had both higher childhood school performance and high occupational complexity.
  - 2<sup>nd</sup> Study**
    - Risk elevated more than 50% in individuals over 75 with the lowest 20% of early-life school grades.
    - Individuals who completed secondary education had lower risk compared to individuals with only elementary education (28% lower risk).
    - Women who had an occupation with high complexity with people were at 60% lower risk of developing dementia compared to those who had an occupation with low complexity with people.



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## Early Life Risk Factors for Alzheimer's Disease, Dementia & Cognitive Decline


- Low Physical Activity and High TV Viewing
  - Studied the association of long-term patterns of low physical activity and high television viewing time over 25 years with cognitive function at mid-life.
  - Study participants with low levels of physical activity over 25 years had significantly worse cognition in mid-life
  - Participants with high levels of TV watching over 25 years also had significantly worse mid-life cognitive function.
  - Study participants with both long-term low physical activity and high television viewing were almost 2x more likely to have poor cognitive function in mid-life.

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## Women and Risk for Cognitive Decline and Dementia

- Almost two-thirds of the 5 million Americans living with Alzheimer's are women
- 60% of Alzheimer's & dementia caregivers are women
- Three new studies suggest there may be biological reasons women are at higher risk than men:
  1. Cognitive Decline 2X as Fast as Men
  2. General Anesthesia and Cognitive Decline
  3. APOE ε4 Alzheimer's Risk Gene and Gender




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## Translating Scientific Evidence to Program Delivery



Alzheimer's & Dementia

Alzheimer's & Dementia | (2015) 1:9



Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective

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### healthy habits for a healthier you



an education program by the alzheimer's association

An education program that helps older adults understand the link between lifestyle and cognitive health. It covers topics such as diet, exercise, social engagement, and mental health. The program is available in multiple languages and formats, including print, audio, and video. For more information, visit [www.alz.org/healthyhabits](http://www.alz.org/healthyhabits).

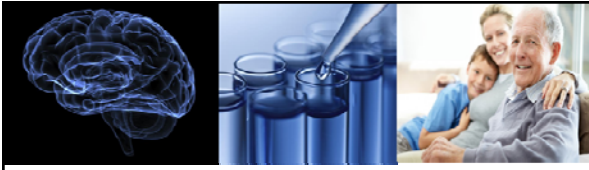
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### 10 WAYS TO LOVE YOUR BRAIN



- Break a Sweat**: Engage in regular cardiovascular exercise that elevates heart rate and increases blood flow. Studies have found that physical activity reduces risk of cognitive decline.
- Hit the Books**: Formal education will help reduce risk of cognitive decline and dementia. Take a class at a local college, community center, or online.
- Butt Out**: Smoking increases risk of cognitive decline. Quitting smoking can reduce risk to levels comparable to those who have not smoked.
- Follow Your Heart**: Risk factors for cardiovascular disease and stroke – obesity, high blood pressure, and diabetes – negatively impact your cognitive health.
- Stump Yourself**: Challenge your mind. Build a piece of furniture. The game of strategy. Be tricky.
- Heads Up!**: Brain injury can raise risk of cognitive decline and dementia. Wear a seat belt and use a helmet when playing contact sports or riding a bike.
- Buddy Up**: Staying socially engaged may protect brain health. Find ways to be part of your local community or share activities with friends and family.
- Take Care of Your Mental Health**: Some studies link depression with cognitive decline, so seek treatment if you have depression, anxiety, or stress.
- Catch Some Zzz's**: Not getting enough sleep over time is problematic with memory and thinking.
- Fuel Up Right**: Eat a balanced diet that is lower in fat and higher in vegetables and fruit to help reduce the risk of cognitive decline.

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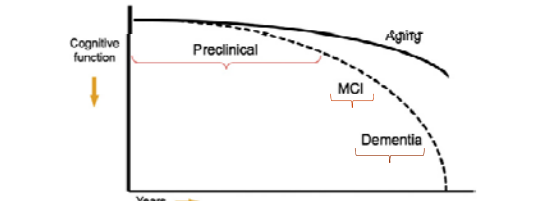
## Biomarkers

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## Continuum of Alzheimer's Disease

Normal

Alzheimer's disease

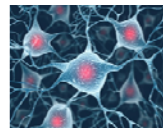


Adapted from Sperling et al. 2011

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## What is a Biomarker?

- Biological marker to measure change
- Reliable predictor and indicator of disease and disease progression
- Example
  - Glucose for Diabetes
  - Cholesterol for Heart disease



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## Amyloid PET Imaging

RED = maximum uptake  
VIOLET = minimum uptake

Clark et al. (2011) JAMA 305(1)

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## New Possibilities for Early Detection (Novel Biomarkers)

- Brain PET Imaging of Inflammation
  - Inflammation in the brain is clearly involved in Alzheimer's
  - Tools to detect inflammation may be helpful in understanding what is happening in the disease and also of research studies of inflammation-targeted therapies.

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## New Possibilities for Early Detection (Novel Biomarkers)

- New CSF Biomarker: Neurogranin**
  - Found only in the brain, involved in brain cell-to-cell communication pathways
  - Baseline levels of neurogranin were significantly higher in individuals with Alzheimer's
  - Levels higher in MCI individuals who progressed to Alzheimer's and were predictive of progression from MCI to Alzheimer's
  - Neurogranin levels were strongly correlated with two other Alzheimer's-related proteins

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## New Possibilities for Early Detection (Novel Biomarkers)

### Saliva

- A small but intriguing study suggests it could be possible to detect Alzheimer's-like proteins in saliva
- Researchers identified proteins in the saliva that differentiated the Alzheimer's and MCI groups, they also predicted worse cognition

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## Modernizing the Diagnosis of Alzheimer's Based on a Continuum

Normal	Pre-clinical	MCI	Alz dementia
APOE Protein or gene "barcodes" Family history Tau/Abeta (CSF, blood, eye) MRI, CT PET, fMRI	Subjective problem in memory or another domain, informant corroborated and measurable on tests; normal overall cognition and ADLs	Clear deficits in 2 or more core cognitive domains; ADLs affected	

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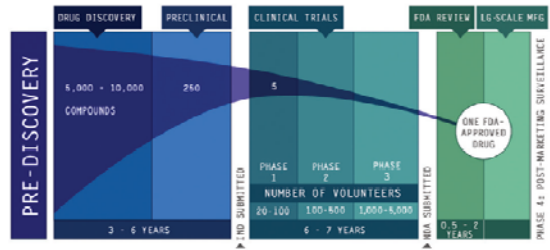
## Interventions

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## Pathway to Develop Interventions

Drug Discovery and Development: A LONG, RISKY ROAD



PhRMA 2012 Annual Report

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## Current Alzheimer's Therapies: Symptomatic

### Cholinesterase Inhibitors

Tacrine (Cognex)

Donepezil (Aricept)

Rivastigmine (Exelon)

Galantamine (Razadyne)

### Glutamate Moderators

Memantine (Namenda)

### Combination Therapies

Donepezil & memantine (Namzaric)



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## Therapeutic Agents in Phase I and II Clinical Trials for Alzheimer's Disease

- AADvac1
- ABT-957
- Allopregnenalone
- ANAVEX2-73
- AZD0530
- BAN2401
- Bexarotene
- BI 409306
- Blood plasma
- Bryostatin 1
- CPC-201
- Crenezumab (MABT5102A)
- DAIO-B
- DBS-f
- E2609
- Encencline
- Exendin-4
- GC021109
- IVIg
- JNJ-54861911
- KHK6640
- Ladostigil
- Levetiracetam
- Liraglutide
- Lu AF20513
- LY3002813
- LY3202626
- MEDI1814
- Mesenchymal stem cells
- Metformin
- MK-7622
- NIC5-15
- Nicotinamide
- PC912
- PX00864
- Rasagiline
- RO4602522
- RPH201
- R-Prampixole
- Sargramostim
- S-Equil
- Simvastatin
- T-817MA
- Tetrahydrobiopterin
- TPI-287
- Transcranial magnetic stimulation (TMS)



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## Therapeutic Agents in Phase III Clinical Trials for Alzheimer's Disease

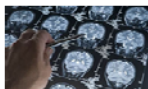
- AZD3293  
Astrazeneca/ Lilly  
BACE inhibitor
- Encencline  
Forum Pharmaceuticals  
Nicotinic receptor agonist
- Gantenerumab  
Hoffman-La Roche  
Monoclonal antibody against beta amyloid Part of DIAN-TU
- Insulin  
Alzheimer's Disease Cooperative Study
- IVIg and Albumin  
Grifols  
Intravenous immunoglobulin
- LU AE58054  
H. Lundbeck  
5HT6 receptor antagonist
- Masitinib  
AB Science  
Inhibitor of c-KIT cell signaling
- MK-8931  
Merck  
BACE inhibitor
- Nivadipine  
St. James Hospital  
Calcium Channel Blocker
- Pioglitazone  
Takeda  
PPAR-gamma activator
- Sodium Oligo-mannurate  
Shanghai Greenvalley Pharmaceuticals
- Solanezumab  
Eli Lilly  
Humanized antibody against beta-amyloid
- TRx0237  
TauRX  
Tau aggregation inhibitor



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## Experimental Drug Trial Results: Potential Disease Modifying Treatments



- **Solanezumab (Lilly)**
  - EXP1 and EXP2 Phase 3 placebo-controlled studies did not meet endpoints
  - Delayed start analysis of sola open label
- **Gantenerumab (Roche)**
  - Humanized Aβ antibody in a 2-year Phase 3 trial in very mild Alzheimer's
  - Dose-dependent reductions in brain β-amyloid and CSF Tau; Aβ42 levels unaltered.
  - Trial did not meet its cognitive endpoints.
- **Aducanumab (Biogen)**
  - Shows solid safety and tolerability profile in Phase 1(b) trial
  - Dose dependent slowing of cognition loss in individuals with mild disease / confirmed β-amyloid in brain
  - Need larger, longer trial (Phase 3) – Biogen has made a \$2 Billion commitment to go to Phase 3

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## Experimental Drug Trial Results: Potential Symptomatic Treatments

- **RVT-101 (Axovant)**
  - Results of a Phase 2b study
  - Advancing to Phase 3 trials
- **TTP488 (vTv, formerly Trans Tech)**
  - Oral antagonist of the Receptor for Advanced Glycation Endproducts (RAGE)
  - TTP488 has been granted Fast Track Status by FDA and is entering Phase 3
- **AVP-923: Dextromethorphan/Quinidine (Avanir)**
  - Investigated for Alzheimer's-related agitation
  - Approved for pseudobulbar affect (involuntary laughing or crying) in MS and ALS
  - Provided significant improvement in agitation in patients with Alzheimer's in 10 week trial



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## Maximizing Independence at Home (MIND at Home)

- 18 month randomized intervention trial including 303 volunteers, 290 caregivers
- Goal: To determine if providing assistance in obtaining appropriate care for older adults with memory problems helps them remain at home longer, as well as improve life quality
- People with help at home able to stay in home 10 months longer than those without help
- Presented at AAIC in 2012



Samus et al 2012 AAIC  
Samus et al 2014 Am J Geriatr Psychiatry

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## Exercise as Treatment: Living Better with Dementia

- Three new trials of aerobic exercise in Alzheimer's, vascular cognitive impairment and mild cognitive impairment
- Exercise or regular physical activity might play a role in both protecting your brain from Alzheimer's, and also living better with the disease

1. Improvement on Psychiatric Symptoms with Mild Alzheimer's
2. Tau Levels in CSF with MCI and Diabetes
3. Improved Memory and Attention with Mild Vascular Cognitive Impairment

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## AAIC Technology & Dementia Preconference

- Organized by the ISTAART Technology Professional Interest Area
- Engages ETAC awardees
- Topics include:
  - Technology integration in clinical trials to monitor intervention effectiveness
  - Global collaborative funding models
  - Technology implications for big data and dementia science
  - Emerging role of technology in dementia research – focus on mobile/ wearable technologies and use of internet

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## Technologies for Intervention and Monitoring



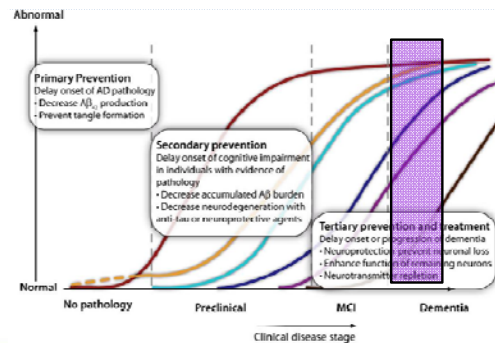
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## Prevention

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## Possible Prevention of Alzheimer's?



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## Slide 39



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- 1 Why is this important for this target audience? Can this group be Istaart members? Is there a recommended PIA for them?

Nancy Cullen,



## Collaboration for Alzheimer's Prevention

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## Alzheimer's Prevention Initiative

### ApoE Trial

- Two Copies of Risk Gene
- 1,300 adults, age 60-75
- Partnering with Novartis – two drugs:
  - CAD106: active immunotherapy
  - Beta secretase inhibitor
- Received \$33.2 million from NIH




ALZHEIMER'S PREVENTION INITIATIVE

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## Alzheimer's Association Leverages Support for API APOE4 Trial


- Alzheimer's Association, GHR Foundation & FBRI \$10 million to the API APOE4 Trial
- Award will enable the trial to:
  - Maximize PET imaging, including Tau, Amyloid and FDG for trial participants
  - Expand the API Registry, including APOE genotyping and online cognitive testing
  - Evaluate two remote genetic counseling approaches (telephone/ video counseling) in a sub-study population



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## Dominantly Inherited Alzheimer's Network Trial (DIAN-TU)

- DIAN: Autosomal dominant Alzheimer's disease (ADAD)
- \$4.2 million award to launch
- Testing three simultaneous drugs:
  - Gantenerumab (Roche, Ab antibody)
  - Solanezumab (Lilly, Ab antibody)
  - TBD
- 22 months later: Received \$6 million from NIH
- A year after that: Received \$23 million additional from NIH



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## DIAN Families Gather at AAIC15

- First ever meeting
- More than 100 participants and family members
- Joined by another 100 researchers, government officials, pharma companies, etc. in the afternoon
- Research updates, educational sessions, support groups
- Shared their unique family stories and impact with others



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## FINGER Study: Recipe of Lifestyle Interventions for Cognition

- Gold standard of testing any type of therapy or intervention – Randomized Control Trial (RCT)
- Large, rigorous study
- First solid evidence that recipe of lifestyle interventions reduces cognitive decline
- Needs to be replicated in more diverse populations



Kivipelto et al., Alzheimer & Dementia 2013

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## \$300 million proposed by US House for Alzheimer's research

- US House of Representatives proposed a bill to increase funding for Alzheimer's research by \$300 million
- If approved, biggest increase in Alzheimer's research funding ever
- Be informed, get involved at [alz.org/advocate](http://alz.org/advocate)



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## What Can You Do Now?

- Learn more about AD and person-centered care
- Talk about your experience
- Participate in Longest Day or Walk to End Alzheimer's
- Talk to your legislators
- Support research
- Maintain overall health



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**Full Access Also Includes:**

- ✓ Alzheimer's Association essentiALZ™ and essentiALZ™ Plus certifications
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Go to [www.healthcareinfoaction.com/pleaseclicktobuy/](http://www.healthcareinfoaction.com/pleaseclicktobuy/)

Approved pre-course training incorporates Alzheimer's Association Dementia Care Practice Recommendations.

- Over 25,000 certified
- Have your curriculum reviewed to meet the Alzheimer's Association Dementia Care Practice Recommendations.
- [www.alz.org/trainingreviews](http://www.alz.org/trainingreviews)

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## Resources to help YOU

By phone  
800.272.3900

In person  
[alz.org/findus](http://alz.org/findus)

Online  
[alz.org/care](http://alz.org/care)

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# THE END OF ALZHEIMER'S STARTS WITH YOU

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[alz.org](http://alz.org)